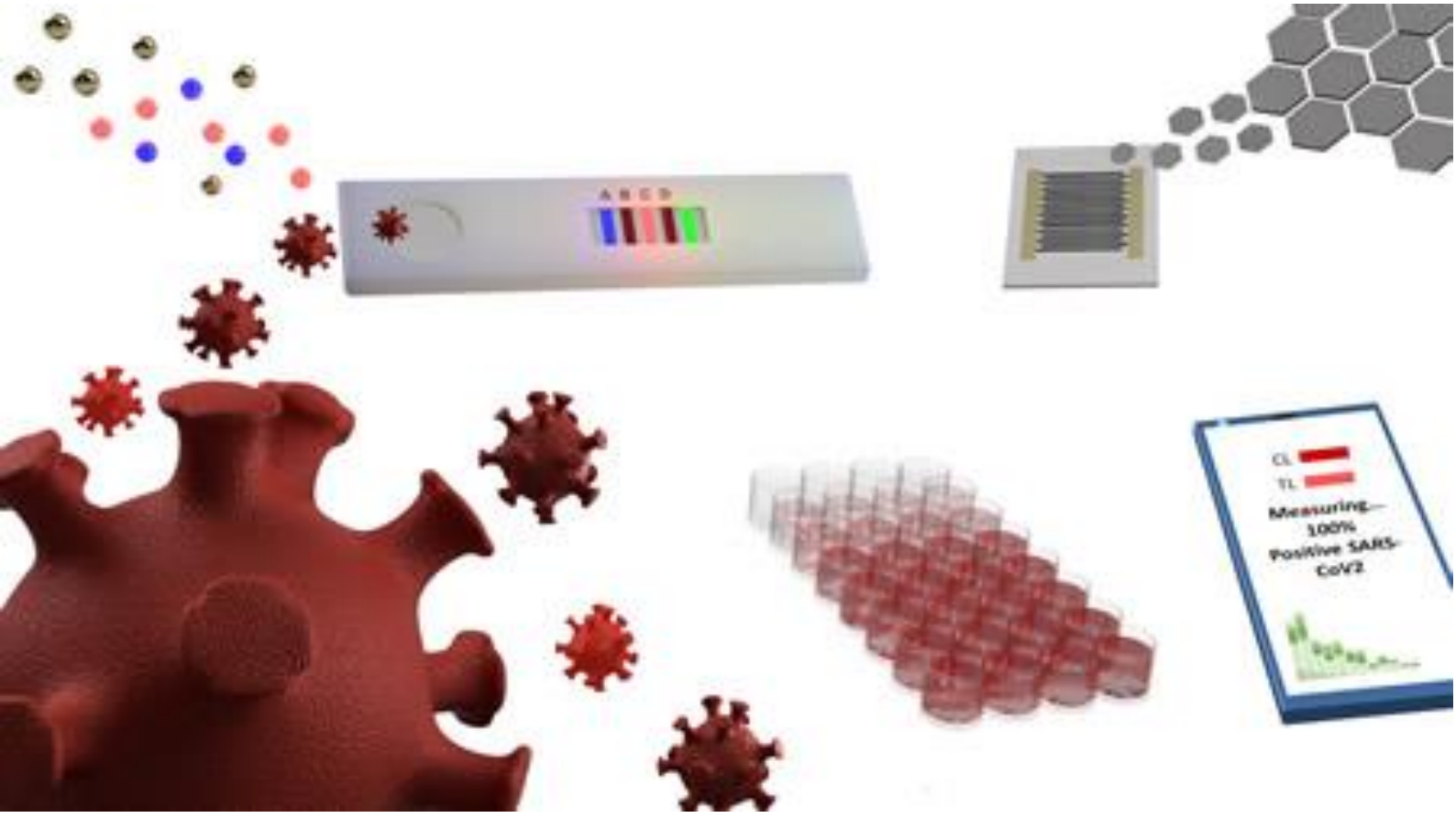
BIOSENSORS FOR PANDEMICS

MAY 06, 2020

CONFERENCE ONLINE



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EXCELENCIA SEVERO OCHOA

FOREWORD

On behalf of the Organising and the International Scientific Committees we take great pleasure in welcoming you for the 1st edition of the Biosensors for Pandemics Online International Conference.

"Biosensors for Pandemics: Reliable and efficient nanotech-based diagnostics in emergency situations" is an Online conference that will address main problems scientific community is facing nowadays for COVID-19 pandemics.

The idea is to get together worldwide well-known experts in biosensing technologies who are working currently in COVID-19 diagnostics or have a great potential for application of their technologies in the near future. This conference is also addressed to specialists in virology, epidemiology and other health areas and communication technologies that are crucial for guiding biosensing community and their diagnostics ideas using biosensors in the right way. A virtual round table providing answers to participants and sharing ideas between speakers is also previewed.

We are indebted to the following Scientific Institutions and Companies for their help and/or financial support:
ICN2 (Spain) and ACS Sensors (USA)

We also would like to thank all the speakers and participants that join us this year.

We truly hope that Biosensors for Pandemics serves as an international platform for communication between science and business.

Hope to see you again online in the next edition of Biosensors for Pandemics.

Biosensors for Pandemics Organising Committee

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The Institut Catala de Nanociencia I Nanotecnologia (ICN2) is a flagship research institute within the CERCA network of centres created and supported by the Autonomous Government of Catalonia to raise Catalan science to the premier international level. The patrons of ICN2 are the Government of Catalonia (Generalitat), the Consejo Superior de Investigaciones Científicas (CSIC), and the Autonomous University of Barcelona (UAB). Its core activities are Frontier Basic and Applied Research in Nanoscience and Nanotechnology, Technology Transfer, and Public Outreach. Currently, ICN2 numbers some 200 staff from over 30 countries, of which about 170 are researchers

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This year, ACS Sensors' is celebrating its 5th anniversary with an impact factor of 6.944. The journal's Editor-in-Chief, J. Justin Gooding (The University of New South Wales) started the journal in 2015 to provide a top forum to publish all aspects of sensing from the conceptual to the applied. The journal is now the 4th ranked analytical chemistry journal and the second ranked journal that publishes primary research based on the impact factor of 6.944. Learn more about the ACS Sensors and its 5th Anniversary Virtual Issue Collection!

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ABSTRACTS

Disposable Silicon-based Micro-qPCR for Rapid Detection of Pathogens

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Rapid screening and low-cost diagnosis play a crucial role in choosing the correct course of intervention e.g., drug therapy, quarantine, no action etc. when dealing with highly infectious pathogens. This is especially important if the disease-causing agent has no effective treatment, such as the novel coronavirus SARS-CoV-2 (the pathogen causing COVID-19), and shows no or similar symptoms to other common infections. We report a disposable silicon-based integrated Point-of-Need (PoN) transducer (TriSilix) that can chemically-amplify and detect pathogen-specific sequences of nucleic acids (NA) quantitatively in real-time. [1] Unlike other silicon-based technologies, TriSilix can be produced at wafer-scale in a standard laboratory (Figure 1); we have developed a series of methodologies based on metal-assisted chemical (wet) etching, electroplating, thermal bonding and laser-cutting to enable a cleanroom-free low-cost fabrication that does not require processing in an advanced semiconductor foundry. TriSilix is, therefore, resilient to disruptions in the global supply chain as the devices can be produced anywhere in the world. To create an ultra-low-cost device, the architecture proposed exploits the intrinsic properties of silicon and integrates three modes of operation in a single chip: i) electrical (Joule) heater, ii) temperature sensor (i.e. thermistor) with a negative temperature coefficient that can provide the precise temperature of the sample solution during reaction and iii) electrochemical sensor for detecting target NA. Using TriSilix, the sample solution can be maintained at a single, specific temperature (needed for isothermal amplification of NA such as Recombinase Polymerase Amplification (RPA) or cycled between different temperatures (with a precision of ±1.3 °C) for Polymerase Chain Reaction (PCR) while the exact concentration of amplicons is measured quantitatively and in real-time electrochemically. A single 4-inch Si wafer yields 37 TriSilix chips of 10×10×0.65 mm in size and can be produced in 7 hours, costing ~US $0.35 per device. The system is operated digitally, portable and low power – capable of running up to 35 tests with a 4000 mAh battery (a typical battery capacity of a modern smartphone). We were able to quantitatively detect a 563-bp fragment (Insertion Sequence IS900) of the genomic DNA of M. avium subsp. paratuberculosis (extracted from cultured field samples) through PCR in real-time with a Limit-of-Detection of 20 fg, equivalent to a single bacterium, at the 30th cycle. Using TriSilix, we also detected the cDNA from SARS-CoV-2 (1 pg), through PCR, with high specificity against SARS-CoV (2003).

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[1] Ultra-low-cost integrated Silicon-based transducer for On-site, genetic detection of pathogens (BioRvix 10.1101/2020.03.23.002931)

FIGURES

Figure 1: (A) Schematic illustration of construction of a TriSilix chip and photographs of the actual device. (B) Wafer-scale fabrication of TriSilix using a 4-inch Si wafer. Each wafer yield 37 chips. (C) Schematic illustration of the functional building blocks of TriSilix that provide trimodal operation for integrated nucleic acid amplification and detection.

Harnessing Digital Medicine and AI to Optimize Combination Therapy for Infectious Diseases

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The process of designing combination therapies for a broad spectrum of disease indications ranging from infectious diseases to oncology has traditionally been based on mechanism-of-action based drug selection followed by dose finding to develop synergistic regimens. While this strategy has led to improved outcomes, drug synergy and globally optimized therapeutic efficacy are very different objectives. A number of factors associated with traditional drug screening substantially complicate its ability to realize globally optimized regimens. For example, effective therapies given at a non-optimal dose can expectedly lead to sub-optimal outcomes. However, dosing also plays a critical role in determining which therapies will ultimately comprise the best course of treatment. As such, when the best drugs and doses for a combination therapy need to be simultaneously identified, this creates a drug/dose space that cannot be reconciled through traditional screening, as even small pools of drugs considered across multiple doses can easily result in over 1 million possible combinations. To address this challenge, our team has developed a suite of platforms that can both select optimal drug combinations (IDentif.AI) and dynamically dose these combinations over time to sustain maximal therapeutic efficacy (CURATE.AI). Our platforms have been validated in multiple interventional clinical studies for organ transplantation, solid cancers, and infectious diseases. This lecture will discuss our study outcomes, and plans for upcoming trials.

Rapid diagnostic tests to fight against COVID-19 pandemics: challenges and opportunities.

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The strategy for screening patients with coronavirus 2019 (COVID-19) infection is based on the use of tests to detect the viral genome in respiratory specimens using molecular biology techniques (namely RT-PCR), and also on the use of serological tests. These two types of tests are available on high-throughput platforms offered by the diagnostics industry to equip medical laboratories. At the same time, rapid diagnostic tests are developing steadily in response to societal demands and the need to test a large number of individuals. In this context, the aim of this communication will be to take stock of the main technological approaches proposed and their current use in clinical practice. We will also address the evaluation of the performance of these rapid tests, which is a key element for their development and their acceptability by the different actors of the health systems

CoNVat Project: Advanced Nanobiosensing Platforms for Point-of-care diagnostics and surveillance of coronavirus

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The dramatic spread of COVID19 pandemics has evidenced the need of novel diagnostic tools that enable rapid testing and screening of the population with sensitivity and specificity levels comparable to laboratory techniques. In fact, reliable and early diagnostics of COVID-19 has become one of the major challenges in the correct management of the Pandemics. Strong efforts are being pursuing at worldwide level to surpass this bottleneck by offering reliable, fast and user-friendly diagnostics tests than can be employed at the point-of-need. Biosensing technology is one of the most well prepared to tackle this challenging goal.

CoNVat project is one of the first projects funded by the H2020 European Union Framework program to fight against COVID-19. Our main objective is to deliver a novel Point-of-Care (POC) Nanophotonics Biosensor platform capable to provide an accurate and fast SARS-CoV-2 coronavirus detection, without requiring complex equipment and for both human and animal reservoirs samples.

CoNVat will provide a unique technology for efficient screening and diagnosis of the SARS-CoV-2 coronavirus infection, providing rapid detection results (less than 30 minutes) and directly from the human/animal sample, without the need of PCR or other time-consuming treatments. The POC biosensor employed is based on proprietary cutting-edge nanophotonic technology that enables ultrasensitive analysis of body fluids in few minutes and in decentralized settings, which has already demonstrated sensitivities at the attomolar (aM) level for direct specific RNA detection and 4 cfu/mL for whole pathogen detection directly in human samples.
The POC biosensor device is being optimized for:

(i) direct detection of SARS-CoV-2 in respiratory body fluids and saliva by incorporating specific antibodies for the capture of complete units of the SARS-CoV-2 virus, for a rapid diagnostics and screening.

(ii) viral RNA analysis in a multiplexed format, including complementary DNA probes that hybridize to exclusive sequences of SARS-CoV-2 RNA, for a more accurate diagnosis and identification of virus strains among different coronaviruses and other clinically relevant viruses.

The **CoNVat** device will be employed for rapid infection detection in pandemic or epidemic outbreaks, but also in prevention and surveillance by routine screening and evaluation of reservoir species. A scheme of the CoNVat project is presented in Fig. 1.

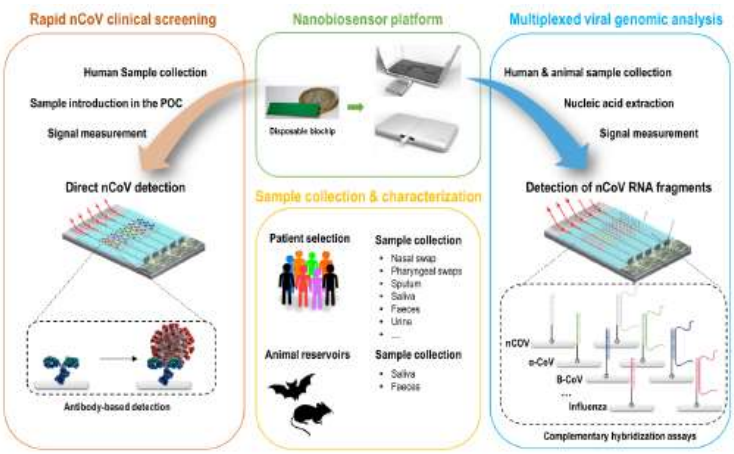

Figure 1: General scheme of the CoNVat project

Perspectives of Biosensors Integrated Point of Care Testings for Personalized Screening of Coronavirus Disease

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Abstract

As the COVID-19 pandemic is rapidly spreading, low-cost, reliable, fast, and sensitive testing methods are urgently required to mitigate the global spread of the COVID-19 pandemic and to screen for immunity among large populations. Over the past decades, diagnostic testing of infectious disease has steadily moved out of the central laboratory and into testing sites closer to patients. This testing modality, referred to as point-of-care testing (POCT), has enabled laboratory service providers to perform testing wherever the patient is located, facilitating disease diagnosis, monitoring, and management. Dramatic technological innovations in POCT have been made during the past few years. For instance, the development of miniaturized biosensing devices with integration of functional materials, artificial intelligent, and internet of things, has been considered the most critical component of POCT for mass public testing; due to the increased test accuracy, fast response, precision, and easier connection and management of data. POCT provide users the ability to perform all steps of the test, from sample collection to test result readout, users can know, within minutes, whether their test result is positive or negative.

Without the need for a trained professional, POCTs are typically designed in a manner that does not require complicated machinery or devices and can ideally be used in an at-home setting by consumers. Anyone and everyone can therefore be tested anywhere and everywhere to allow them immediately to act to seek professional help, which is especially essential during the COVID pandemic.

In this talk, we describe a novel design that combines the traditional POC lateral flow strip tests and electrochemical impedance sensor with a commercialized smartphone-enabled glucometer for portable and quantitative detection of a non-glucose target. The concept is demonstrated by using an oxidative DNA damage biomarker and the protein biomarker of Zika virus. We establish a novel method that transforms the detection of the target to the detection of an nanozyme based converting enzymatic reaction for enabling quantitative analysis. Considering the inherent advantages of the personal glucose meter, the demonstration of this device, therefore, may inspire you the new opportunities for the development of an ASSURED i.e., affordable, sensitive, specific, user-friendly, rapid, robust, equipment free, and deliverable systems for COVID infection diseases.

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Paper-based nanobiosensors as point of care for pathogens detection

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Abstract

An efficient detection of pathogens is strongly related to biosensors. Unfortunately, the cost of biosensors and the lack of equipped centers and trained people are probably the hardest obstacles to the diffusion and use of these devices in pandemics situation as the one we are already living. Biosensors field is progressing rapidly and the demand for cost efficient platforms is the key factor for their success. Physical, chemical and mechanical properties of cellulose in both micro and nanofiber-based networks combined with their abundance in nature or easy to prepare and control procedures are making these materials of great interest while looking for cost-efficient and green alternatives for device production technologies. Both paper and nanopaper-based biosensors are emerging as a new class of devices with the objective to fulfil the “World Health Organization” requisites to be ASSURED: affordable, sensitive, specific, user-friendly, rapid and robust, equipment free and deliverable to end-users. How to design simple paper-based biosensor architectures? How to tune their analytical performance upon demand? How one can ‘marriage’ nanomaterials such as metallic nanoparticles, quantum dots and even graphene with paper and what is the benefit? How we can make these devices more robust, sensitive and with multiplexing capabilities? Can we bring these low cost and efficient devices to places with low resources, extreme conditions or even at our homes? Which are the perspectives to link these simple platforms and detection technologies with mobile phone communication? I will try to give responses to these questions through various interesting applications we have been developing so far for the detection of various biomarkers related to pathogens.

Electrochemical biosensors for pathogen detection

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Diagnostic tests and devices based on electrochemical biosensors are being increasingly exploited as a valuable alternative to standard laboratory instrumentation for clinical diagnosis and as simple, inexpensive and point-of-care testing systems. Electrochemical biosensors are usually highly specific, sensitive, portable, and easy to operate. They are often designed to be affordable and to have a fast response that correlates well to different pathogen concentrations in different matrixes. Therefore, electrochemical biosensors hold the potential to contribute to the solution of a pandemic like we are living nowadays, especially regarding timely real-time detection, screening and diagnosis of pathogen-triggered diseases in working conditions, closer to the patient, in a reduced time-scale of testing and with minimal requirements of samples volume.

This talk is aimed to discuss novel electrochemical biosensors that have been developed in our group for diagnosis and monitoring of pathogens, including viruses, bacteria and parasites. It will highlight innovative approaches regarding i) Biosensors for the specific and highly sensitive detection of *Streptococcus agalactiae*, in a straightforward format [2], ii) Nanogenosensors for differential diagnosis of Zika virus and its discrimination among related viruses such as dengue and chikungunya and iii) Nobel bioreceptors based on glycans for the detection of *Toxoplasma gondii*. The talk will highlight the enormous potential of electrochemical biosensors for tackling real problems in today´s world and will remark their opportunities for multiple applications in clinical diagnosis and monitoring.

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Computational Microscopy and Sensing

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Deep learning is a class of machine learning techniques that uses multi-layered artificial neural networks for automated analysis of signals or data. The name comes from the general structure of deep neural networks, which consist of several layers of artificial neurons, each performing a nonlinear operation, stacked over each other. Beyond its main stream applications such as the recognition and labelling of specific features in images, deep learning holds numerous opportunities for revolutionizing image formation, reconstruction and sensing fields. In fact, deep learning is mysteriously powerful and has been surprising optics researchers in what it can achieve for advancing optical microscopy, and introducing new image reconstruction and transformation methods. From physics-inspired optical designs and devices, we are moving toward data-driven designs that will holistically change both optical hardware and software of next generation microscopy and sensing, blending the two in new ways. In this presentation, I will provide an overview of some of our recent work on the use of deep neural networks in advancing computational microscopy and biomedical sensing systems.

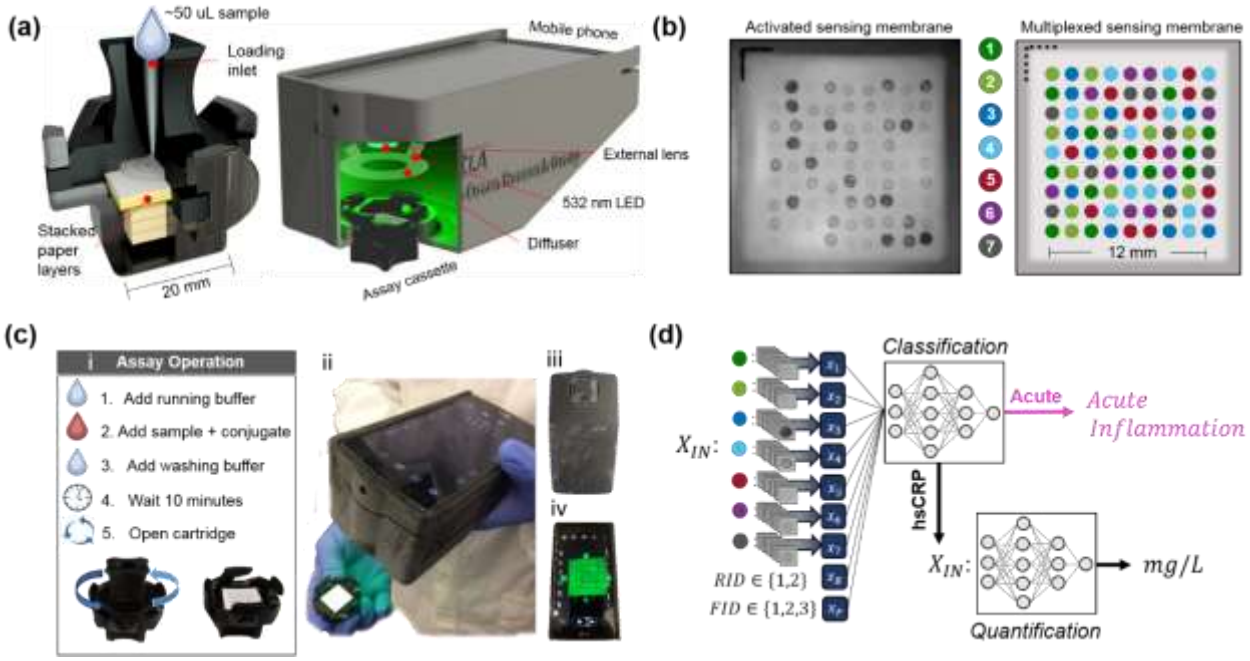

Figure 1: Deep Learning-enabled Point-of-Care Sensing: https://www.biorxiv.org/content/10.1101/667436v1

Plasmonic Biosensors for Ambient Viruses and Bacteria

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Abstract (Arial 11)

The tiny invisible airborne pathogens, especially viruses, bacteria and their components, may cause health impacts even with minute amount. My group has developed sensors for total bioaerosol quantification [1] and for highly accurate SARS-CoV-2 detection [2].

To quickly evaluate the total bioaerosols concentration, we developed a localized surface plasmon resonance (LSPR) biosensor based on succinimidyl-ester-functionalized gold nanoislands (SEF-AuNIs) for quantitative bioaerosols detection. The detection limit of our proposed SEF-AuNIs sensors for model bacteria *E. coli* and *B. subtilis* can go to 0.512 cells/ml and 1.69 cells/ml respectively. To demonstrate the capability of this bioaerosols sensing technique, we tested aerosol samples collected from Bern (urban station), Basel (suburban station) and Rigi mountain (rural and high altitude station) in Switzerland, and further investigated the correlation with endotoxin and PM10. The results substantiated that our SEF-AuNIs sensors could be a reliable candidate for total bioaerosols detection and air quality assessment.

Our dual-functional plasmonic biosensor combining the plasmonic photothermal (PPT) effect and LSPR sensing transduction provides a promising solution for COVID-19 virus detection. The AuNIs functionalized with complementary DNA receptors can perform a sensitive detection of the selected sequences from SARS-CoV-2 through nucleic acid hybridization. For better sensing performance, the thermoplasmonic heat is generated on the same AuNIs chip when illuminated at their plasmonic resonance frequency. The localized PPT heat is capable to elevate the in situ hybridization temperature and facilitate the accurate discrimination of two similar gene sequences. Our dual-functional LSPR biosensor exhibits a high sensitivity with the lower detection limit down to the concentration of 0.22 pM and allows precise detection of the specific target in a multi-gene mixture. The virus sensor can serve as an alternative to the standard PCR methods for COVID-19 diagnosis, but more prominently, may provide fast and continuous monitoring of the ambient viruses.

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FIGURES

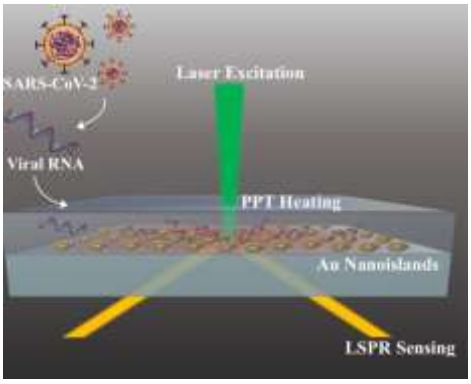

Figure 1: Dual-functional plasmonic biosensor combining the PPT effect and LSPR sensing.

Graphene-on-Polymer films for low cost flexible & disposable biosensors

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We are developing (1) a technology platform that exploits the sensing features of monolayer graphene, an atomically-thin layer of pure carbon (2) for its promising perspectives in biomedical applications, especially for embedded devices and wearables.

For that purpose, we have developed (1) biocompatible (3) films based on graphene-on-polymer for enabling sensing layers which have proven both in-vitro (4,5,6) and in-vivo (7) real-time sensing and diagnostics on the skin as well as on open wounds for healing assessment (1) and for implants (7).

I will present the capabilities of the films and the perspectives for enabling RFID connected wearables for remote patient monitoring as well as disposable devices for rapid point-of-care diagnostics.

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FIGURES

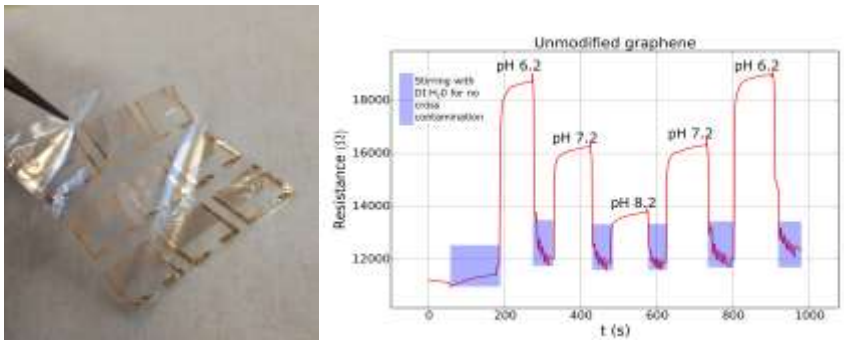

Figure 1: Left sensors on polymer , Right : time traces of pH Sensors made of graphene-on polymer devices.

Antibody-gated indicator releasing mesoporous materials: a potential biosensor platform for rapid diagnostic tests

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The urgent necessity to carry out reliable and relevant analytical measurements directly at a point-of-need is one of the current drivers for the development of miniaturised analytical systems, quick tests and wearables. Despite their simplicity, this type of tests must guarantee analytical relevance and reliability like laboratory-based analysis, e.g., in terms of sensitivity, selectivity, immunity against false positives and false negatives as well as robustness and repeatability. Keeping in mind the high sensitivity offered by gated indicator-releasing micro- and nanoparticles due to their inherent features of signal amplification, we performed several optimisations to develop a potential biosensor platform for use in rapid tests. Conceptually, these gated materials are closely related to drug delivery systems, consisting of high porous materials usually closed with macromolecular “caps” and loaded with indicator molecules that are released in presence of a target analyte. However, the key difference between the two types of functional materials is that many drug delivery systems should deliver their cargo over a longer period, often many hours, whereas the gated materials prepared for sensing should show fast release kinetics, on the order of <5 min.

With the aim to optimise and adapt gated materials for sensing purposes, we prepared in this work several antibody-gated materials for small-molecule sensing. The materials consisted of porous silica particles containing indicator molecules in the pores and certain hapten molecules grafted to the particle surface close to the pore openings. The pores were then capped with antibodies binding to these haptens, thus inhibiting the escape of the indicators from inside of the pores. In presence of the corresponding analyte, the antibody is displaced from the surface of the material, allowing the escape of the indicators. This allows the detection of the analyte indirectly through an inherent signal amplification. In this work, the insecticide permethrin, a type-I pyrethroid, was selected as target model, because type-I pyrethroids play an important role in airplane disinfection. A first in-depth study of the various chemical tuning options of such antibody gated systems was performed. Different mesoporous silica supports, different functionalisation routes and different loading sequences were assessed. The materials’ performances were evaluated by studying their temporal response behaviour and detection sensitivity, including the tightness of pore closure (through the amount of blank release in absence of analyte) and the release kinetics. Our results indicate that the better the paratope-accommodating Fab region of the antibody “cap” fits into the host material’s pore openings, the better the closing/opening mechanism can be controlled. Because such materials can be used in various different formats from suspension assays[1] via microfluidic chips[2] to test strip-based lateral flow assays,[3] such materials present a powerful analytical particle platform for the sensitive analytics and diagnostics outside of a laboratory, realising sensitivities down to the µg kg^{-1} range in less analysis times of less than 5 min as we have recently demonstrated.[4]

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Optofluidic fiber platform for molecule sensing

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Considerable advances have been achieved with optical sensors throughout the years, which today find real world applications in diverse areas. For chemical and biosensing, a number of methods based on, e.g., photoluminescence and Raman scattering, allow for obtaining chemical composition information of analytes. In particular, surface enhanced Raman scattering (SERS) can achieve detection at single molecule concentrations. Optofluidic sensors, which combine the compactness and practicality of microfluidics with the high sensitivity of optical sensing, present a high potential for practical, reliable and low sample volume testing. Even though most optofluidic sensors rely on integrated optics on chips and planar structures, structures that are based on optical fibers containing micron-scale fluidic channels can take advantage of the well-established optical fiber industry, with cost effective optical sources, detectors and components widely available. In addition, with channels of few to tens of microns in diameter, as little as nanoliter sample volumes are required. Our group has a long-term experience with optofluidic fiber structures, with a fluidic fiber dye laser, e.g., demonstrated [1]. This expertise has now been used in combination with the functionalization with graphene oxide of the internal walls of microstructured fibers [2], for the preparation of a sensitive and ultralow volume SERS sensor [3]. A fiber with an 80-μm-diameter central capillary was functionalized in a 2-step process, first with graphene oxide, and subsequently with gold nanorods with a ~15-nm diameter and a ~50-nm length (Figure 1A). Graphene oxide plays a triple role, mediating the attachment of the nanorods in the fiber, suppressing photoluminescence from the analyte and stabilizing the SERS signal [4]. Centimeter long sections of the fiber were tested as optofluidic SERS platforms, placed under a WITec Alpha 300R confocal Raman microscope, with an excitation wavelength of 633 nm. Rhodamine 640 and Rhodamine 6G were used as analytes and were inserted into the fibers in aqueous solutions. We highlight that volumes as low as a few hundreds of nanoliters were sufficient for the measurements. Figure 1B shows the obtained SERS spectra for Rhodamine 640, in which case concentrations as low as 10^{-9} M still presented the analyte's characteristic modes. Figure 1C shows that sub-second integration times were sufficient to obtain low noise and temporally stable spectra, allowing for fast analysis. The developed sensing platform can be adapted to be selectively sensitive to specific biomolecules, such as viral proteins, potentially providing highly sensitive and precise tests with ultralow-volume requirements.

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FIGURES

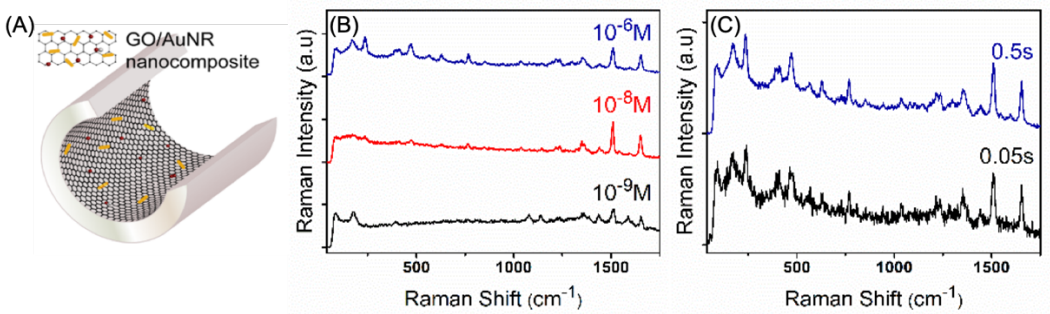

Figure 1: (A) Schematic representation of the capillary fiber internally coated with GO/AuNRs. SERS spectra of Rhodamine 640 solutions for various concentrations (B) and for different integration times at 10^{-6} M (C).

A rapid and sensitive bioelectrical biosensor for the detection of the SARS-CoV-2 S1 spike protein based on membrane-engineered cells

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Abstract

As a result of the COVID-19 pandemic, novel diagnostic tools are needed to reliably monitor of infected individuals, particularly including asymptomatic patients and/or during the first days following of infection. Therefore, we developed a novel biosensor for the SARS-CoV-2 S1 spike protein antigen. The biosensor was based on measuring changes in the bioelectric responses of membrane-engineered mammalian Vero cells bearing the human chimeric spike S1 antibody, according to the principles of the Bioelectric Recognition Assay [1] and the technology of Molecular Identification through Membrane Engineering [2]. The biosensor was able to detect the viral antigen in three minutes without any prior sample processing and with a high specificity (pg/ng level) and selectivity against other virus-associated proteins. In addition, we have coupled our approach with a Point-of-Care recording device which can be operated by lay users with minimum training and operated via a smartphone.

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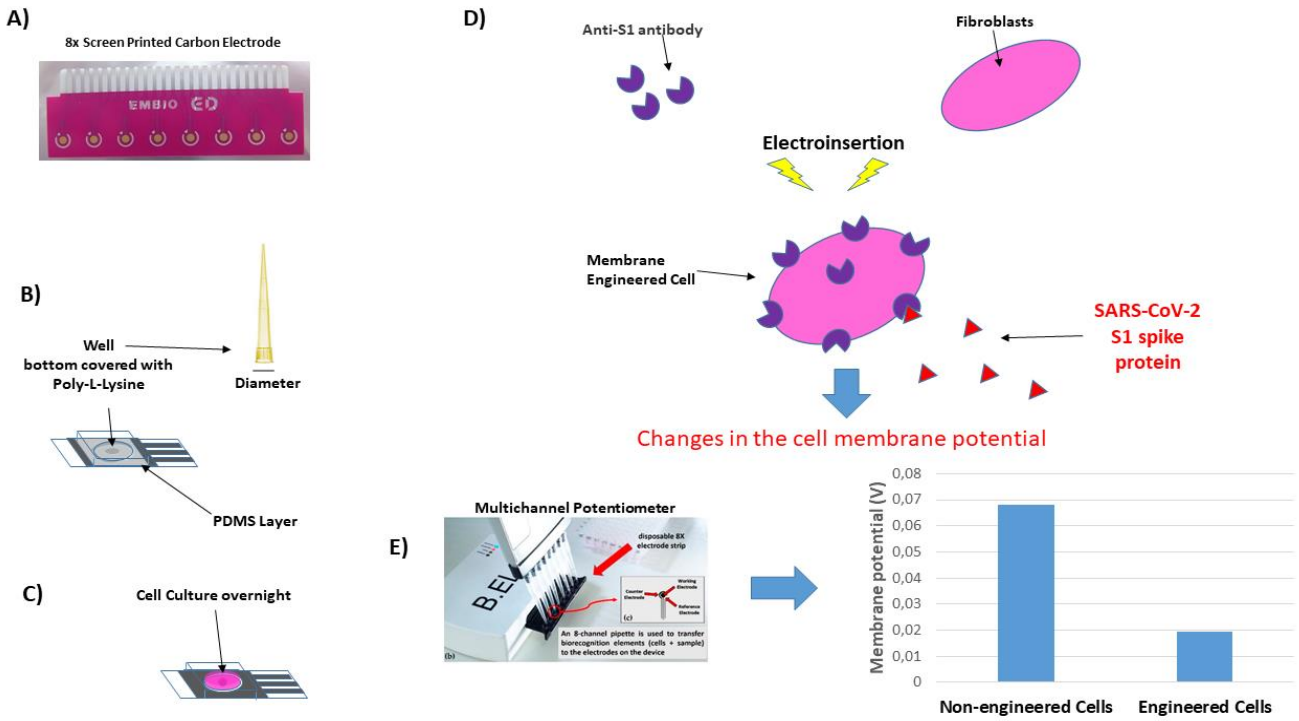

Figure 1: Graphical abstract presentation of the process for developing a Bioelectic Recognition Assay for the detection of the SARS-CoV-2 S1 spike protein antigen using membrane-engineered cells as biorecognition elements.

An innovative Fiber Optic- Surface Plasmon Resonance (FO-SPR) biosensor as a potential tool for SARS-COV-2 detection

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Fiber Optic – Surface Plasmon Resonance (FO-SPR) technology has been recognized as a remarkable optical sensing tool in various fields of life science, agro-food sector and medical diagnostics, as it can provide efficient characterization and real-time quantification of various biological entities [1]. Potential applications can span from studying interactions between proteins, lipids, nucleic acids, to even low molecular weight molecules such as drugs [2-4]. Moreover, these systems possess some other interesting features such as acceptable costs, compact instrumentation, immunity to electromagnetic interferences and remote sensing capabilities [5]. In the FO-SPR technology (see Figure 1), the light is guided through a metal-coated multimode FO to yield propagating plasmonic waves at the interface obtained with the analysing environment. Sensitive changes in the refractive index of light are then triggered by any biological interaction occurring at this interface, and subsequently processed into a graphical representation [6]. The developed FO-SPR sensor can be applied in an automated setup for both immuno- and aptamer based bioassays, rivalling with the ELISA and PCR golden standards [3,4].

Hence, in the near future we are attempting to employ the FO-SPR system to efficiently detect the SARS-COV-2 antigen, using both antibodies and aptamers as specific bioreceptors. In this scenario, it is expected that FO-SPR sensing performance competes with the state-of-the-art technologies in terms of faster detection (less than 60 min) and higher sensitivity.

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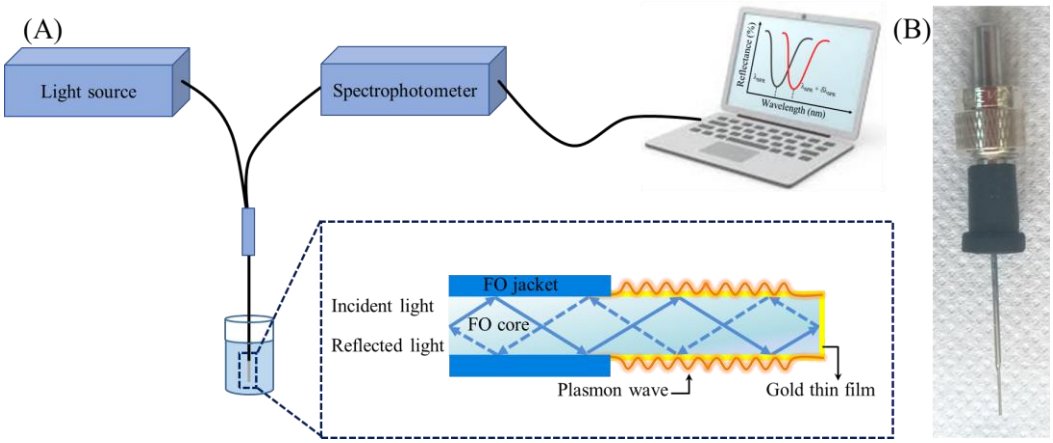

Figure 1: Fiber optic-surface plasmon resonance (FO-SPR) sensing platform. (A) Schematic of the experimental setup; (B) Image of the fabricated FO-SPR sensor.

Smartphone-based wireless point–of–care platform for potential electrochemical detection of SARS-CoV-2

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COVID-19 (coronavirus disease 2019), provisionally called 2019-nCoV infection and officially declared by WHO to be a pandemic on March 11, 2020, is a respiratory tract infection caused by severe acute respiratory syndrome (SARS)-CoV-2, which mainly results in pneumonia and upper/lower respiratory tract infection [1]. Cell culturing, enzyme-linked immunosorbent assay (ELISA), or reverse transcription polymerase chain reaction (RT-PCR) are some of the conventional methods used for disease diagnosis. However, according to some earlier reports, a majority of these methods require expensive reagents and equipment as well as well-trained personnel. In addition, they often have limited speed, sensitivity or specificity [2]. On the other hand, electrochemical biosensors have presented high sensitivity and selectivity real-time detection of pathogens without the requirement of additional processing steps or reagents. Nevertheless, using low energy wearable and wireless electronic devices are required for a rapid, versatile and low-cost point-of-care electroanalysis [3–5]. In this study, low-cost and wide energy efficiency electronic platform for a rapid and versatile electroanalysis, is shown. The device of 28.7 mm × 70.10 mm is powered by a 3 V coin cell battery and performs some of the most common electroanalytical techniques of chronoamperometry (CA), differential pulse voltammetry (DPV) and square wave voltammetry (SWV). These tests can be carried out for more than 24 uninterrupted hours. Additionally, the electronic platform using “Bluetooth Low Energy” protocol for both receiving the parameters from the user and sending the test results to a smartphone where a custom app has been developed and installed. The App not only allows to visualize the results in real time but also exports them in a file .csv or .jpg for further analysis. Finally, the device has been electrically tested through precision resistance load bank. The results obtained show two operating voltage ranges: ±720 mV with steps of 60 mV and ±492 mV with steps of 40 mV, a working current range from 5 µA to 750 µA (full scale), and an energy consumption less than 10 mW. Based on the work developed in [3], where a genosensor on gold films for enzymatic electrochemical detection of a SARS virus through a square wave format with frequency of 50 Hz, amplitude of 50 mV and potential between −0.15 and +0.3 V is shown, these platform may allow a rapid and versatile diagnostic (SARS)-CoV-2 if the system is coupled with a biosensor of this type that includes an appropriate gene of (SARS)-CoV-2 as target.

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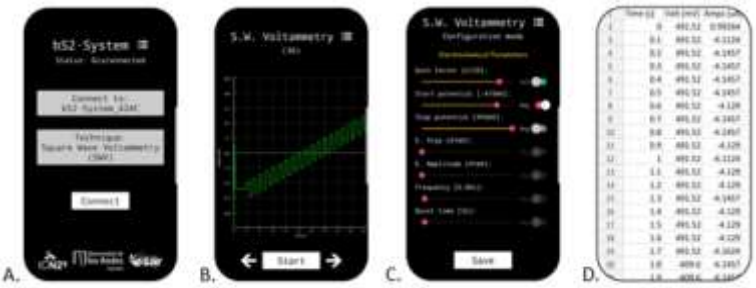

Figure 1: Custom app. A) Main screen. B) SWV graphical result. C) Configuration screen. D) Exported result.

Faster and economic detection of SARS-CoV-2 using isothermal amplification techniques

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Abstract

With the dimension of the SARS-CoV-2 pandemic all over the world, showing highly contagious rates and severe complications, an urgent need exists for faster detection methods to identify infected people, and slow down the contagion networks. RT-qPCR is the primary, and crucial, tool employed for the detection of different pathogens, and became the standard methodology for this particular virus [1]. Despite its high sensitivity to detect the presence of viral RNA in a sample, this technique is slow and needs complex equipment and specialized work force to perform the analysis. For this reason the number of tests accomplished is limited, and can lead to a decrease in subjects tested, and no measures can be implemented to control cross-contamination with others. Isothermal amplification have been extensively studied due to its advantages when compared to traditional PCR for the detection of pathogenic bacteria and virus in patients. As they perform at constant temperature the equipment needed is much simpler, and the reaction may be performed even in a water bath. This characteristic also allow an easier integration in miniaturized devices, and a complete automatization of the analysis can be reached, reducing the complexity and the cost of the analysis [2]. Our group works in the development of new methodologies for the detection of pathogens based in nucleic acid detection, thus directly applicable for the detection of viral RNA of SARS-CoV-2. We have applied several isothermal amplification techniques, including Loop-mediated isothermal AMPlification (LAMP) and Recombinase Polymerase Reaction (RPA) for pathogen detection. With the addition of a pre-step for reverse transcription of RNA into cDNA, both techniques can easily be applied for the detection of viral RNA. Another advantage of these techniques is the possibility to combine them with different naked eye detection strategies, what simplifies the interpretation of the results. Efforts have been made to validate LAMP to be used in different applications, and already some studies have shown as an alternative to RT-qPCR for the detection of SARS-CoV-2 [3,4] Despite RPA has not been yet tested for the detection of this virus, its advantages in terms of speed and simplicity of the reaction, can improve the analysis. This poster will compare and summarize different isothermal amplification techniques which present a real potential for a simple, economic and faster detection of SARS-CoV-2.

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Nanobioconjugates for signal amplification in electrochemical genosensors

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Abstract

Nanobioconjugates are hybrid materials that result from the coalescence of biomolecules onto nanomaterials surfaces [1]. They have demonstrated the ability to dramatically increase the signal response of a biorecognition event when assembled in biosensors [2]. In this context, nanobioconjugates hold the potential to solve the limitations of conventional clinical assays in terms of analysis time, detection limits and costs. Biomolecules that integrate the nanobioconjugates include proteins, antibodies, aptamers, carbohydrates, and single and double DNA strands, among others. The use of a specific biomolecule depends on the biosensor application. For example, DNA is frequently used in the development of genosensors associated with pathogenic infections such as COVID-19 [3], Zika virus and other infections transmitted by vectors [4, 5], detection of bacteria, cancer biomarkers, among others [6]. Biomolecules are bounded to nanomaterials to build the nanobioconjugates, which are commonly assembled in biosensing platforms, either modifying the transducer or as a signaling tag, to enhance the signal response.

This work aims to show a general strategy for the design of a nanobioconjugate for the amplification of the electrochemical signal recorded in genosensors for the detection of viral infections. As a proof-of-concept, we developed an electrochemical sandwich-type biosensing platform for the differential detection of RNA of the Zika virus and its discrimination against Dengue and Chikungunya related arboviruses [4]. And a nanobioconjugate based on gold nanoparticles (AuNPs) and DNA where a ruthenium complex, intercalated in between the DNA strands, served as a signal electrochemical reporter [5]. The resultant nanobioconjugate increased the signal response of the electrochemical genosensor dramatically, allowing for the ultrasensitive detection of RNA of the Zika virus in real serum samples from infected patients in concentrations down to fM. The approach demonstrated to be useful for the detection of viral RNA levels of clinical relevance and holds the potential for the development of electrochemical biosensors to fight pandemics.

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Lateral flow devices for COVID-19-related biomarkers

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In December 2019, an outbreak of severe acute respiratory syndrome caused by a novel coronavirus (SARS-CoV-2) was originated in Wuhan, Hubei province, China, escalating into a global pandemic in just three months. The disease, officially named COVID-19, has saturated healthcare systems worldwide, thus demonstrating the urgent need to deploy rapid and reliable diagnostic tools. Along with contention measures such as social distancing and good hygienic practices, the use of diagnostic devices during the early stages of the pandemic can have a major impact on limiting the spread of the virus. In this context, lateral flow assays (LFAs) offer advantages compared to traditional techniques that depend on nucleic acid amplification due to their lower cost, shorter time of assay and ease of use. Most LFAs for COVID-19 diagnostic target immunoglobulins G and M (IgG/M) in blood for the assessment of acquired immunity against the virus. Alternatively, some LFAs target viral proteins of the SARS-CoV-2 structure, allowing for direct detection of the virus before the onset of symptoms. This poster will present: 1) a general outline on the operation of LFAs, 2) the two main approaches used during the current pandemic (IgG/IgM and viral protein detection), and 3) novel strategies, such as LFAs coupled to nucleic acid amplification.

Development of a lateral flow test for rapid pyrethroid detection

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The WHO (Word Health Organization) defines “disinfection” as the procedure whereby health measures are taken to control or kill the insect vectors of human diseases including dengue, yellow fever and malaria.[1] After the unprecedented spread of the Zika virus (South America, Brazil) in 2016,[2] the employment of type-I pyrethroids for airplane disinfection on inbound flights from the tropics thus increased in recent years. However, means to control for proper spraying to guarantee effective disinfection and avoid possible onset of symptoms in passengers and crew members, especially children and sensitized subjects, underlines the necessity to develop sensing schemes for the rapid detection of these pesticides directly at the point-of-use.[3] The aim of the presented work was the development of such a simple, rapid and effective method for pyrethroid analysis. The analysis will provide a semi-quantitative estimation of the insecticide levels, in order to have a control over the amount necessary to efficiently kill mosquitoes, while maintaining non-hazardous concentrations inside the passenger and crew cabins.

An antibody-gated indicator-releasing mesoporous material[4-6] was thus developed to class-selectively indicate type-I pyrethroids. The material shows various new features from the reported ones such as a pore size better adapted to the antibody caps, a localized hapten grafting and secondary poly(ethylene glycol) (PEG) functionalisation, all contributing to the fact that now micron-sized scaffold particles can be used without compromising kinetics or blank release. The implementation into PEGylated glass fibre membranes allows for lateral-flow assay-based analysis, employing a smartphone for readout. It was possible to detect Permethrin (type-I pyrethroid) at concentrations down to 1 ppb in less than 5 min, using a 3D-printed case as the strip holder and a smartphone for signal readout.[7] The reported method is not only a simple alternative for testing for pesticide residues on airplanes but is modular and can thus be adapted for many different analytes and field analytical scenarios for instance in point-of-care and point-of-need diagnostics.

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Improving sensitivity of organic electrochemical transistor with modified PEDOT-functionalized gate electrodes

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Abstract
Organic electrochemical transistors have emerged as a solid platform for sensing biologically relevant species including proteins [1], nucleic acids [2], metabolites [3] and pathogens [4]. The presence of the biochemical events at the gate electrode interface endows unique sensitivities compared to classical electrochemical sensors due to the signal amplification at the organic channel [5]. Despite the continuous effort has been devoted to enhance the channel properties, the gate electrode plays a critical role to effectively transduce the biochemical binding event in a shift of the effective potential that ultimately lead to the channel doping/dedoping. One strategy to amplify the signal generated by the biochemical event is to utilize more sensitive material as a gate electrodes with nanocomposites of conjugated polymers and 2D materials [6].
In this study, organic channel based on poly(3,4-ethylenedioxythiophene):poly(styrene sulfonic acid) (PEDOT:PSS) with different gate electrodes including PEDOT:PSS:MXene, PEDOT:PSS:GrapheneOxide (GO), and PEDOTOH:ClO_4 were used as electrochemical sensor for uric acid, ascorbic acid, and dopamine. We found that the device with PEDOT:PSS:MXene gate electrode characterized at the gate voltage of 0.2V shows the highest sensitivity. The gate operation condition was determined by performing cyclic voltammetry measurements. The detection limit of the transistors was obtained about 100 nm which is better than a conventional electrochemical sensors. Our results suggest that PEDOT:PSS:MXene gated transistors could be used to sense low abundance biological species such as SARS-CoV-2.

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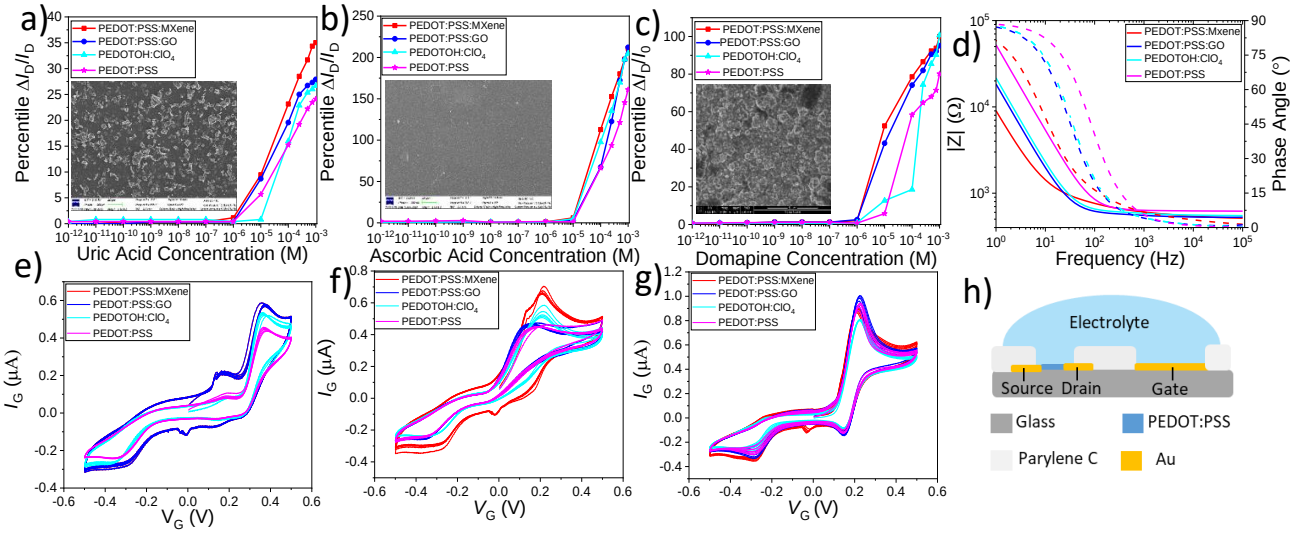

Figure 1. Sensitivity of transistors measured with a) uric acid, b) ascorbic acid, and c) dopamine for different gate electrodes, and d) their impedance spectra. Cyclic voltammetry measurements determines the optimum transistor operation condition for e) uric acid, f) ascorbic acid, and g) dopamine. h) Device schematic

Photonic Platform For Detection Of Significant Low Amount Of DNA

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Liquid biopsy has the potential to revolutionize the future of cancer diagnostics and disease management. The biomarkers for cancer present in blood are very diluted and difficult to measure. Droplet digital PCR (dPCR), real time PCR and Next Generation Sequencing are techniques that can measure minimum concentrations of biomarkers such as free circulating DNA fragments relevant to cancer diagnostics. The adoption of these techniques has been held back by complicated workflow, specific reagents, costly equipment and slow read out times.
Optics and photonics technologies, and high-sensitivity molecular diagnostic tests, already play key roles in the practice of healthcare. These technologies are essential for developing advanced tools for observing and measuring symptoms and treating patients with less invasive, more cost-effective methods.
Our technology could be a promising tool for early cancer detection. The principle of the our photonic detection system is based on exposing a sample of wavelength shifting material coupled to free DNA to light of certain wavelength and detecting afterwards the wavelength shifted light. The amount of shifted light for a given amount of input light provides information about the amount of free DNA in the sample. Thus, to optimize the signal to background ratio is of significant importance. Current systems are using photodiodes to detect the light. These devices have a low internal gain and a relatively large dark current, leading to the fact that at least few thousand photons are needed for detection. The developed setup is using photomultipliers (PMT) for the detection of the light. This kind of sensor has a high internal gain and allows therefore the detection of single photons. Furthermore, PMTs allow to measure the arrival time of the different photons with high precision. The combination of low detection threshold and timing information will allow to detect significant lower amounts of free DNA (at picomolar range). Moreover, the detection of low amount nucleic acid without amplification or sequencing opens the market for detection of another diseases such as: (I) Viral diseases (COVID-19..) by viral RNA or (II) Nosocomial infections by pathogenic bacterial DNA.

Equivalent electrical model circuit for COVID-19 electrochemical detection

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Abstract
Human respiratory infections caused by different pathogenic threats are a severe risk for the population worldwide [1]. Recently, an unprecedent outbreak of the newly designated Coronavirus disease 2019 (COVID-19) [2] has caused, to date, over 169000 deaths around the globe [3]. The societal and economic impact are still to be realized. While research around the globe has shown a remarkable amount of fast track results, it has also been questioned the readiness level of health systems in different countries. As an immediate counter measure to avoid catastrophic scenarios, the accurate and timely diagnosis of potential cases is required [4]. Currently, diverse methods are available to perform fast (<2 h) detection, however, instrumentation and reagents costs are considered a major drawback for routine application.

Electrochemical technologies have proven to accomplish the requirements for fast and economically amendable screening tools, different groups have demonstrated applicability of electrochemical biosensors for human influenza (H1N1) [5], rabies [6], human papilloma virus [7], among others. One of the main advantages of electrochemical technologies is that it allows to obtain readily accountable results, which translates in market products that require little training, which make them perfect candidates in emergency situations. On the other hand, the design and development of devices based in electrochemical technologies requires a careful understanding of each element that would partake in the final measurement. As part of this endeavor, a proper modelling and characterization of the target is required. In this work we, present the equivalent electrical model circuit for different measurement strategies focused in the COVID-19 viral particle (virion), ranging from the single particle electrical characteristics, to suspension dispersed virus (colloid) and immobilization. The basic model is based in the dielectric properties of the virion structure, represented by the single shell and the dual shell spherical model [8]. The results provide a simple capacitive representation which can be used for the more complex scenarios, in which the diffusive effect of the suspension medium and the immobilization molecules should be accounted for in order to avoid misreading and, correspondingly, misdiagnosis.

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Silicon nanowire-based field-effect transistor array for multiple and rapid pathogen detection

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The recent outbreak of the pandemic Coronavirus disease [1] has demonstrated the need of highly sensitive and fast biosensors to detect pathogens at an early stage. Direct antigen or toxin detection rather than DNA amplification or patients´ immune response analysis allows such detection in order to take immediate actions. Nanomaterial-based field-effect transistors (FETs) have demonstrated to be efficient transducers that can be modified with the corresponding bioreceptors for antigen detection with high sensitivity [2]. Here, we present a chip containing an array of 16 FETs with silicon nanowires as semiconductor channel [3]. The nanowires are defined in a honeycomb shape by an electron-beam lithography process [4], giving good mechanical stability and enhanced contact area with the sample. This area is covalently functionalized with antibodies against three different markers of pathogens, namely VP40 protein of the Ebola virus, B subunit of Cholera toxin, and Staphylococcal enterotoxin B. The array responds to the presence of the analytes in femtomolar concentrations with no cross-reaction, allowing to discriminate a lethal and potentially pandemic virus like Ebola from others that could show similar initial symptoms.

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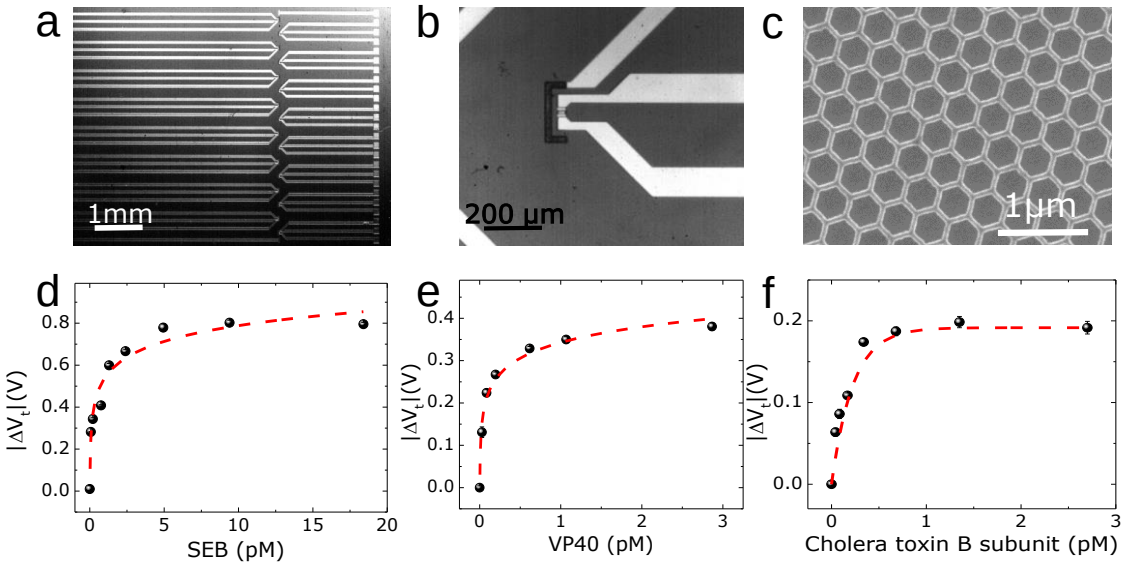

Figure 1: Sensor array and biosensing response. (a) Array of FETs, (b) Individual FET, (c) Magnification of the nanowires. (d), (e) and (f) show biosensing response for Staphylococcal enterotoxin B (SEB), VP40 from Ebola, and Cholera toxin B subunit.

Electrical probing of SARS-CoV-2 spike protein via a graphene field-effect transistor

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Graphene is a two-dimensional material with excellent electronic properties and chemical stability. We combined the unprecedented sensitive graphene field effect transistor (Gr-FET) with highly selective antibody/antigen interaction to develop immunosensors towards facile and fast detection of SARS-CoV-2 (and potentially SARS-CoV). It uses a field effect transistor structure with graphene as the channel material and body fluid environment as the liquid gate. The graphene surface is combined with SARS-CoV spike glycoprotein S1 subunit antibody (CSAb) or human angiotensin converting enzyme 2 (ACE2) through non-covalent crosslinking[1]. During the test, the spike glycoprotein S1 antigen (including receptor binding threshold, RBD) of the SARS-CoV-2 binds to the CSAb and ACE2 on the graphene surface[2,3], inducing a change in the source-drain conductance of the Gr-FET via field effect.

At present, the lowest detection limit concentrations we have achieved is 0.2pM (CSAb) and 0.1nM (ACE2) in the laboratory stage. If assuming a linear sensing response, we may deduce a limit of detection (LOD) as low as ~10fM at a signal-to-noise ratio of 1. Therefore, our developed Gr-FET-based antigen/antibody biosensors provide an alternative to resolve early diagnosis, as well as rational design of neutralizing antibody locking methods to resolve this ongoing public health crisis.

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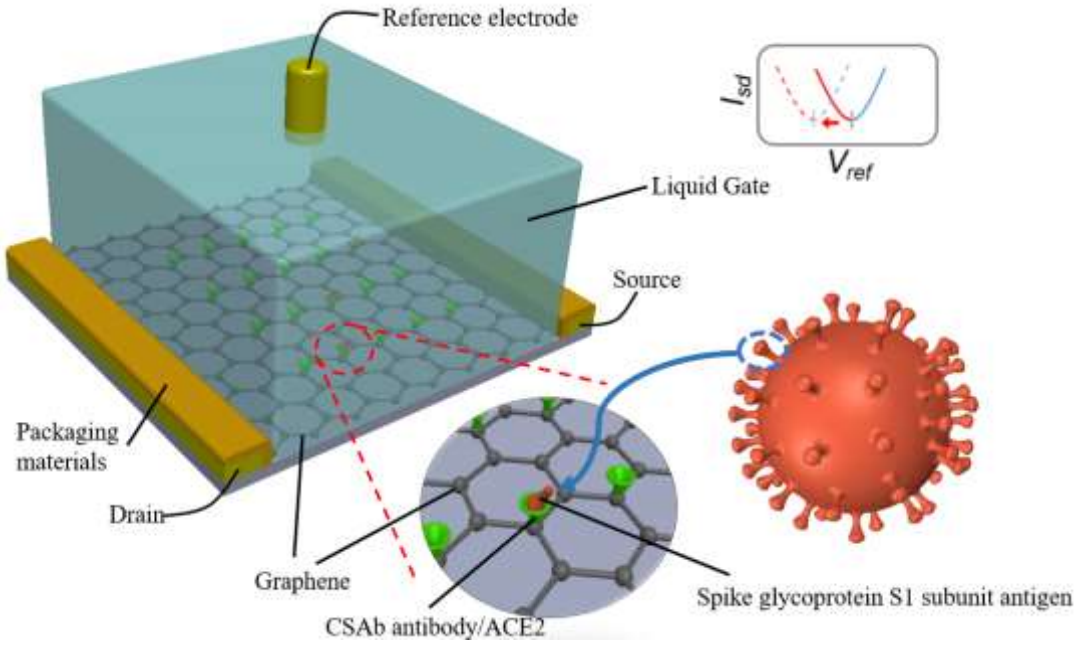

Figure 1: Schematic of GFET-based coronavirus antigen / antibody detection sensor

Electrical detection of amyloid-β aggregates using membrane integrated microfluidic transistors

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Abstract
Alzheimer's disease (AD) is a neurodegenerative disorder associated with a severe loss in thinking, learning and memory functions of the brain. There is currently no treatment that can effectively stop AD. Some drugs can however slow down the progress. Thus, early detection of AD is the key to manage the disease and develop better treatments. A common pathological change found in AD-affected brains is the accumulation of a peptide named amyloid-β (Aβ) that can form plaques. In this work, we design an organic electrochemical transistor (OECT) for *in vitro* detection of Aβ aggregates [1]. The OECT channel is integrated with a nanostructured isoporous membrane which has a strong affinity for Aβ aggregates. As Aβ aggregates are captured by the membrane, they block its pores that are smaller in size than the protein. As such they impede the vertical ion flow towards the channel and change the transistor characteristics (speed and output current). The sensor thus does not rely on fluorescent labels or redox molecules. Combining the high transconductance of the OECT with the precise porosity and selectivity of the membrane, the device detects the presence of Aβ aggregates in human serum samples with excellent sensitivity. Moreover, a microfluidic channel, where minute amounts of fluids can be precisely processed, stand as an ideal platform to provide a compact size of the device, a short detection time, and low analyte consumption. This is the first-time demonstration of a biofunctionalized, nanostructured, and isoporous membrane integrated with a high-performance microfluidic based transistor for biosensing. This robust, low-power, non-invasive, and miniaturized sensor aids in the development of point-of-care tools for early diagnosis of AD. We would now like to convert this OECT into a Coronavirus detection device by replacing the proof-of-concept recognition module with very recently published nanobody versions that recognize SARS-CoV-2 and MERS surface proteins [2]. The human ACE2 receptor protein, to which the virus binds with high affinity, will be evaluated as an alternative recognition module. Sensor performance will be tested with recombinant SARS-CoV-2 RBS (receptor binding domain of the spike protein) fusion proteins as described in the literature. We will also try to create more realistic dummy virus particles by decorating unrelated protein shells with the larger trimeric spike protein.

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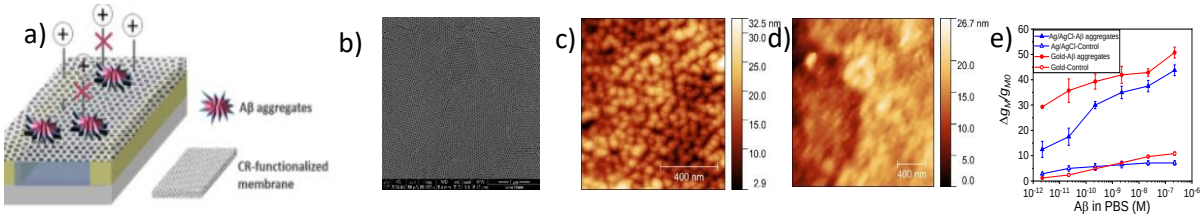

Figure 1: a) Schematic of target molecule binding on nanoporous membrane (NP) and b) its SEM image. c) and d) is the AFM images of NP before and after target molecules binding. e) is the sensitivity curve obtained by calculating the change of transconductance as a function of concentration.

Ultrathin Polydopamine Films with Phospholipid Nanodiscs Containing a Glycophorin A Domain

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Inspired by a mussel adhesive, polydopamine (PDA) has earned great acclaim as a multifunctional coating. Its easy synthesis, the ability to adhere to virtually any surface and its biocompatibility makes polydopamine an interesting material for preparing films used in various fields of research ranging from energy to environmental to biomedical. Here, we use electropolymerization to provide highly controlled deposition of polydopamine and other catecholamines on conductive surfaces. Motivated by the precise control achievable by electropolymerization, polydopamine films can be fabricated on conductive substrates with nanometre thickness and outstanding elastic moduli. Since electropolymerization only occurs at the conductive surface, it is possible to embed non-conductive materials within the PDA matrix. We were able to directly incorporate phoshoplipid nanodiscs with glycophorin A domain into the polycatecholamines to provide functional films and membranes. AFM-IR-measurements revealed that the nanodiscs were retained in the film, emphasizing that electropolymerization is a mild process. Moreover electrochemical tests further proved the availability of the lipids after embedding (figure 1) indicating that the nanodiscs were not completely overgrown by PDA. This approach opens many new avenues for creating hybrid films with novel properties and increased stability. Polydopamine provides a versatile foundation for the design of hybrid membranes paving the way for new biomimetic materials leading to the development of cell mimicking nanocomposites. The formation of complex biosensing platforms by, for instance, developing microfulidic devices with incorporated transmembrane receptors would be possible.

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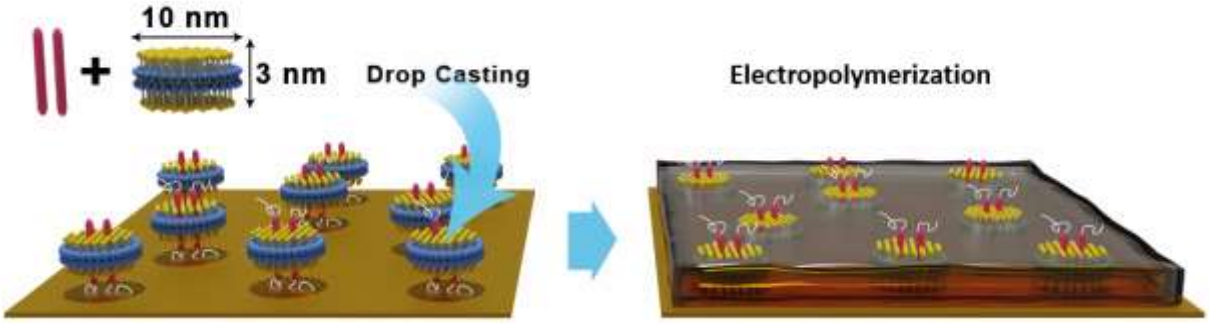

Figure 1: Schematic representation of the process to embed Phospholipid nanodiscs into polydopamine matrix on gold substrate.

Multianalytical Point-of-Care device for the diagnosis of viral infections

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Abstract

We propose a portable device with disposable cartridges for the diagnostic of Covid-19. The technology is based on magnetic sensors able to perform molecular and serologic tests in different cartridges. The device is composed of an electronic reader and disposable biochips with an array of magnetic sensors (Fig.1). Each biochip has 6 sensing sites for the interrogation of multiple target analytes (genes, antibodies, antigens), per sample. The use of magnetic markers coupled to on-chip magnetic attraction allow an increased sensitivity able to detect down to hundreds of target molecules per microliter of sample in shorter times [1,2]. The proposed technology has been validated for various clinical applications. Namely, in the detection of viral genes (Zika, Dengue and Chikungunya virus), bacteria [3], 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. Major assets include, low cost (< 10€/test), multiplex (6 probes/test) and fast time to results (< 1 h).

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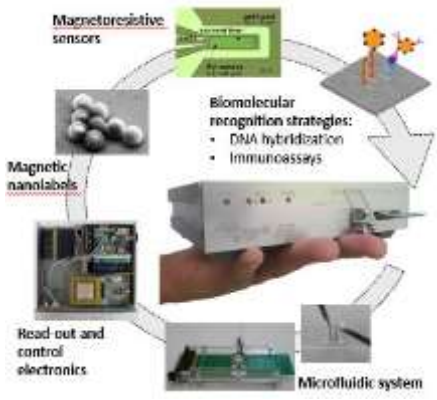

Figure 1: INESC MN portable diagnostic platform

Electrochemical detection of multiple RNA targets using MXene/duplex-specific nuclease: A path towards simultaneous detection of SARS-CoV-2 and H1N1 influenza virus

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Rapid and sensitive detection of SARS-CoV-2 in an affordable fashion is vital for the early diagnostics of the COVID-19. Moreover, with the inevitable emergence of the upcoming seasonal influenza (flu), it is highly important to differentiate influenza virus from SARS-CoV-2 in order for the healthcare professionals to prescribe the most appropriate medications. We have developed a novel biosensor for the concurrent detection of two short RNA strands (microRNA-21 and microRNA-141) that is being upgraded for the SARS-CoV-2 and H1N1 influenza virus. A MXene-$Ti_3C_2T_x$ is synthesized and modified with 5 nm gold nanoparticles (AuNP@MXene) and drop-casted on a home-made dual screen printed gold electrode (SPGE). Two DNA probes ($Base^{21}$ and $Base^{141}$) are identically immobilized on each working electrodes to form $Base^{21}$/AuNP@MXene/SPGE and $Base^{141}$/AuNP@MXene/SPGE). Two magnetic particles (MPs) are conjugated with two different ssDNAs labelled with ferrocene (Fc) and methylene blue (MB), which are partly complementary to the target RNAs. After target binding and the DNA:RNA heteroduplex formation, the DNA is cleaved by duplex-specific nuclease (DSN) leaving the target RNA intact for further reactions. The cleavage, releases the over-hanged labelled ssDNAs to be hybridized with their corresponding $Base^{21}$/AuNP@MXene/SPGE and $Base^{141}$/AuNP@MXene/SPGE following by two discrete electrochemical signals arising from MB and Fc. AuNP@MXene provided spacious accordion-like host for immobilization of vast numbers of DNAs and represented a great charge mobility by offering 4 times higher electrochemical signal than that of the AuNPs alone. The proposed biosensor could detect both target RNAs in 80 min with the detection limits of 204 aM and 138 aM and a wide linear range from 500 aM to 50 nM demonstrating promising features for the fabrication of practical devices.

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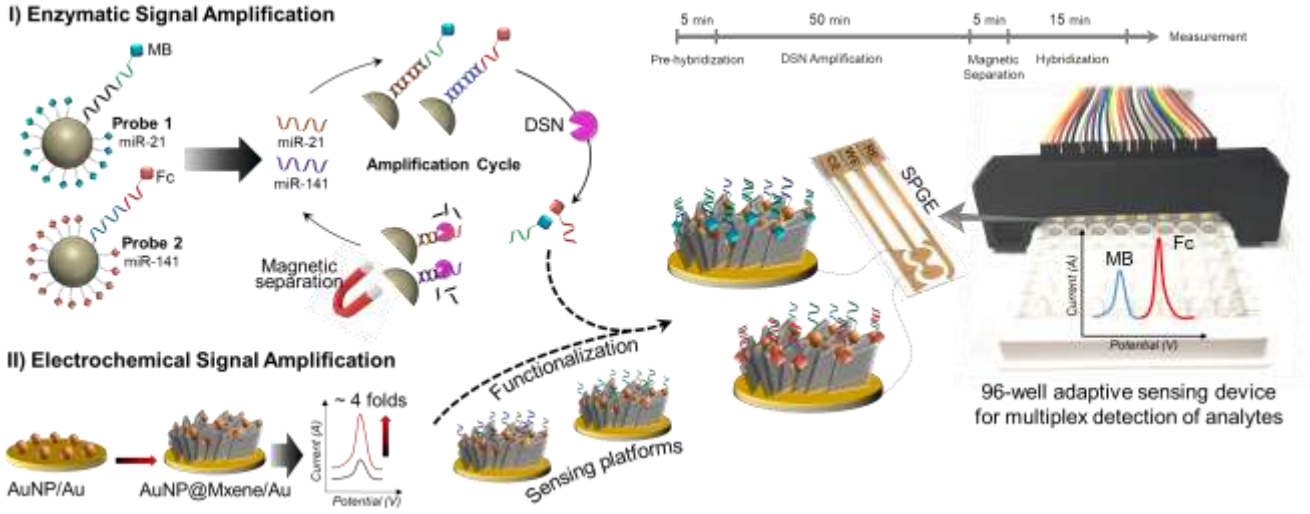

Figure 1: Schematic diagram of the multiple detection of target RNAs.

Nano-Illumination Microscopy as a fast-low-cost chip-sized technique to face pandemics

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Over the past few decades, virologists, epidemiologists and other health sectors have issued alerts about new viruses that could lead to global pandemics. The need for rapid and effective methods to diagnose viruses is of paramount importance to prevent its massive spread among the population. Most viruses vary in size from 20 nm to 250-400 nm, but only the largest ones (700 nm-1 µm) can be seen with a traditional optical microscope. Although some optical super-resolution techniques achieve a resolution of tens of nm, these are complex and require expensive setups. Lensless microscopy is a low-cost alternative, but its resolution is limited by the pixels size on the camera. Recently, a new type of microscope based on nano-illumination microscopy (NIM), was presented [1, 2]. The NIM setup consist in a 2D array of GaN based nano-LEDs used to illuminate the sample while the resulting light is sensed by a photodetector. The sample is placed on top of the light source and the photodetecting device close to the sample (< 1 mm). The LEDs in the array can be switched individually or forming custom patterns, and can be used to observe the transmitted light through the sample or excite fluorescent dyes on it. So, by mapping the sample with the LEDs, morphological as well as molecular information can be obtained. The resolution in NIM microscopy is given by the LED pitch, which can be reduced to the pixel size with an adequate setup. The important aspect of NIM microscopy is that it relies on the LED size and this is continuously being reduced [3]. In this work, we will present a microscope built by using a 2D array of nano-LEDs with a state-of-the-art size of 5 µm LEDs, emitting at ~465 nm. But we will demonstrate how super-resolution with smaller LEDs than the diffraction limit will be obtained in no time. Figure 1 shows the principle of operation of the NIM microscope with a fly wing sample. The LEDs are switched one by one and the light is measured by a photodetector camera. At the same time the NIM image is reconstructed by associating the intensity measured at the photodetector to each LED position. As no lenses or expensive setups are involved the microscope is affordable by anyone. In addition, a complete setup can be produced on a chip size, available to be plugged in mobile phones. We acknowledge the European Union by the support through the European project ChipScope (737089).

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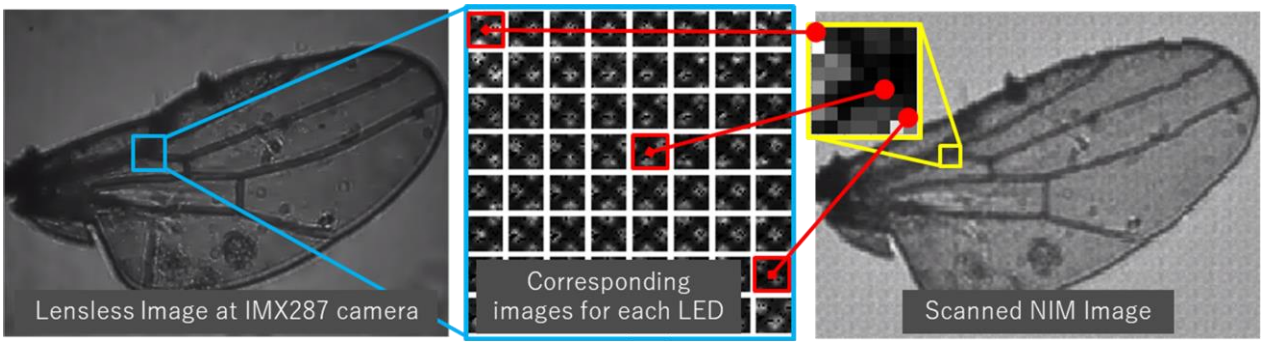

Figure 1: NIM method and extended image of a wing fly obtained by scanning with piezo motors.

Silicon nanowire sensor for immunological treatment - another approach for fighting pandemic

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Abstract

As of April 28, 2020, a pandemic called coronavirus disease 2019 (COVID-19) has spread to every continent of the world, infecting around three million people, and taken nearly 200,000 lives [1]. Although such deadly events are not new throughout human history, they often cause fear and uncertainty, mostly because of lacking information about the new strain of the virus. Insight about the virus and its working mechanism is perhaps important yet understanding the human immune response is the key to reducing mortality. Our immune system reacts differently depends on ages, genders, races, and health background. That explains dissimilar COVID-19 progression in patients where some develop critical conditions while others only have mild symptoms [2]. Accumulating evidences suggest patient with severe COVID-19 symptoms is due to cytokine - a common name for a broad spectrum of small proteins important in cell signalling, especially in the immune system - dysregulation [3-5]. Therefore, many studies have suggested a screening of cytokine profiles together with other immune cells responses for the determination of correct treatment [3,5]. Meanwhile, nanosensors such as silicon nanowire (SiNW) own advantages of being sensitive to small molecules, rapid and label-free [6]. In this poster, we demonstrate the use of a SiNW sensor in immunotherapy research, more specifically, in a system of switchable T-cell expressing chimeric antigen receptors (CARs). The sensor showed better sensitivity and a much lower limit of detection compare to standard ELISA tests. Moreover, thanks to its compatibility with CMOS technology which enables mass production, reproducibility is ensured [7]. Since the cytokine release syndrome (CRS) found in COVID-19 patients is also observed in patients receiving CAR-T therapy [4], the knowledge and tools generated by the SiNW sensor developed in this field of study may benefit the community. In the end, a full understanding and control of our immune system might be the key to fight any other pandemic in the future.

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Portable and real time DNA detection system using graphene transistor

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ABSTRACT
With the fast rising confirmed case due to the novel coronavirus disease (COVID-19) all over the world, a rapid, low-cost and non-laborious point of care (POC) diagnostic tool is urgently required. Graphene, an excellent two dimensional (2D) material with 1-atom thick carbon provides a new route towards ultrasensitive biomolecular detection for disease early diagnosis. In this study, we developed a portable and real time DNA detection system based on multi-array graphene field effect transistor (GFET) integrated with a miniaturized Arduino output reading platform and an automatic micropump. Single layer graphene was applied as channels where biorecognition elements immobilized. To optimize probe DNA (pDNA) (amine-tagged, 35 mer) immobilization and to preserve graphene structure and functionality, 1-pyrene butyric acid succinimidyl ester (PBSE) linker was chosen since it could be attached to graphene through the π- π stacking [1]. To minimize the non-specific binding, ethanolamine (ETA) was applied prior to the addition of target DNA (tDNA). Signal acquisition was performed in a quick response time with a liquid gating setup [2] using 0.01x phosphate buffer solution (PBS). Preliminary results demonstrated successful surface modification and DNA hybridization signal of the pDNA and 1µM tDNA with Dirac point (V_{Dirac}) shift of ~90 mV. The integrated GFET system is also potential to detect specific viral RNA which carries the same charge as DNA, as well as for multiplex detection through multi-array configuration towards more rapid, portable and inexpensive detection highly needed in pandemic scene like in nowadays COVID-19 outbreak period.

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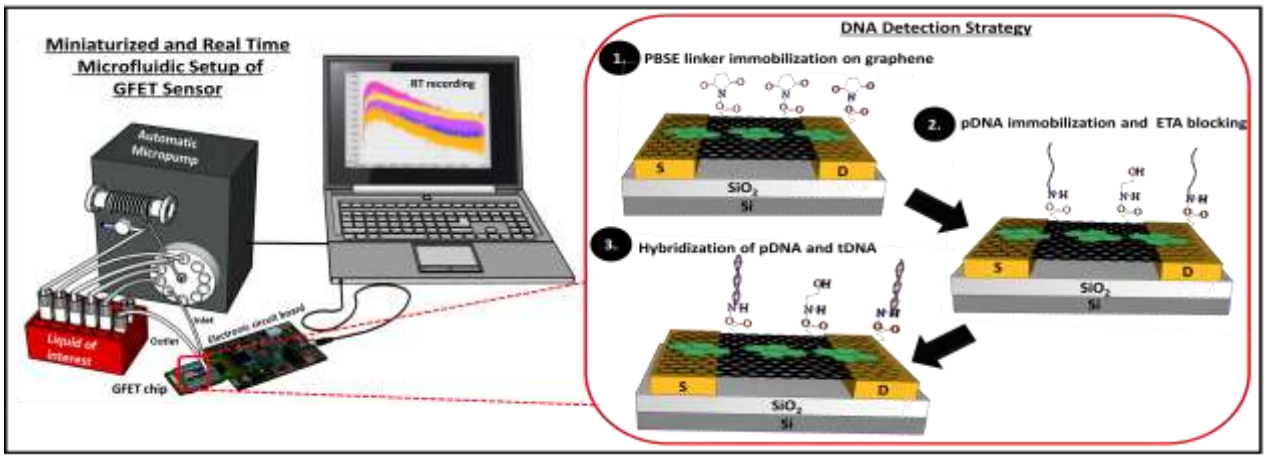

Figure 1: Miniaturized and RT setup of GFET sensor for DNA hybridization test and DNA detection strategy.

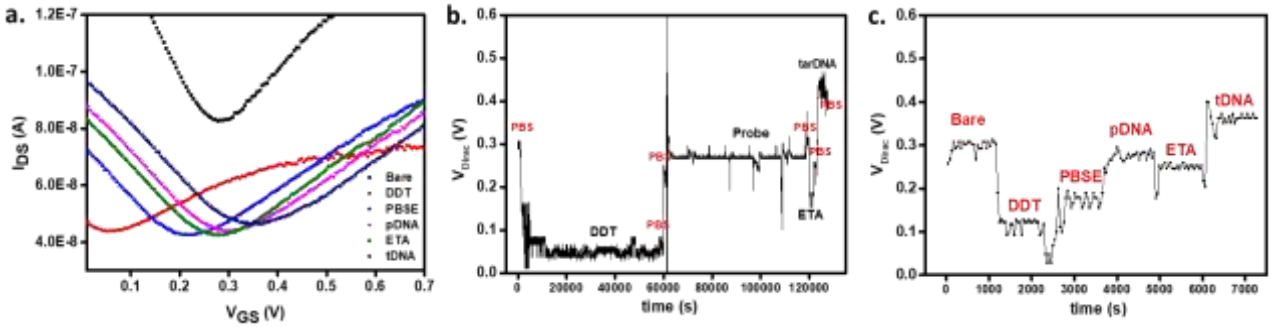

Figure 2: a. I/V transfer curve characteristics, b. RT Dirac point screening and c. extracted signals of each steps of GFET surface modification and DNA hybridization detection using 1 µM target DNA.

Electrochemical sensors for pandemics management: a review of current diagnostic devices and new rapid-deploy systems

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Abstract
Electrochemical biosensors have been impacting the research community since the 60s with the first generation of glucose oxidase biosensor. These devices have been allowing for quantitative and rapid detection of almost any type of analyte in a short time and with point-of-care (PoC) readout. Despite, the consumer market came to know almost only the glucometer, these systems have a huge applicability and the potential to overcome the limitations of their widespread optical cousins, the Lateral Flow Assays (LFAs) overall in terms of sensitivity.
Situations like the one we are living with SARS-CoV-2 virus, from local outbreaks to pandemics would radically change their impact on our societies if these tools would come to be rapidly available. The easy connection of the readout systems to the web would allow real-time monitoring of the spread, planning of effective actions to limit it, modelling and obtaining accurate prevision to minimize the economical and societal impacts.
In this work, we present and shortly discuss the recently proposed electrochemical systems for the detection of the SARS-CoV-2 and other viruses and of the immunization against them [1,2], for this we will space from voltammetry- and impedance-based sensors to graphene field effect transistors (GraFETs) [3,4]. Moreover, we introduce and discuss ideas we are currently exploring in our lab to produce scalable printed biosensors for rapid-deploy for the PoC. Electrical biosensors (with potential for SARS-CoV-2 detection) are based on the use of various printing technologies (inkjet- and screen-printing, stamping etc.) and the use of nanomaterials to improve their electro-catalytic or receptors binding capabilities. They (may) take advantage of recently developed antibodies and aptamers (specific to the virus surface proteins) immobilized on the electrodes' surface using various strategies.
We propose three approaches: the first one is a simple impedance-based label-free and mediator-free system and a low-cost smartphone based readout (Figure 1a, b, c), which has already been tested with a model protein and showed LOD in the nM range.
The second approach is based on the same concept but using a nicotinamide adenine dinucleotide (NADH) redox mediator and either the aforementioned impedance readout system or the widespread glucometer for the readout (Figure 1d, c, d). Finally, the third approach uses a labelled sandwich one with enzymatic amplification (glucose as substrate, glucose dehydrogenase enzyme, and NADH as product) being both low-cost and easy-to-use readout technologies (Figure 1e, c, f).

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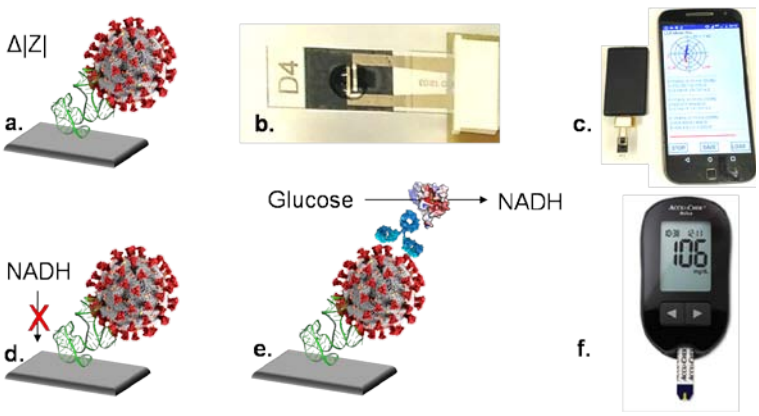

Figure 1: Schematic of the proposed SARS-CoV-2 virus detection strategies. Label-free detection of the impedance variation due to virus-aptamer binding (a) on the printed electrodes surface (b) readout by impedance commercially available app. (c). Reduction of NADH mediator access sites onto the electrode surface due to virus-aptamer binding (d) and readout by impedance (c) or commercially available glucometer (f). Labelled sandwich detection using glucose dehydrogenase as enzymatic label for signal amplification (e) and readout by glucometer (f).

Proposal of Antibody-Based Biosensor and portable potentiostat as a potential virus detection of COVID

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The spread of the COVID-19 virus is at the pandemic level, and it has become a global problem; this situation leads us to find new ways to control its advance. Moreover, the best way found to stop its advance is to track people infected. The governments had been used molecular techniques such as Polymerase Chain Reaction (PCR) to identify the virus presence in the patients. However, although this is an effective method, the time to obtain the measurement is high. However, some research groups had developed electronic biosensors based on antibodies, which are potentially faster than the molecular ones. An example works like the biosensor developed by [1], which uses electrodes functionalized with antibodies to give a measurement of the Human Papilloma Virus (HPV) presence in a sample. Also, more recent research from [2] presents another antibody-based biosensor for tuberculosis, and [3] shows a biosensor that detects Zika virus-specific antibodies. Finally, with the technology developed by us [4], a portable, low-cost potentiostat which can perform cyclic voltammetry and custom electrodes for the device. This device works at 3,3V, and it is powered by the USB power of the host system. The potentiostat weights about 20g and its dimensions are 4,45 cms of width, 5,34 cms of length, and around 2 cms of height. This device could make cyclic voltammetry at 1.5Vpp at a scan rate of 12 mV/s, it can measure currents from microamperes to a maximum of 10mA, has a UART communication through a USB-Serial converter, and the software refreshes the newly acquired data every 60ms. Additionally, the software allows exporting all data from the applied voltage against the measured current to a .csv file and the corresponding images. Furthermore, the device and electrodes developed by us are fast to manufacture due to the techniques used. Also, portability is a huge advantage as a portable measurement system. On [1], the authors used impedance measurements to detect the presence of the HPV in a sample. These results were achieved by the change of impedance magnitude that occurs when the virus binds to the antibody. We propose that with our device, we could observe similar differences in the CV using an antibody-based biosensor due to the similarity in size between the HPV and COVID-19. Finally, building a biosensor functionalizing the surface with COVID-19 antibodies could allow us to had a fast procedure to test the presence of the virus on the patients, this in addition to actual measurement methods, will allow us to reach more people and to track and identify the infected patients, which will aid to stop the spreading speed of the COVID-19.

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FIGURES

Figure 1: Portable potentiostat and electrode for electrochemical measurements

Smartphone-Based Multiplex 30-minute Nucleic Acid Test of Live Virus from Nasal Swab Extract

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Rapid, sensitive and specific detection and reporting of infectious pathogens is important for patient management and epidemic surveillance. [1] We demonstrated a point-of-care system integrated with a smartphone for detecting live virus from nasal swab media, using a panel of equine respiratory infectious diseases as a model system for corresponding human diseases such as COVID-19. [2] Specific nucleic acid sequences of five pathogens were amplified by loop-mediated isothermal amplification (LAMP) on a microfluidic chip and detected at the end of reactions by the smartphone. Pathogen-spiked horse nasal swab samples were correctly diagnosed using our system, with a limit of detection comparable to that of the traditional lab-based test, polymerase chain reaction, with results achieved in ~30 minutes.

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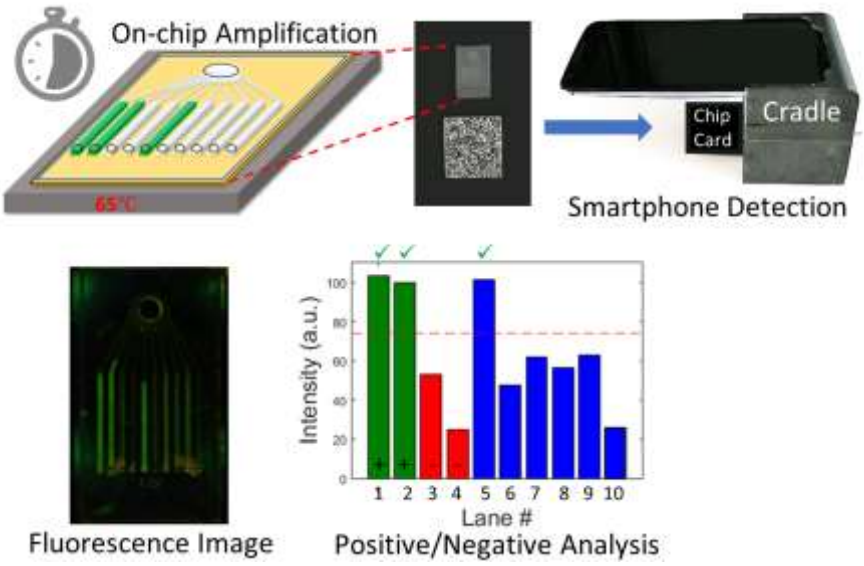

Figure 1: Detection protocol: extracted nucleic acids from samples will be mixed with fluorescence dye and LAMP reagents to perform 30-min amplification at 65 °C on a silicon microfluidic chip. The amplified chip will then be inserted into a customized detection cradle for fluorescence imaging by a smartphone. Qualitative results will be obtained by analysing fluorescence intensities in reaction channels.

Real-time detection of viral surface antigens using hybrid graphene-gold Nanosensors

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Point-of-care (POC) diagnostics for disease detection are fast, cheap & easy to use in comparison to laboratory tests, requiring highly trained staff, large/expensive equipment & long time-to-result[1]. There has been rapid growth of POC diagnostics in recent years with increasing emphasis on resource-limited settings[2], particularly relevant to diagnosis of hepatitis - a major global health problem affecting almost 400 million people worldwide[3]. A nanosensor based on a graphene resistor functionalized with AuNPs (Gold Nanoparticles) is demonstrated for the real-time detection of hepatitis B surface antigen (HBsAg). Graphene–AuNP hybrid structures are of particular interest in sensing applications because they display individual properties of graphene and AuNPs, but can also exhibit additional synergistic properties[4]. Real-time 2-point resistance measurements, performed using varying concentrations of hepatitis B surface antigen (HBsAg), show a linear dependence of resistance change against the logarithm of HBsAg concentration (log[HBsAg]). A limit of detection of 50 pg/ml was observed[5]. Moreover, the hybrid biosensor platform has potential to be applied to other viral proteins or any biomarker of interest.

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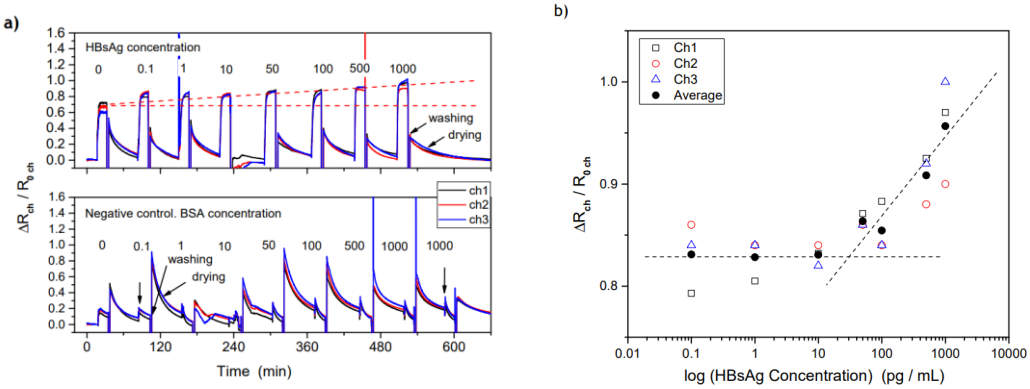

Figure 1: a) Graphene channel resistance response to the time- dependent application of HBsAg concentrations in pg/ml (top) and at various BSA concentrations in pg/ml (bottom). Where $\Delta R = R_{channel} - R_{0\ channel}$, and $R_{0\ channel}$ is the initial resistance measurement. b) Normalized graphene channel resistance against log HBsAg concentration.

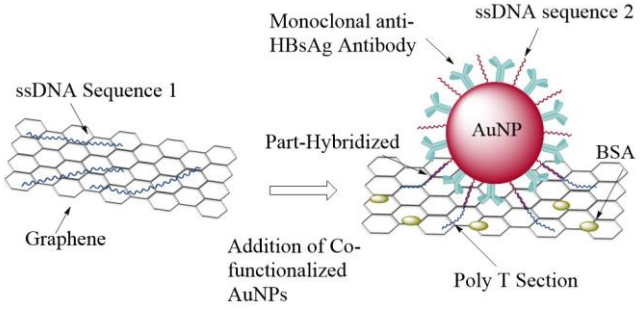

Figure 2: Graphene-AuNP hybrid manufacture through part-hybridization of ssDNA sequences.

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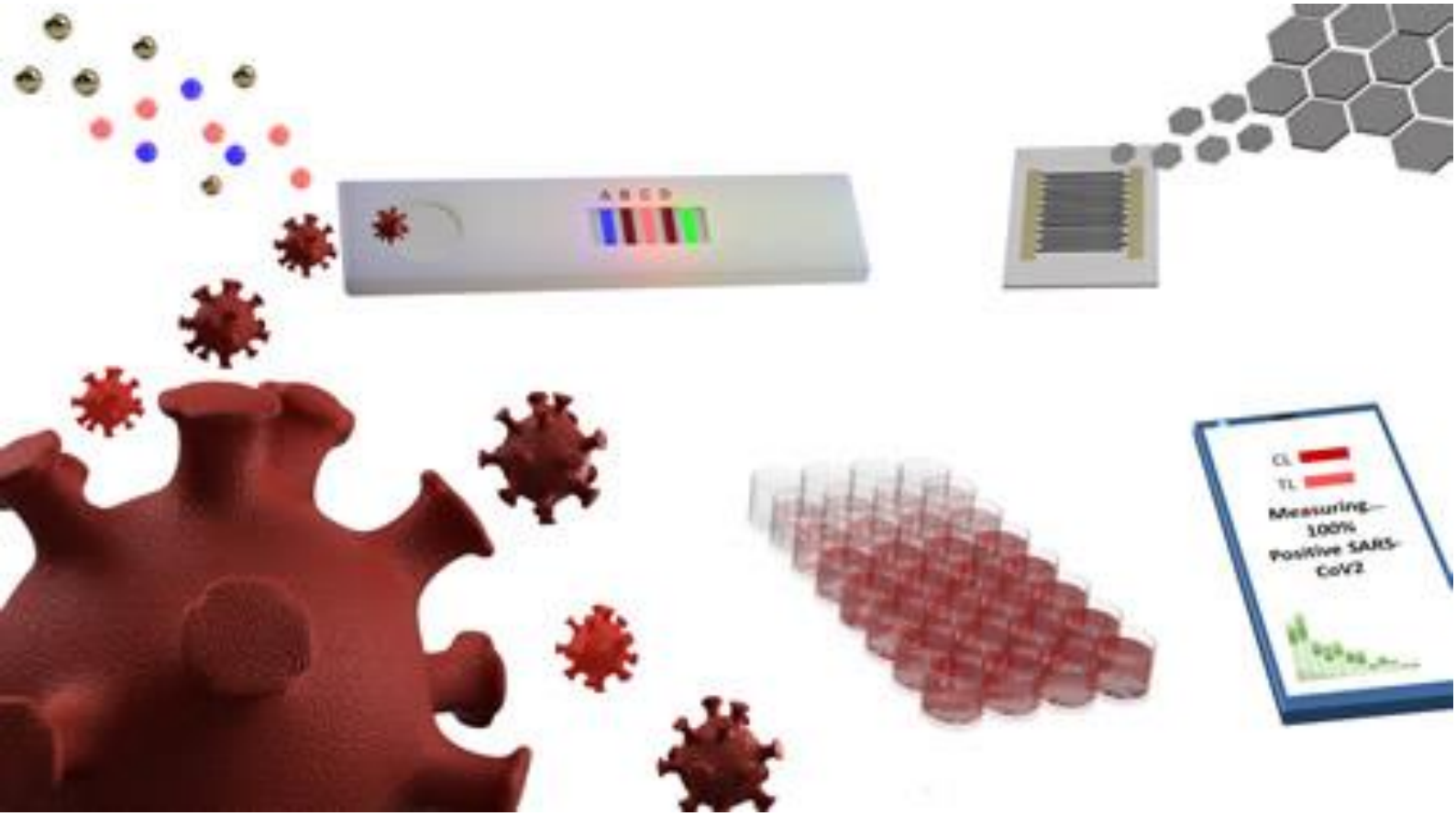

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