





ELECTRICAL NANOBIOSENSORS FOR ENVIRONMENT DIAGNOSTICS

Prof. Arben Merkoçi Nanobioelectronics & Biosensors Group ICREA & Institut Català de Nanociéncia i Nanotecnologia (ICN2) Barcelona, Spain e-mail: <u>arben.merkoci@icn2.cat</u>



Summer School Sustainable nanosensors for water pollution detection Tirana, Albania 22-25 March 2023

BIST

Barcelona Institute of Science and Technology



Generalitat de Catalunya





Table of contents

About ICN2 and the NBB Group

Diagnostics and PoC

Electrical sensors examples

Conclusions

2

3

The Catalan Institute of Nanoscience and Nanotechnology (ICN2)



Institut Català de Nanociència i Nanotecnologia



BIST Barcelona Institute of Science and Technology







UAB Universitat Autònoma de Barcelona



ICN2 is part of BIST

BIST of Catalon

THE BARCELONA INSTITUTE OF SCIENCE AND TECHNOLOGY

 The BIST – a private foundation created in 2015 - is a leading institution of multidisciplinary research encompassing seven top Catalan public research centres of excellence.

NANOBIOELECTRONICS AND BIOSENSORS

The Group

Focuses on the **discovery** and **technological development** of cutting edge nanotechnology and nanomaterials to create **simple and cost effective nanobiosensing platforms.** We do this by controlling their architectures on both the **nano** and **macro** scales with the objective to link these two worlds.



Application areas:

- **Diagnostics**
- Environmental Monitoring
- Food quality
- Safety / security
 Other industrial
 - Other industrial applications

Technology transfer:



OUR RESEARCH

<u>Nanomaterials</u>

Graphene and 2D materials, Metal nanoparticles, quantum dots

Paper-based

Lateral flow assay, hybrid electrochemical/LFA, optical redout

Printing technologies

Inkjet printing, screen printing, graphene transfer electrodes, FET-based biosensors, electrochemical readout

Fully integrated PoC devices

Smartphone based, wearables, wireless readout



Table of contents

About ICN2 and the NBB Group

Diagnostics and PoC

Electrical sensors examples

Conclusions

2

3



PLENTY OF POSSIBILITIES FOR NANOBIOSENSORS







PLENTY OF POSSIBILITIES FOR NANOBIOSENSORS





3. Tethering mediator on protein



5. Immobilization into a redox polymer



Nanotechnology: New source of possibilities to improve biosensors. Most of expectations comes from the fact that matter behaves differently at the nanoscale -> Plenty of new possibilities emerge from nanomaterials.



Binding characteristics •



- Nanochannels
- Nanostructured surfaces. ٠

nanotubes http://www.naturphilosophie.co.uk/gr aphite-graphene-kitchen-blender/

BIOSENSORS CAN BE EVERYWHERE



Medical devices



Wearables



Smart Phone



Smart TV



Smart Fridge



Environment control



Smart washing machine



Smart houses







Food/plant control

Smart cities

Integration of biosensors with real world applications





Navruz I, et al. Lab Chip, 2013, 13, pp. 4015-4023



Nimerosky A, et al. **PNAS**, 111, 33, pp. 11984–11989



Gallegos D, et al. Lab Chip, 2013, 13, pp. 2124-2132



Feng S, et al. ACS Nano. 2014, 8(3),pp. 3069–3079.



Diagnostic devices to be used at the Point of Care need to be REASSURED:

- Real-time connectivity
- Ease of Specimen collection
- Affordable
- Sensitive

he

- Specific
- User-friendly
- Rapid and Robust
- Equipment-free
- Delivered

Substrates

- Paper
- Flexible/sustainable
 plastics



Transducers

- Metallic NPs
- Graphene
- Aptamers

Readers

- Naked eye
- Smartphones
- Portable readers





- Low-cost and abundant material
- Easy to manufacture
- Recyclable & sustainable
- Microfluidic properties









- Plasmonic properties
- Electrocatalytic materials
- Conductive nanoinks
- DNA-based bioreceptors





OUR CHALLENGES

1 Can we make diagnostic devices completely non-invasive?

2 Can we ensure continuous / real time (bio)monitoring?

3 Which partners & expertise's we need to develop devices for real applications that generate (bio)data?



4 How to make cheap/low cost devices that can be disposable?

5 How to correlate (sensor)data to get insights about the body?

Nanobiosensors

Nanomaterials

- Gold Nanoparticles
- Quantum dots
- Iridium Oxide
 Nanoparticles
- Gold Nanoclusters
- Graphene





Readout

Electrochemical and optical sensors, including smartphone sensing and portable readers

Sci Rep 7, 976, 2017

Substrate

- Paper
 - Nitrocellulose
 - Cellulose
- Plastic

Anal. Chem. 92, 4209, 2020

- ♦ PET
 - PDMS



- Cancer
- Leishmania
- Pesticides
- Bacteria
- Pollutants



ACS Nano 14, 2585, 2020

WHY DO WE NEED FAST AND EFFICIENT DIAGNOSTICS?

COVID-19: A tremendous real world example

Showing the necessity of efficient diagnostics for the protection of us all

an an

We are living through a global crisis:

252 million infected 5 million death

DIAGNOSTICS TOOLS ARE CRUCIAL

12/11/2021

How COVID19 changed the scenario

The development of new diagnostic devices is a process characterized by several bottlenecks. Most of them related to sub-optimal interactions between the actors involved, i.e.:

- The scientists
- The clinics
- The regulatory bodies
 - The companies



What can we do to change the status quo?

Merkoçi et al. 2021 Nanodiagnostics to Face SARS-CoV-2 and Future Pandemics: From an Idea to the Market and Beyond **ACS Nano**. https://doi.org/10.1021/acsnano.1c06839

Ubiquitous fabrication of nanobiosensors



Centralized production of nanobiosensors









With appropriate materials, inks, and easy protocols, a consumer printer can be used to fabricate advanced nanobiosensors, successfully facing supply chain interruptions and democratizing these technologies

DEMOCRATIZE THE DIAGNOSTICS The present Our future

- Innovative nanomaterials and nanotechnologies
- In-situ and easy production
- Low-cost scalability
- Portability
- Sensitive, reproducible
- Equipment-free







DEVELOPMENT OF SUISTANAIBLE NANOBIOSENSORS



Table of contents

About ICN2 and the NBB Group

Diagnostics and PoC

Electrical sensors examples

Conclusions

2

3

Electrochemical Biosensors

Fabrication technologies

Detection methods

- Amperometric
- Potentiometric
- Conductometric
- Impedimetric
- Field effect



ACS Nano 10, 853, 2016





2D Mater. 7, 024006, 2020

Chip fabrication and electrode integration

PDMS Chips COC Chips (Collaboration. J.L.Viovy) softlithography process



Simple and low cost fabrication techniques

C institut**Curie**



Chip fabrication and electrode integration



Electrode fabrication



Bioelectronics & Biosensors Group 28

Paper-based biosensors



Why to move biosensors to paper format?

Paper...

... is formed by cellulose.

- Low-cost and aboundant material.
- Easy to manufacture
- Recyclable & biosustainable.

...has a porous matrix.

- Several reactions can be carried out within it.
- The porosity can be modified.
- Capillary forces creates autonomous microfluidics making "zero energy" device!

RECYCLABLE

PAPER

- ... is easily tunable.
 - Its microfluidics by porosity.
 - Its architecture.

... is compatible with nanomaterials

- Printing of nanomaterials
- Easy nanoplasmonics

Claudio Parolo, Arben Merkoçi. Chem. Soc. Rev., 2013, 42, 450 - 457

Paper based biosensors

....

Simple is the best

- Dipsticks

- Lateral Flow strips

- Microfluidic devices



https://www.microessentiallab.com/





http://www.cliawaived.com



www.dfa.org

Type of paper-based biosensor	Possible detection methods	Advantages	Disadvantages
Dipstick	• Optical	 Easy design Fast optimization	Just one stepOnly optical detectionMostly no quantification
LFA	OpticalElectrochemical	 Versatile Flow Electrochemical detection Possible quantification 	 Long optimization times Long fabrication Sample volume (around 100 μL)
μPAD	OpticalElectrochemicalChemiluminescenceMEMS	 Versatile Flow Different detection methods Quantification Small sample volume (less than 10 μL) Massive production 	• Long optimization times

Electrochemical lab-on-paper for heavy metal detection



The quantification of lead and cadmium in aqueous samples

from 10 to 100 ppb with a limit of detection of 7 and 11 ppb respectively.



Merkoçi et al., Anal Bioanal Chem (2015) 407:8445-8449



CNT / LOC and capillary electrophoresis-based analysis



Electrophoresis 28, 1274–1280, 2007

BIOSENSOREMOVAL NanoTechnologies

Phenol detection and removal



BIOSENSOREMOVAL NanoTechnologies



Merkoçi et al., Nano Research, 2017, Vol 10 (7), pp 2296-

Graphene Oxide-Poly(dimethylsiloxane)-Based Lab-on-a-Chip Platform for Heavy-Metals Preconcentration and Electrochemical Detection



Merkoci et al., ACS Appl. Mater. Interfaces 2017, 9, 44766–44775



Au-NP-based detection of bacteria







DIRECT VOLTAMMETRIC DETECTION OF Au-NPs



A. Merkoçi et al., Biosensors and Bioelectronics, 2013, 40, 121–126



AgNP-ink jet printed reference electrode in paper or plastic



Inkjet-printed sensing platforms using nanomaterial-based inks and other materials

No need for clean room at all!



Merkoçi et al. Advanced Functional Materials, 20, 6291–6302. 2014

Merkoçi et al. Anal. Chem. 86, 10531-10534. 2014

A plug, print & play inkjet printing and impedance-based biosensing technology operating through a smartphone for clinical diagnostics



The concept in a nutshell:

- Draw your biosensor on your PC
- Load nanomaterials in your consumer inkjet printer
- Print your nanobiosensor
 - Functionalize it with aptamers
 - Connect it to your smartphone
- Get your result!

1.

3.

4.

We fabricated a nanobiosensor based on aptamers NGAL.

NGAL (Neutrophil Gelatinase-Associated Lipocalin) NGAL in urine is a biomarker of acute kidney infection (AKI) and of liver cirrhosis

Water Activated Graphene Oxide Transfer Using Wax Printed Membranes for Fast Patterning of Electrical Devices



Baptista-Pires, Mayorga-Martínez, Medina-Sánchez, Montón, Merkoçi, ACS Nano 2016, 10, 853-860

Water Activated Graphene Oxide Transfer Using Wax Printed Membranes for Fast Patterning of Electrical Devices



Baptista-Pires, Mayorga-Martínez, Medina-Sánchez, Montón, Merkoçl, ACS Nano 2016, 10, 853-860

Water Activated Graphene Oxide Transfer Using Wax Printed Membranes for Fast Patterning of Electrical Devices



Baptista-Pires, Mayorga-Martínez, Medina-Sánchez, Montón, Merkoçl, ACS Nano 2016, 10, 853-860

Transfer onto flexible substrates





pubs.acs.org/acssensors

🔤 🕲 🖲 🖻

One-Step Laser Nanostructuration of Reduced Graphene Oxide Films Embedding Metal Nanoparticles for Sensing Applications

Annalisa Scroccarello,[#] Ruslan Álvarez-Diduk,^{*,#} Flavio Della Pelle, Cecilia de Carvalho Castro e Silva, Andrea Idili, Claudio Parolo, Dario Compagnone, and Arben Merkoçi^{*}

Cite This: https://doi.org/10.1021/acssensors.2c01782 Read Online

ACS Sens. 2023, Publication Date: February 3, 2023







(A) SEM micrograph of the GO film after laser treatment.(B) Raman spectra of the GO (black line) and rGO (red line) film.

(C) C 1s XPS spectrum of the GO film. (D) C 1s XPS spectrum of the rGO film obtained via laser treatment. All the analyses were performed after the film integration into the sensor.

SEM micrographs and XPS spectra of the MNPs@rGO films formed with the laser treatment. (G) XPS spectrum of the Au 4f of the Au@rGO film. (H) XPS spectrum of the Ag 3d of the Ag@rGO film. (I) XPS spectrum of Pt 4f XPS spectra of the Pt@rGO films. All the analyses were performed after the film integration into the sensor.

DOI:

ACS APPLIED MATERIALS & INTERFACES

www.acsami.org

Laser Reduced Graphene Oxide Electrode for Pathogenic Escherichia coli Detection

Lei Zhao, Giulio Rosati,* Andrew Piper,* Cecilia de Carvalho Castro e Silva, Liming Hu, Qiuyue Yang, Flavio Della Pelle, Ruslán R. Alvarez-Diduk, and Arben Merkoçi*





This proof-of-concept sensing platform could detect *E. coli* between 917 and 2.1×10^7 CFU/mL, with a LOD of 283 CFU/mL, within the clinically relevant range for *E. coli* in human urine.

Research Article

Wearable and fully printed microfluidic nanosensor for sweat rate, conductivity, and copper detection with healthcare applications

We fabricated a printed nanosensor to be applied on the skin for copper detection in sweat:

- Active sweat stimulation (reverse iontophoresis)
- Sweat rate compensation
- Continuous monitoring
- Microfluidic (low vol.)









Biosensors and Bioelectronics 202, 114005, 2022

25

Wearable and fully printed microfluidic nanosensor for sweat rate, conductivity, and copper detection with healthcare applications

Por (a) * Epidermis Sweat gland Dermis Inkjet printed AgNPs Blood Subcutaneous vessels Wax laver fatty tissue everse iontonhoresis Layer 2 (b) electrode (transparent PET) Skin surface Bottom side Layer 1 (biadhesive) (skin) Printed wax Top side insulation (sensing channel) Screen-printed HM sensor Laver 3(biadhesive tape) 2 cm (e) Patterned micro. chamber and -channel Screen-printed Laver 4 (transparent PET) sensor Bottom side (sensing channel) connectio 畿 Anisotropi Inkjet conductivity and Printed wax conductive volume sensors insulation highhesive tane (c) Screen-printed Inkjet-printed Cu sensor Inkjet-printed volume senso Reverse iontophoresis conductivity electrode (g) PET laver Biadhesive laver Contacts pads Hydrogel pads

Scheme of the skin tissue vertical structure

Cross-section of the microchannel, profilometry of the gap between two printed Ag electrodes (Inset left) and 3D profilometry of the open microchannelborder (Inset right) (a), cross-section of the copper detection chamber (b), and SEM picture of the SPCE working electrode (c)



Biosensors and Bioelectronics 202, 114005, 2022

Wearable and fully printed microfluidic nanosensor for sweat rate, conductivity, and copper detection with healthcare applications



a) Staircase calibration of he <u>conductivity nanosensor</u> impedance with NaCl at a frequency of 10 kHz. <u>CF</u> diagnosis relevant ranges marked with colors (green=healthy, orange=suspicious, red=pathological)
b) admittance <u>calibration curve</u>

c) pictures of the microfluidic channel in correspondence to 1 μl colored dye drops at the device inlet

d) impedance of the <u>conductivity sensor</u> at 10 kHz in correspondence to artificial sweat introduced drop-by-drop

e) impedance of the volume sensor at 10 kHz with artificial sweat introduced drop-by-drop and calibration of the volume nanosensor by means of its admittance (inset).

Biosensors and Bioelectronics 202, 114005, 2022





Innovative monitoring tools for river and lake water quality, and a new business model for 2020 and beyond





Laboratory set-up for *in-situ* and automatic heavy metal sensing measurements



Yang, Qiuyue, Merkoçi et al. "Development of a heavy metal sensing boat for automatic analysis in natural waters utilizing anodic stripping voltammetry." voltammetry."

ACS ES&T Water 1 12 (2021): 2470-2476



Autonomous boat for heavy metal sensing measurements





Yang, Qiuyue, Merkoci et al. "Development of a heavy metal sensing boat for automatic analysis in natural waters utilizing anodic stripping voltammetry." ACS ES&T Water 1 12 (2021): 2470-2476



originated from F-Ba-Pb-Zn mine vein

Yang, Qiuyue, Merkoci et al. "Development of a heavy metal sensing boat for automatic analysis in natural waters utilizing anodic stripping voltammetry." ACS ES&T Water 1 12 (2021): 2470-2476



Navigating performance













Our review articles



www.nanobiosensors.org



Received 11th July 2012 DOI: 10.1039/c2cs35255a

Our review articles



<image><text><text><text><text>

Chem Soc Rev

Chemical Society Reviews

Attomolar analyte sensing techniques (AttoSens): a review on a decade of progress on chemical and biosensing nanoplatforms

Sruthi Prasood Usha, 🔞 ^a Hariharan Manoharan, ^a Rehan Deshmukh, ^a Ruslan Álvarez-Diduk, 🔞 ^b Enric Calucho, ^b V. V. R. Sai 🔞 ^{• a} and <u>Arben</u> <u>Merkoçi</u> 🔞 ^{• bc}



Trends in Chemistry



Available online 25 April 2022 In Press, Corrected Proof ⑦

Review

Paper-based biosensors for cancer diagnostics

Claudia Pereira ^{1, 2, 3, 9}, Claudio Parolo ^{1, 4, 9}, Andrea Idili ^{1, 5}, Roger R. Gomis ^{6, 7}, Lígia Rodrigues ^{3, 8}, Goreti Sales ², Arben Merkoçi ^{1, 7}, 8 🖻



www.nanobiosensors.org

materialstoday

Electrochromism: An emerging and promising approach in (bio)sensing technology

Mohammad Amin Farahmand Nejad ^{1,2,‡}, Saba Ranjbar ^{1,‡}, Claudio Parolo ¹, Emily P. Nguyen ¹, Ruslan àlvarez-Diduk ¹, Mohammad Reza Hormozi-Nezhad ^{2,3}, Arben Merkoçi ^{1,4,}

Electrochromic sensors





Our review articles



Toward Integrated Molecular Lateral Flow Diagnostic Tests Using Advanced Micro- and Nanotechnology Ana Rubio-Monterde, Daniel Quesada-González*, and Arben Merkoci* Cite this: Anal. Chem. 2023, 95, 1, 468-489



Table of contents

About ICN2 and the NBB Group

Diagnostics and PoC

Electrical sensors examples

Conclusions

2

3

Conclusions

Electrical nanobiosensors represent a great alternative for environment monitoring

These devices and related fabrication technologies offer unpresented alternative for the democratization or monitoring systems

Nanomatarials can be easily coupled to paper-based platforms to build cost/efficient nanobiosensors

Nanomaterials exhibit unprecedented properties as either electrical or optical transducer for biosensing applications

Their properties and related platforms can enable:

- Connection to a variety of (bio)receptors and nanomaterials
- Simple assay procedures and avoid time consuming labours
- Compatibility with mobile phone technology and other smart environment monitoring systems.



Our sponsors & Colaborators

























Thank you very much! Shumë faleminderit!

QUESTIONS?

arben.merkoci@icn2.cat









Barcelona Institute of Science and Technology



Generalitat de Catalunya



