Finanziato dall'Unione europea NextGenerationEU

Ministero dell'Università e della Ricerca

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

HEAL ITALIA ROADSHOW
TECNOLOGIE E INNOVAZIONE
INNOVATION ON THE ROAD

PRIMO CONVEGNO NAZIONALE DEL CENTRO DI MEDICINA DI PRECISIONE – HEAL ITALIA PER LE MALATTIE RARE

www.ancona.centridimedicinadiprecisione.it

Responsabile scientifico
Prof. **Gianluca Moroncini**

UnivPM – Ancona
Aula Montessori
Facoltà di Medicina
e Chirurgia

venerdì 28 febbraio
14:30 → 18:30
sabato 1 marzo
09:00 → 13:00

Progetto "Health Extended ALliance for Innovative Therapies, Advanced Lab-research, and Integrated Approaches of Precision Medicine (HEAL ITALIA) Codice PE00000019, CUP I33C22006900006 – finanziato dal PNRR M4C2 I1.3 – DD MUR 341 del 15/03/2022

HEAL ITALIA

CENTRO DI MEDICINA DI PRECISIONE™

UNIVERSITÀ POLITECNICA DELLE MARCHE

Azienda Ospedaliero Universitaria delle Marche

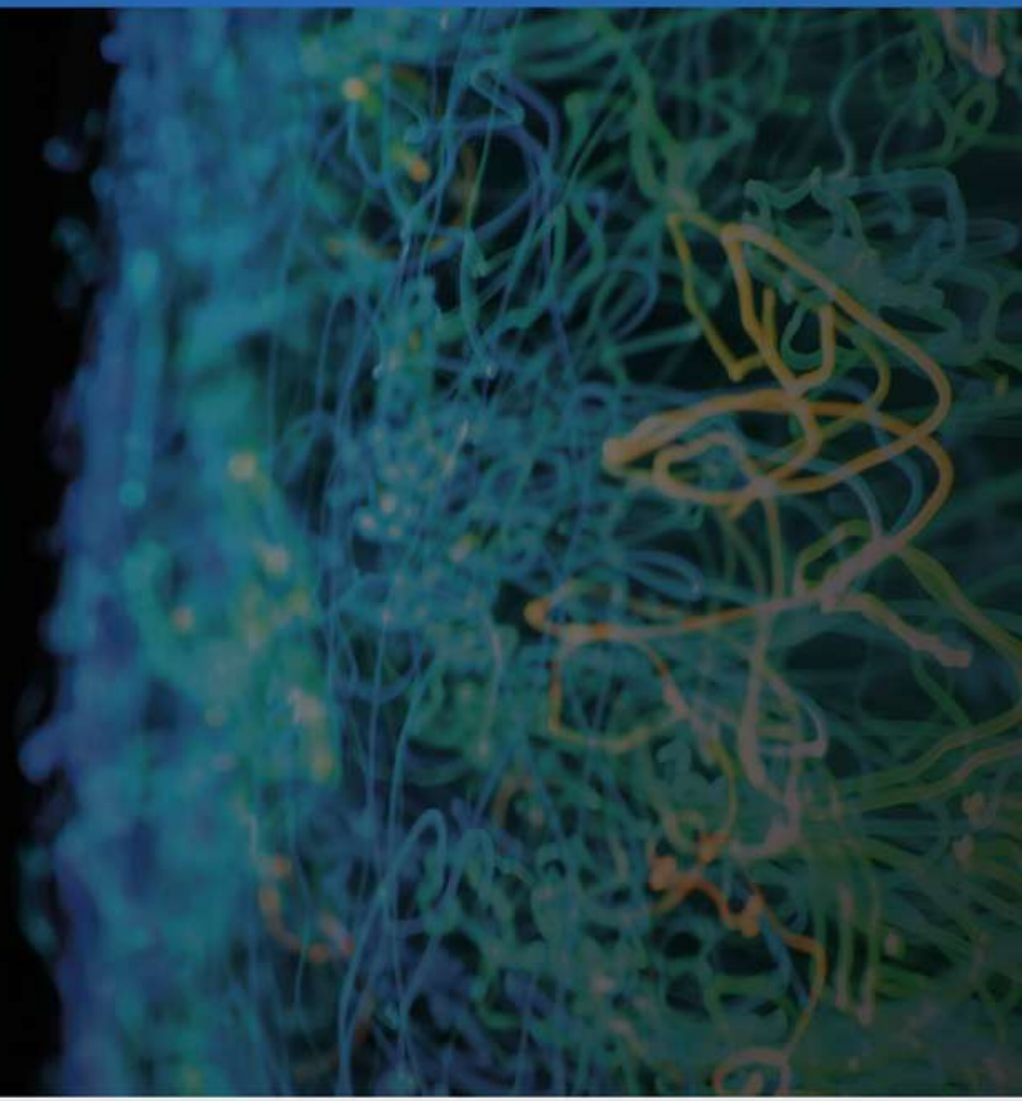
MARCHE BIOBANK

Comune di Ancona

Ancona città sana

Provider:
Tonidigrigio
www.tonidigrigio.it

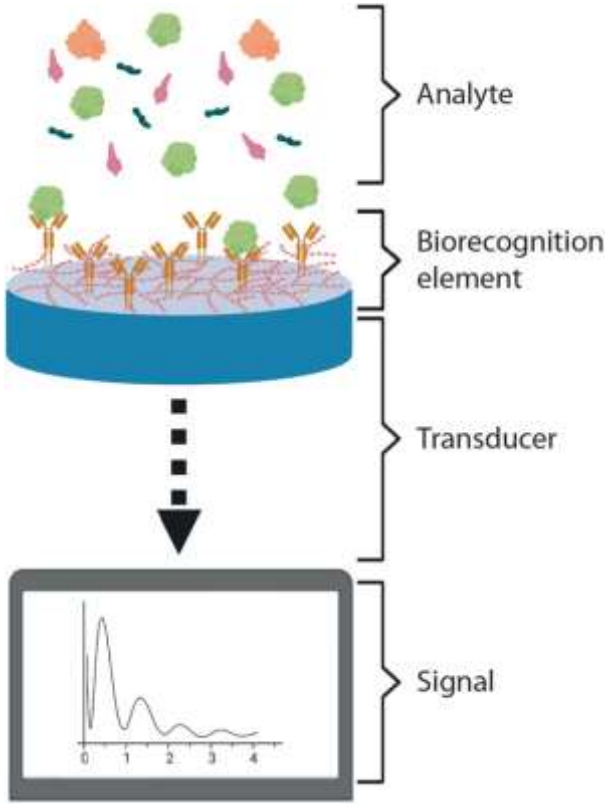
Biosensori elettronici organici: un'opportunità per le diagnosi di Malattie Rare



Carlo Augusto Bortolotti

Università di Modena e Reggio Emilia

What is a biosensor?



FIGURES of MERIT:

Selectivity

Sensitivity

Limit of Detection (LOD)

Repeatability and reproducibility

OTHER FEATURES:

Time to response

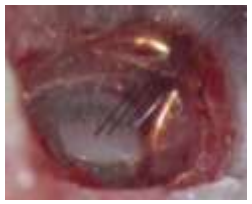
Portability

Ease of use

Label-free

Bioelectronics is a bridge between man-made electronics and biology

IONIC (mostly) signals ⟷ *ELECTRONIC currents*



Electroceutical devices, actuators, stimulators, controllers, drug delivery

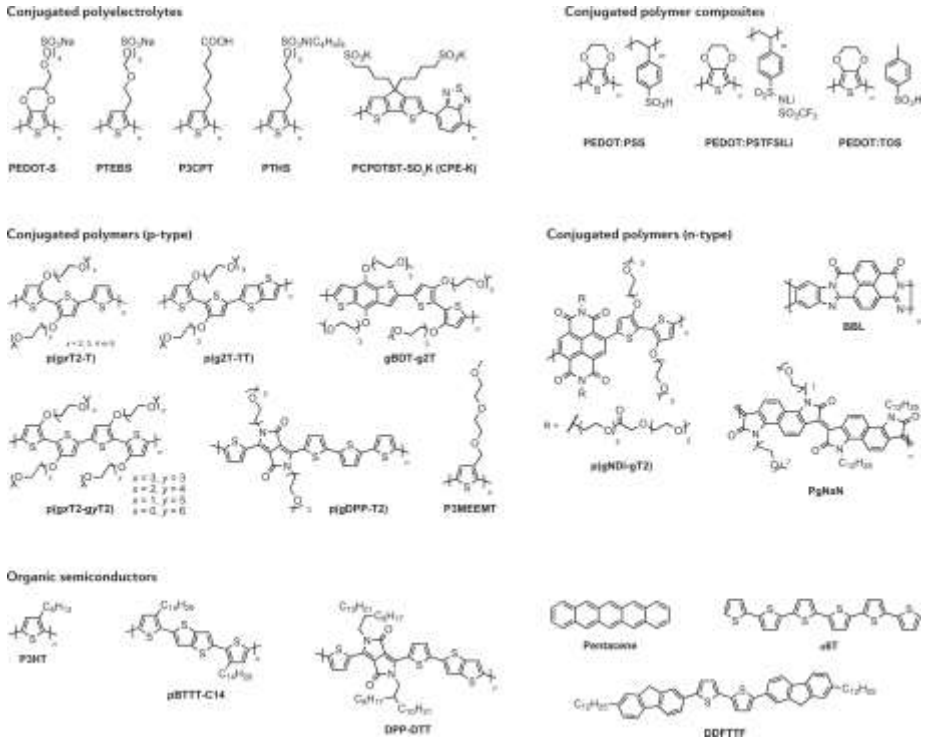
regulate the physiology and processes of cells, tissues, and organs ⟵

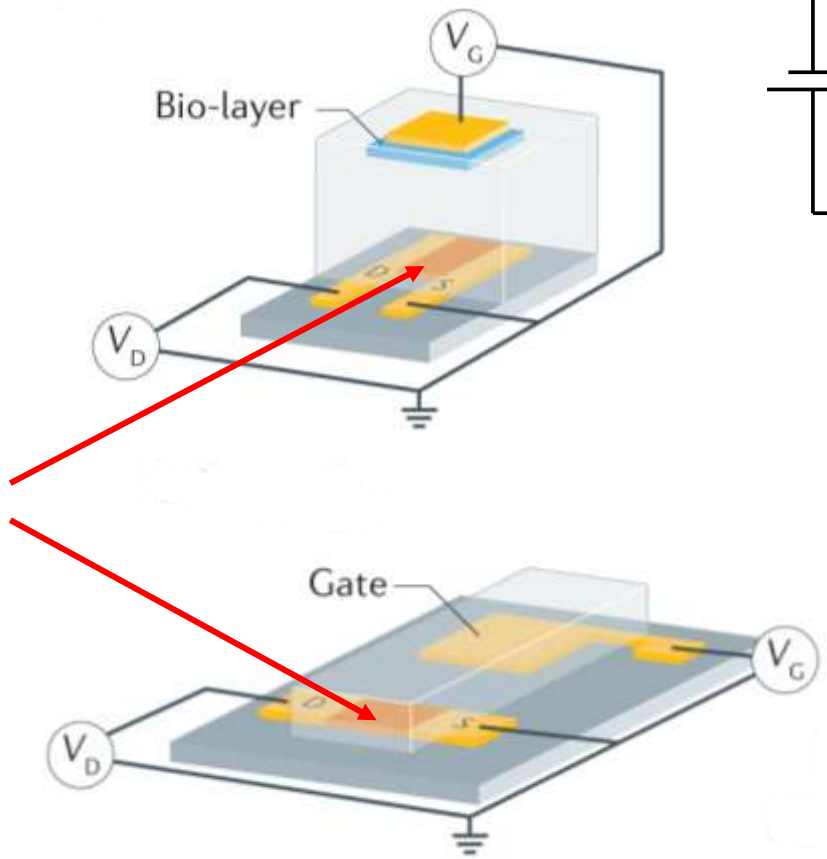
Biosensors

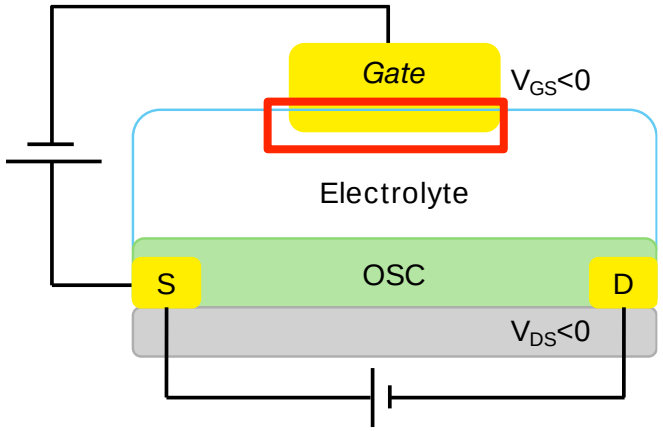
sense, record, and monitor different signals and physiological states ⟶

Simon et al., Chemical Reviews, 2016

Electrolyte-Gated Organic Transistors EGOTs

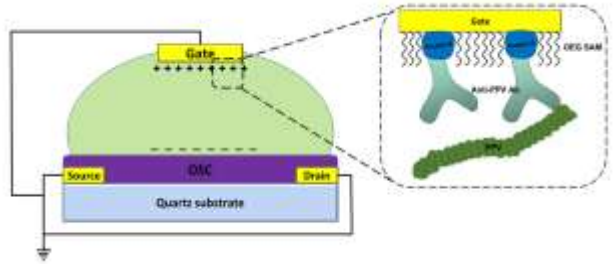






F. Torricelli et al., Nature Reviews Methods Primers, 2023

High sensitivity and ultra-low limit of detection can be achieved with EGOT biosensors



Berto et al., Analytical Chemistry, 2016, 88, 12330-12338
Berto et al., Sensors and Actuators B: Chemical, 2019, 281, 150,156.
Parkula et al., Analytical Chemistry, 2020, 92, 9330-9337.

Monitoring inflammatory processes through cytokines quantification:
Interleukin-4, Interleukin-6 and TNFalpha, LOD 1 pM/300 fM

Monitoring axonal damage biomarkers: detection of NF-L with sub-pM LOD

Monitoring plant infections through virus detection in leaf extracts:
Plum Pox Virus (destroys Prunus plants), LOD 180 pg/ml

Monitoring food adulteration or water pollution through urea detection

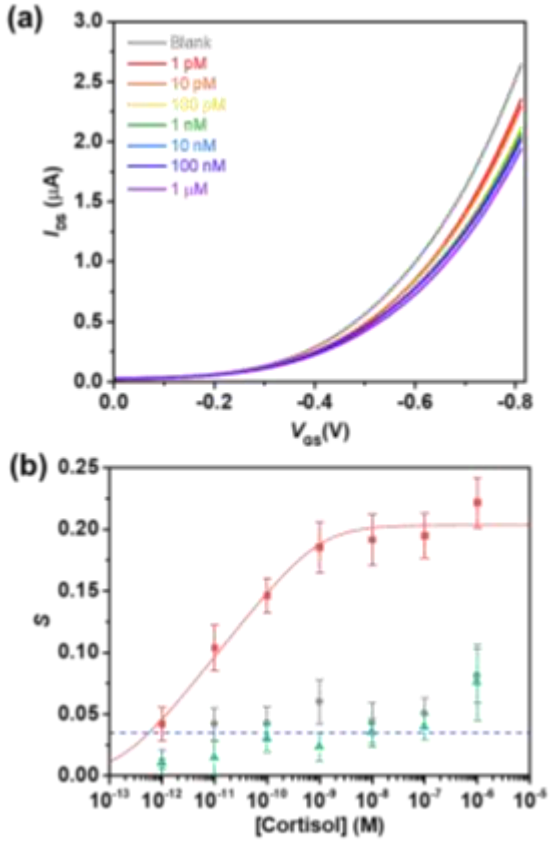
Detection at different lengthscales

An EGOT-based biosensor for cortisol

Detection of anti-drug antibodies with EGOTs

EGOT-based detection of extracellular vescicles

BSA/CNT hybrids-based EGT as cortisol biosensor



Dose curve: 10–1000 pM concentration range in solution, with an estimated limit of detection (LOD) of 0.6 pM.

Generalization of a multi-sites Langmuir model by considering the presence of a large number of binding sites on the electrode surface, with different binding energies (U), that are uniformly distributed in the range $U_{min} < U < U_{max}$

$$S = \frac{S_{max}}{2A} ln\left(\frac{1+K_{avg}\, e^{A}\, c}{1+K_{avg}\, e^{-A}\, c}\right) \quad \text{with } A = \frac{1}{2\, k_B T}(U_{max} - U_{min})$$

Control experiments:
Green triangles → only SAM
Grey dots → SAM+ antibodies non-specific for cortisol

Paradisi et al., Chemistry: A European Journal, 2023, e202301704

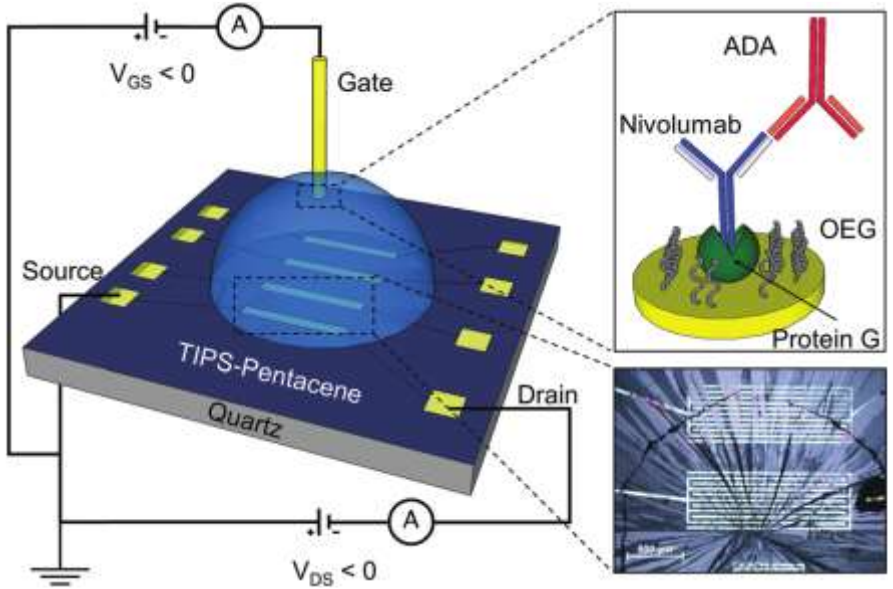
Detection at different lengthscales

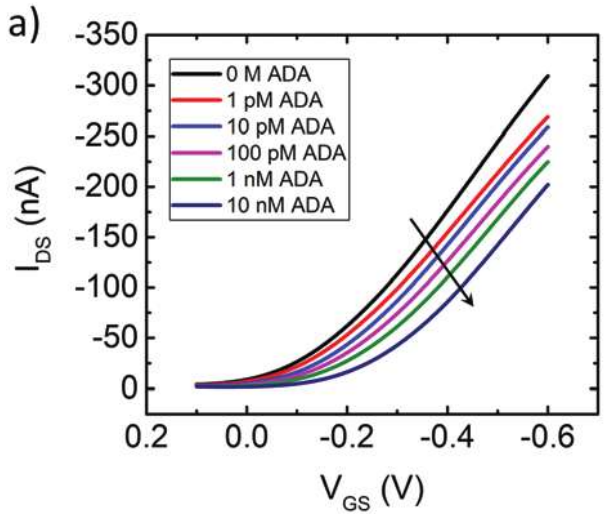
An EGOT-based biosensor for cortisol

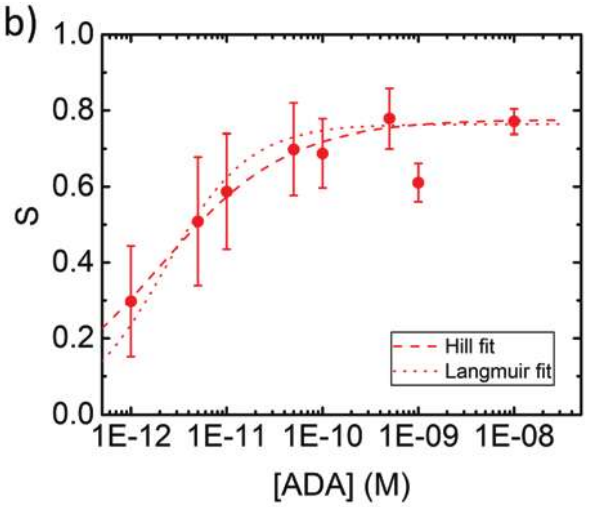
Detection of anti-drug antibodies with EGOTs

EGOT-based detection of extracellular vescicles

Anti-drug antibodies can be detected with EGOTs







$$S = S_{\max}\frac{(K_{\mathrm{H}}^{\alpha}[\mathrm{ADA}]^{\alpha})}{1 + K_{\mathrm{H}}^{\alpha}[\mathrm{ADA}]^{\alpha}}$$

Hill model
$K_H = (5.1 \pm 0.9) \times 10^{11}$

Cooperativity exponent
$\alpha = 0.64 \pm 0.07$

Estimated LOD = 100 fM

Sensi et al., Chem. Commun., 2021, 57, 367--370

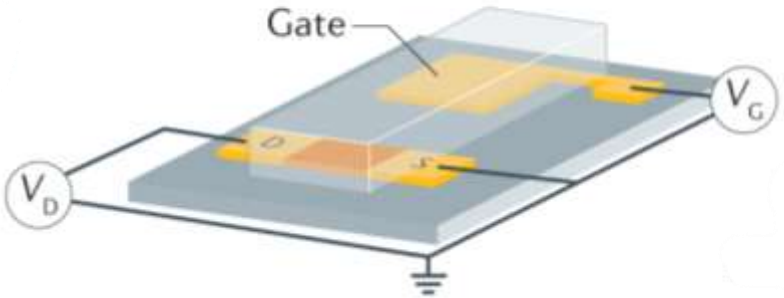
Detection at different lengthscales

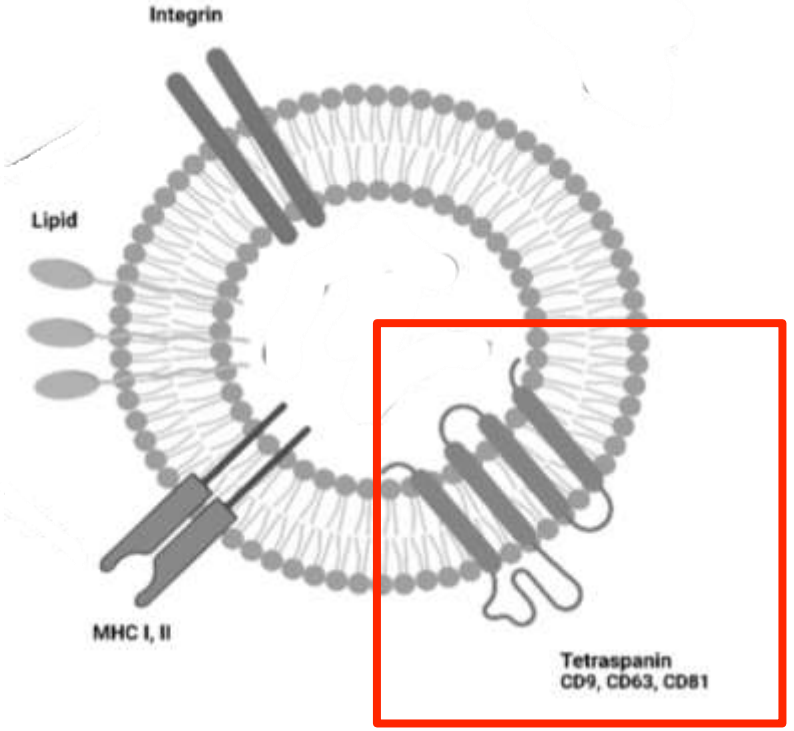
An EGOT-based biosensor for cortisol

Detection of anti-drug antibodies with EGOTs

EGOT-based detection of extracellular vesicles

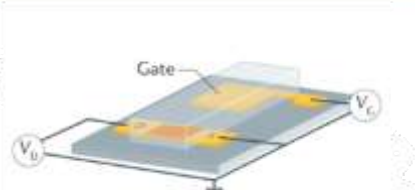
Detection of extracellular vescicles

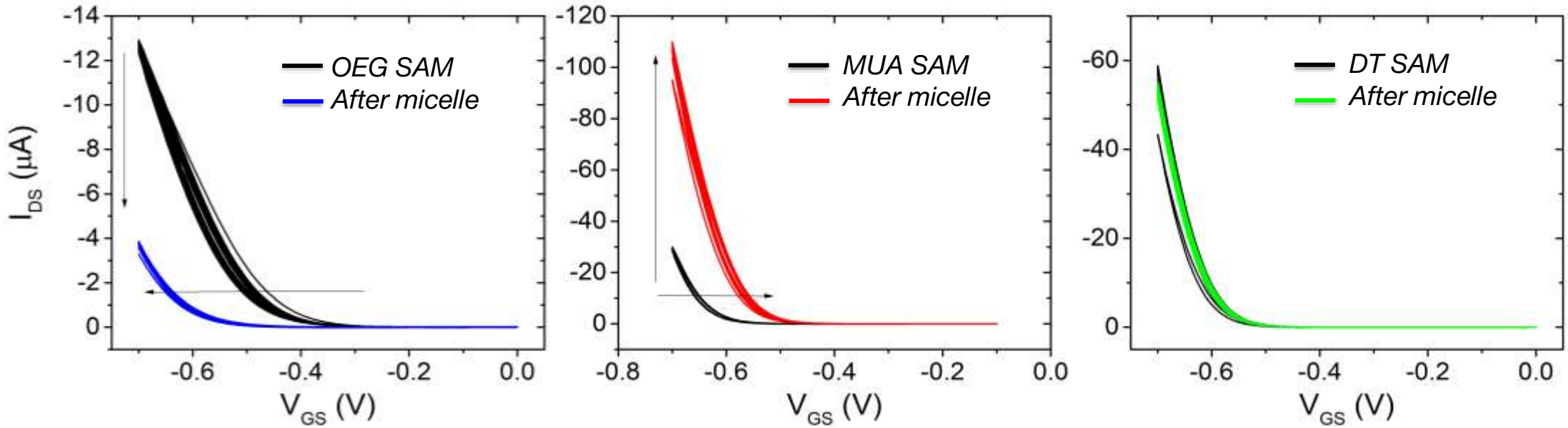


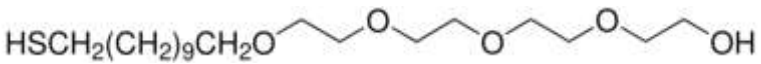


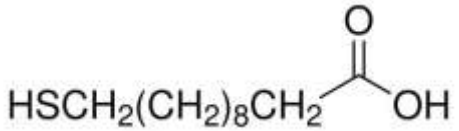
I. Mastrolia, C.A. Bortolotti, M. Dominici et al., Biology, 2023

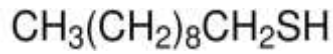
Gate functionalization









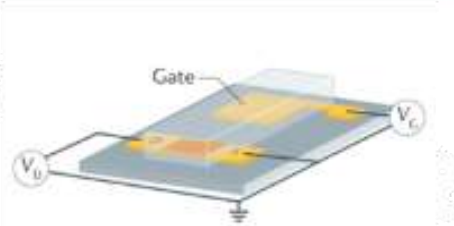


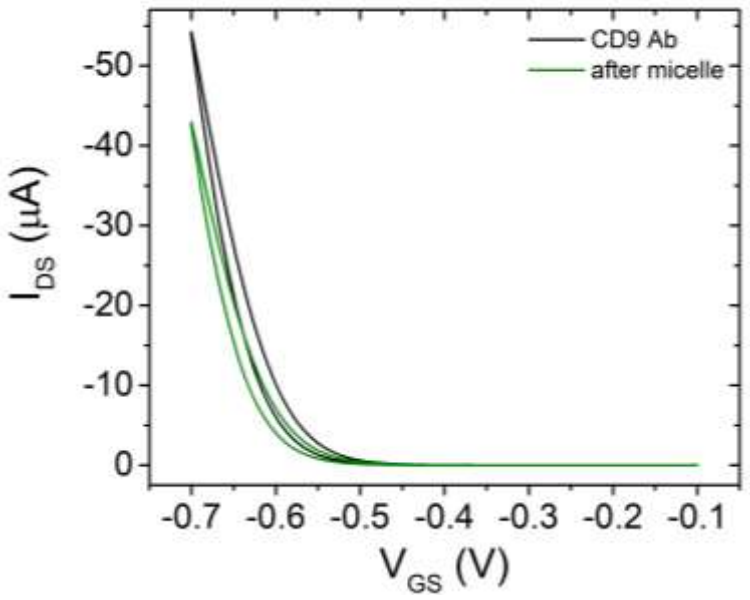
Collaboration with M. Dominici, A. Toss, I. Mastrolia, V. Catani @ UNIMORE – UNPUBLISHED RESULTS

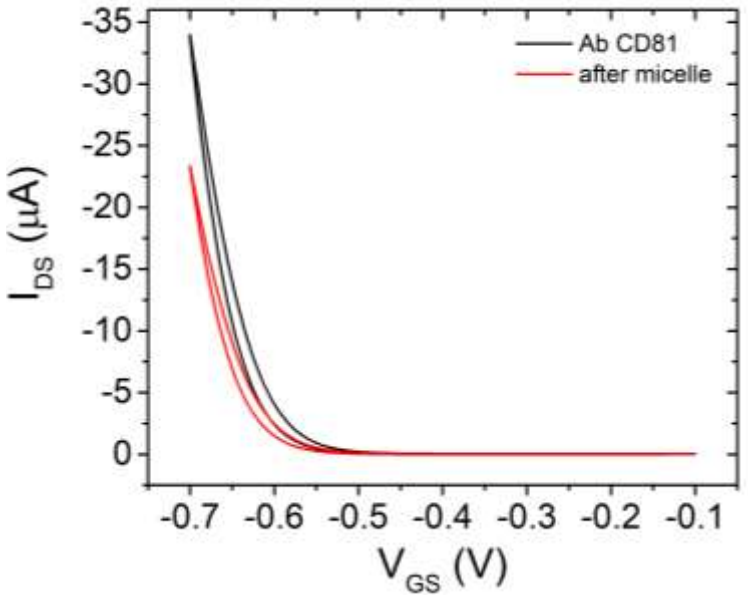
Detection of EVs

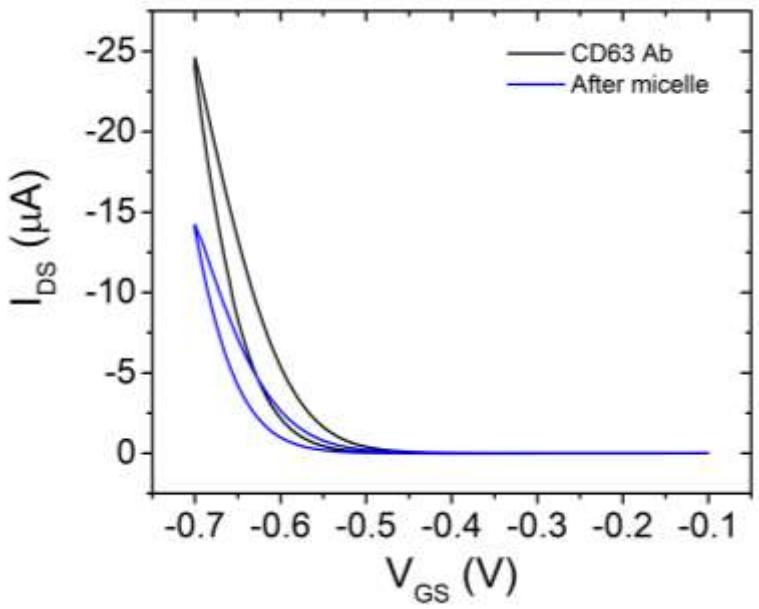
Vescicles concentration ≈ 10^{14} micelle/ml in water

Gate functionalization protocol:
i. MUA:DT (1:9)
ii. EDC:NHS
iii. Ab
iv. Ethanolamine + BSA









Current I_{DS} reduction ≈ 22%

Current I_{DS} reduction ≈ 31%

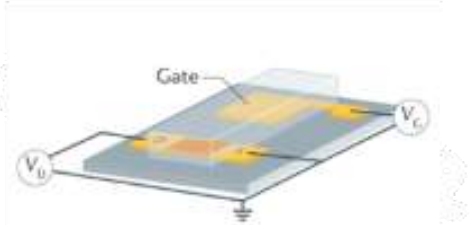
Current I_{DS} reduction ≈ 42%

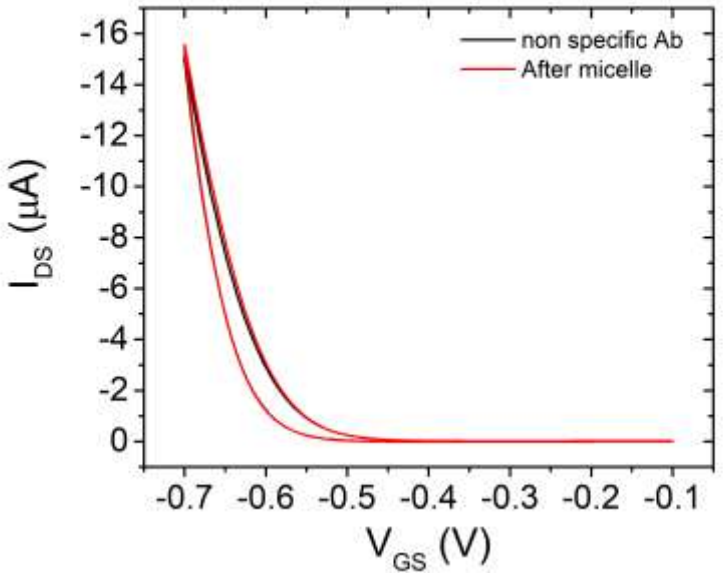
Collaboration with M. Dominici, A. Toss, I. Mastrolia, V. Catani @ UNIMORE – UNPUBLISHED RESULTS

First round of control experiments

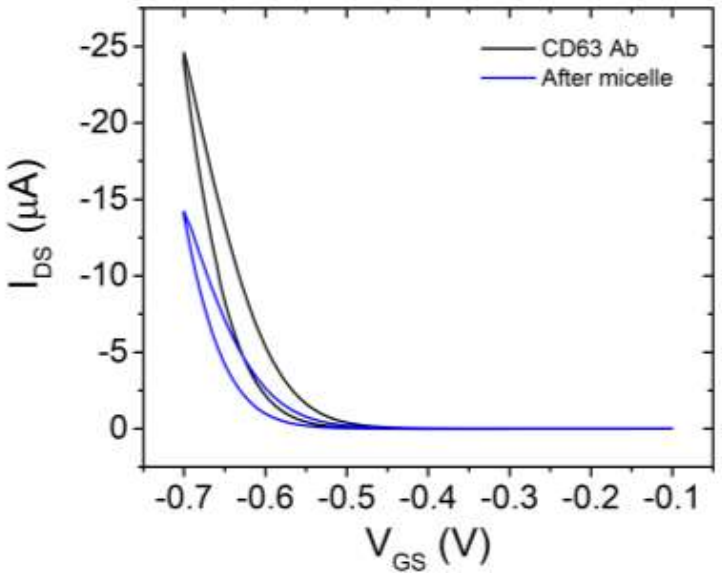
Vescicles concentration ≈ 10^{14} micelle/ml in water

Gate functionalization protocol:
i. MUA:DT (1:9)
ii. EDC:NHS
iii. Ab
iv. Ethanolamine + BSA





Current I_{DS} reduction ≈ 0%



Current I_{DS} reduction ≈ 42%

Collaboration with M. Dominici, A. Toss, I. Mastrolia, V. Catani @ UNIMORE – UNPUBLISHED RESULTS

Conclusions and Perspectives

EGOT-based biosensors allow for detection in a remarkably large lengthscale range, allowing to address problems of clinical relevance.

Sensing performances that are able to even surpass those of state-of-the-art analytical methods can be achieved by:
- rational design of the device architecture,
- innovative active materials,
- ad hoc designed immobilization strategies of the biorecognition element.

Analysis of the device response yields information beyond the analytical purposes, allowing for elucidation of binding thermodynamics and kinetics

Acknowledgements

Fabio Biscarini

Marcello Berto

Matteo Sensi

Alessandro Paradisi

Massimo Dominici

Ilenia Mastrolia

Pamela Manco

Kateryna Solodka

Marco Borsari

Virginia Catani

Angela Toss

UNIVERSITY of MODENA and REGGIO EMILIA M. Pinti, A. Cossarizza, C. Salvarani, A. Conti, G. Pellacani

UNIVERSITY of SHEFFIELD N. Amdursky

Funding

The research leading to these results has received funding from the European Union – NextGenerationEU through the Italian Ministry of University and Research under PNRR – M4C2-I1.3 Project PE_00000019 "HEAL ITALIA"

HEAL ITALIA

MARIE CURIE ACTIONS

BORGES

Marie Skłodowska Curie European Training Network (MSCA-ITN-ETN)
www.borges.unimore.it

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement no. 813863

The authors also acknowledge contribution of the Italian Ministry of Foreign Affairs and International Cooperation.

FONDAZIONE DI MODENA

UNIMORE UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

Fondazione Umberto Veronesi