Electrolyte-Gated Transistors Biosensors for Healthcare Applications

Matteo Sensi, Marcello Berto, Pierpaolo Greco, Carlo Augusto Bortolotti and Fabio Biscarini

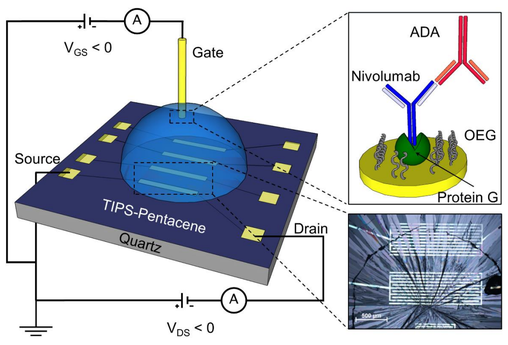
Contact: matteo.sensi@unimore.it

Abstract Electrolyte gated transistors (EGT) based on organic semiconductors and graphene derivates are emerging in the field of biosensing for point of care applications thanks to their high signal amplification, sensitivity, and possibility to be deposited on flexible substrates. We present four examples to demonstrate the possibility to use this technology to develop biosensors for different healthcare applications, by just selecting the most effective device architecture and material.

We conclude that EGT are promising biosensors in the field of healthcare applications, although steps are still needed to bring them at the point of care.

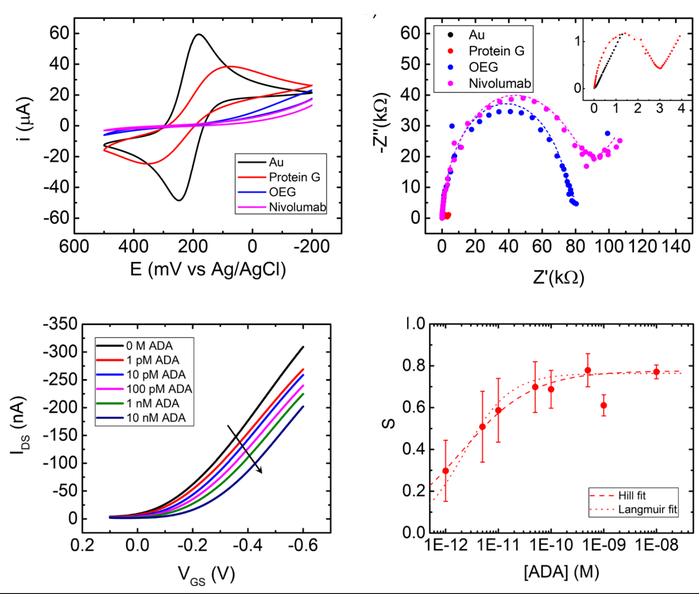
Anti-Nivolumab antibody EGOFET immunosensor

Healthcare challenge: patients treated with the immunotherapic drug Nivolumab (for melanoma) develop anti-drug antibodies. Early detection of ADAs is urgent to avoid ineffective treatment and change the therapy according to the response of the patients.



- Electrolyte-Gated Field-Effect Transistor (EGOFET)[1]: quartz subtrate, patterned with TIPS-Pentacene semiconductor.
- Nivolumab (probe) immobilized on the gold top gate electrode by means of protein cys-Protein G.

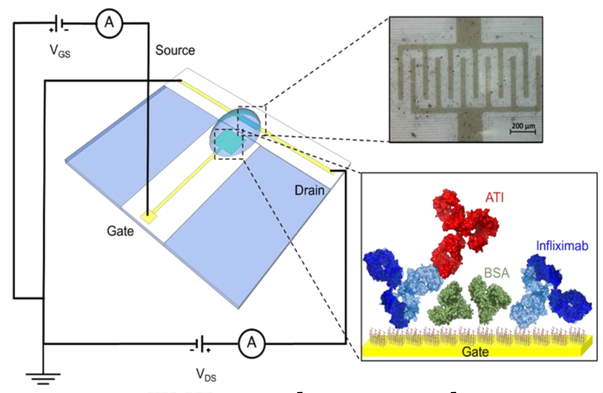
- The signal (S) of the device exposed to the ADAs, calculated as the normalized difference in source-drain current (I_{DS}), shows a monotonic trend with [ADA].
- The device saturates around 1 nM and shows a theoretical LOD of 100 fM.[2]

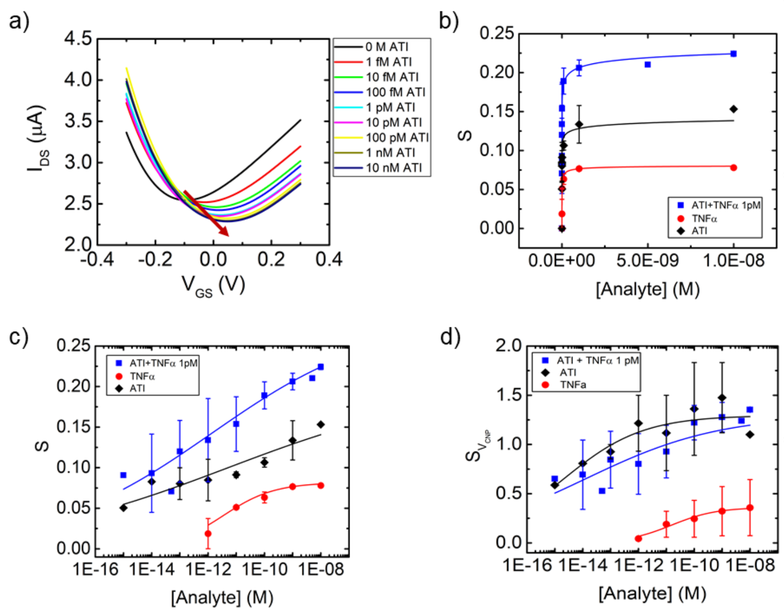


Flexible rGO-FET for Anti-Infliximab detection

Healthcare challenge: treatment with the biological drug Infliximab (for autoimmune diseases) induces the production of anti-drug antibodies (ATIs).

- Flexible PET device, printed gold interdigitated electrodes covered with a reduced graphene oxide film.
- Infliximab, as probe, immobilized on the planar gold gate electrode (on PET), by means of a thiols SAM. To reduce nonspecific absorption on the gate, we introduced BSA, which also increases the buffer complexity.

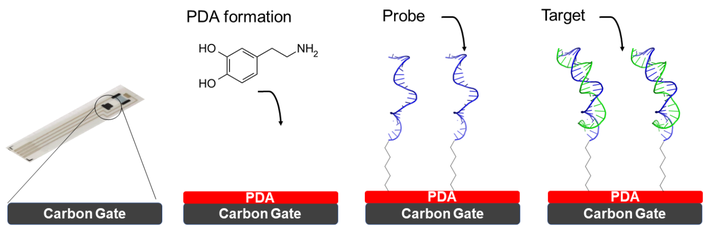




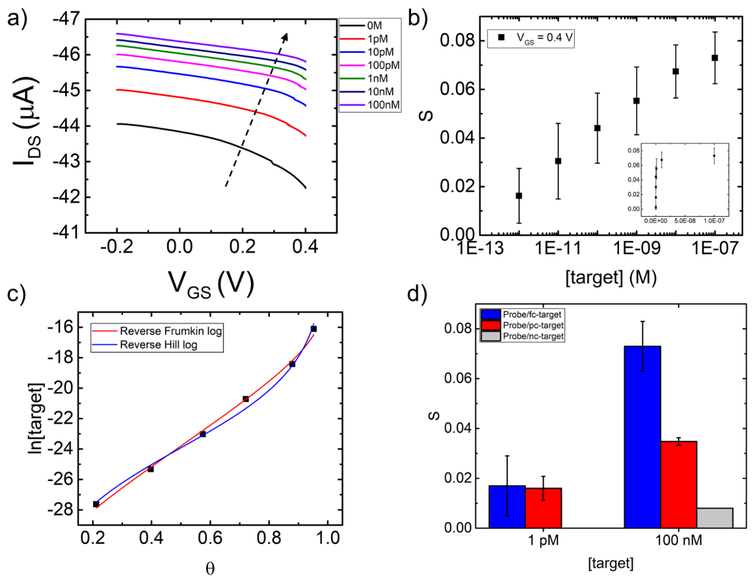
- TNFα is the natural target of the drug, so we tested the device in presence of both TNFα and ATIs.
- The voltage of the Dirac point is the best figure of merit to evaluate the ATIs detection, since it's only slightly affected by the presence of TNFα.
- Developmnet microfluididcs platform to perform controlled tests with real patients' samples in progress

OECT genosensor with Polydopamine functionalization

Healthcare challenge: biosensors for the detection of oligonucleotides (genosensors) are relevant for many health-related issues[3], not last the COVID-19 pandemic that we are experiencing. The immobilization of DNA probes is mainly done on gold electrodes, by means of thiolated-oligo o a thiolated-SAM exposing functional groups. We instead propose the use of carbon ink gate electrodes, functionalized with a polydopamine film (PDA). Oligonucleotides with and amine modification at 5' can spontaneously bind to the PDA film.

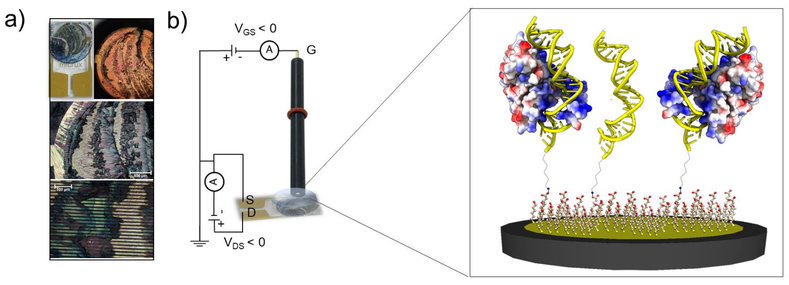


- C/PDA/oligonucleotide used to modulate the current of an Organic Electrochemical Transistor (OECT), fully printed on PET, with a PEDOT:PSS channel.
- In presence of increasing [complementary oligo], we observe an increase of the channel current, due to the intrinsic negative charge of DNA.
- The genosensor showed a different response in presence of partially and non-complementary target sequences, leading to the possibility to study DNA hybridization with EGTs.

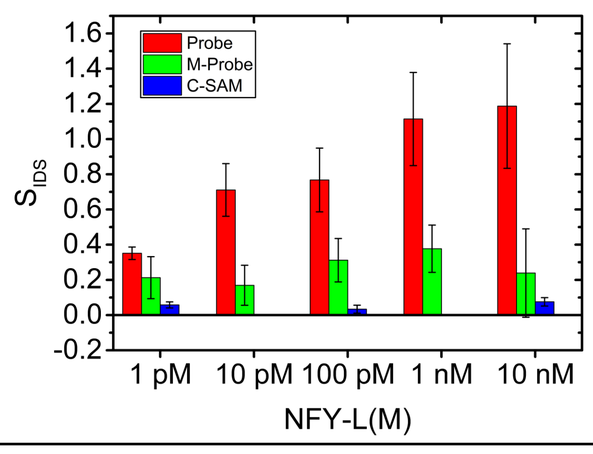


Transcription factors biosensor

Healthcare challenge: the expressions of different isoforms of rhe transcription factor NFY is related to specific stages of lung and breast cancer progression. Detection the isoforms could lead to stratification of patients and development of personalized medicine plans.



- To detect the NFY long and short isoforms, we immobilized on a gold gate electrode a double strand oligonucleotide, containing the NFY target sequence, called CCAAT-box. The electrode was used to gate an EGOFET, with TIPS-Pentacene as active material.
- The response of the device is monotonic with increasing [NFY-long].
- A set of control experiments, where the probe was mutated or omitted, confirms the specific binding of NFY to the probe sequence.



Conclusions and perspectives

- Electrolyte-gated transistors show high sensitivity, low LOD and can be ideally used for any probe/target couple.
- The substrates and materials can be adapted to the health issue studied, to optimize the response of the device.
- Association constants of the probe/target couple can be extracted from biosensing data.

To improve:

- ➢ Optimization of device stability in complex media.
- ➢ Test with samples from patients.

Acknowledgements

- A. Cossarizza, M. Pinti, C. Salvarani, A. Conti, G. Pellacani, C. Imbriano, S. Gentile, M. Palmieri, G. Migatti, A. Ricci (UNIMORE)
- P. Livio, R. Furlan de Oliveira, P. Samorì (UNISTRA)
- M. B. González-García, P. Fanjul-Bolado (LEITAT)
- J.M. Cabot, J. Ricart (METROHOM DROPSENS)

Bibliography

1. Burtscher, B.; Allison, P.; Urbina, M.; Diacci, C.; Borghi, S.; Pinti, M.; Cossarizza, A.; Salvarani, C.; Berggren, M.; Biscarini, F.; et al. Sensing Inflammation Biomarkers with Electrolyte-Gated Organic Electronic Transistors. Adv. Healthc. Mater. 2021, 2100955.
2. Sensi, M.; Berto, M.; Gentile, S.; Pinti, M.; Conti, A.; Pellacani, G.; Salvarani, C.; Cossarizza, A.; Augusto Bortolotti, C.; Biscarini, F. Anti-Drug Antibody Detection with Label-Free Electrolyte-Gated Organic Field-Effect Transistors. *Chemical Communications* **2021**, *57* (3), 367–370 .
3. Selvaraj, M.; Greco, P.; Sensi, M.; Saygin, G.D.; Bellassai, N.; D'Agata, R.; Spoto, G.; Biscarini, F. Label Free Detection of MiRNA-21 with Electrolyte Gated Organic Field Effect Transistors (EGOFETs). Biosens. Bioelectron. **2021**, *182*, 113144.