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Soft matter films interfaced to electronic devices: capacitance-modulated field effect transistors integrating protein layers

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SOFT MATTER FILMS INTERFACED TO ELECTRONIC DEVICES: CAPACITANCE-MODULATED FIELD EFFECT TRANSISTORS INTEGRATING PROTEIN LAYERS

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\textsuperscript{4}University of Manchester, UK.
**OFET = Organic Field Effect Transistor**

point-of-care (POC) testing: clinical tests to be performed at the site of patient care

Sensors: Portable, cheap (disposable) and easy to operate
Why organic electronics?

- Low cost
- Large area

Flex plastic substrate

Wereable sensors

Organic electronics @UNIBA

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Organic field-effect transistor OFET

OFET biosensor

Response = $\Delta I/I_0$

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Bao’s group @Stanford

Thrombin sensor LOD 100 pM
Hammock et al. ACS NANO 2013, 7, 3970

Katz group @Johns Hopkins University

Glial fibrillary acidic protein (GFAP) sensor
LOD 1 ng/mL = 20 pM
Huang et al. Chem. Sci. 2014, 5, 416

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How does it work?

Journal of Materials Chemistry C

REVIEW

Electrochemical processes and mechanistic aspects of field-effect sensors for biomolecules

Weiguo Huang, Abdou Karim Diallo, Jennifer L. Dailey, Kalpana Besar and Howard E. Katz*

J. Mater. Chem. C, 2015, 3, 6445

Angew. Chem. Int. Ed. 2015, 54, 12562
How does it work?

\[ I_{DS} = \frac{W}{2L} C \mu_{FET} \cdot (V_G - V_T)^2 \]

- \( V_T \) = voltage threshold
- Depends on chem. Pot charge carriers
- It is affected by electrically charged analytes

Dielectric layer capacitance
- \(?\)
- good performance requires high capacitances, i.e. high-\(k\) dielectrics in form of very thin films

OFET detections are possible only for:
1) charged analytes
2) at salt concentration low enough so that the Debye’s length is larger than the analyte size.
electrolyte-gated field-effect transistor: An alternative approach to high-capacitance gate dielectric


Porcine Odorant Binding Protein (pOBP)
Porcine Odorant Binding Protein (pOBP)

- shuttle odorant molecules
- soluble proteins, can be expressed in bacterial systems at low-cost
- highly stable

19 kDa

Krishna Persaud e Elena Tucconi
The University of Manchester,
Sensitive biosensing (LOD 100 pM) of electrically neutral analytes

What is going on? Carvone 150 Da; pOBP 19 KDa

The response is dominated by capacitance
MD simulations of pigOBP F$^{88}$W

PDB code: 1E00
System size: ~ 46278 atoms.
pH: ~ 5.5
Force field: CHARMM27 + TIP3P water.
Cutoff van der Waals: 12 Å.
Electrostatic interactions: PME with direct sum cutoff at 12 Å.
Constraints: SHAKE for all R-H bonds
Time step: 2 fs
NAMD 2.9 on FERMI supercomputer @CINECA

NPT ensemble (298 K, 1 atm) with Nosè-Hoover Langevin barostat (oscillation period 200 fs, decay coefficient 100 fs) and Langevin thermostat (damping coefficient 1 ps$^{-1}$).
Total simulation time: 25 ns

G. Lattanzi

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• Only a single state can be defined for S (+) carvone:

- Interaction
- Planarity of carvone

The complex pOBP-carvone is different for S(+) and R(-) carvone

• Two different states can be defined for R (-) carvone:

- Interaction
- Planarity
- Reorientation of carvone
The response is dominated by capacitance

A CHANGE 2.4 % of the total surface of the protein ACCOUNTS FOR THE OBSERVED RESPONSE

\[ R(-)\text{-Carvone} \quad \rightarrow \quad C_{OBP} \approx C_w \]
\[ S(+)\text{-Carvone} \quad \rightarrow \quad C_{OBP} = C_p \]

high dielectric percolative path, “water channel”
neutral ligand detection in the picomolar concentration range. a minute change in protein layer capacitance modulate a water-gated OFET, allowing for chiral differential detection with large enantiomeric discrimination factor

Insight on the energy of ligand binding to immobilized proteins

For details

Capacitance-modulated transistor detects odorant binding protein chiral interactions

Mohammad Yusuf Mulla¹, Elena Tuccori², Maria Magliulo¹, Gianluca Lattanzi³, Gerardo Palazzo¹, Krishna Persaud² & Luisa Torsi¹
Electrolyte-gated field-effect transistor: An alternative approach to high-capacitance gate dielectric


Good EGOFET performances require short Debye's length

\[ C_{GCDL} = \frac{\varepsilon \varepsilon_0}{\lambda} \propto \sqrt{i_s} \]

This is an issue in biosensing
the Debye’s screening length $\lambda$ is the length-scale at which a charged analyte can be electrically probed at the detector interface.

No detection when $\lambda <$ the distance at which the recognition event takes place

Hammock et al. 2013, ACSnano, 5, 3970
OFET detections should be possible only at salt concentration low enough so that \( \lambda \) is larger than the analyte size.

**BUT**

Large \( \lambda \) means small gate capacitance = unperforming OFET and this should be prejudicial for the use of EGOFETs as biosensors.

2013-2014: workable sensing at a distance larger than \( \lambda \) are reported

Magliulo et al. *Adv. Mater.* 2013, 25, 2090 [ionic strength=0.16 M \( \lambda \)=0.7 nm]

Huang et al. *Chem. Sci.* 2014, 5, 416 [ionic strength=0.08 M \( \lambda \)=3 nm]


Need for a systematic study of a sensor response as a function of the Debye’s length and the distance at which the binding event takes place.
scheme of phospholipid BIOEGOFET fabrication

Spin coating

PE-CVD
Acrylic acid + ethylene + argon

PL-OSC conjugation
1) EDC-NHS
2)Phosphatidylethanolamine

BIOEGOFET

<table>
<thead>
<tr>
<th>$I_{DS}$ ($\mu$A)</th>
<th>$V_{DS}$ (V)</th>
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<tr>
<td>0.0</td>
<td>-0.1</td>
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<td>-0.4</td>
</tr>
<tr>
<td>0.0</td>
<td>-0.5</td>
</tr>
</tbody>
</table>

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Tuning the distance at which the binding event takes place

Streptavidin (SA) binds to biotin

Biotinylated Antibody (aB) against CRP

aB is bound by the SA

C-reactive protein (CRP) is the antigen of the aB

Tuning $\lambda$: dilution
Response = $\Delta I/I_0 = (I_{DS} - I_0)/I_0$

In PBS!!

PBS
Ionic strength = 0.160 M
$\lambda = 0.7$ nm
To tune $\lambda$: dilution
The sequential binding of the three proteins is reproducibly probed at salt concentration typical for human blood.

CRP sensing in human serum
\[ \frac{\Delta I}{I_0} = \frac{\Delta C}{C_0} + \frac{2\Delta V_T}{(V_G - V_{T,0})} \]

\[ I_{DS} = \frac{W}{2L} C \mu_{FET} \cdot (V_G - V_T)^2 \]

the response to the analyte is mainly capacitive
Why the capacitance changes??

The charges on the protein backbone are fixed. The free counterions cannot leave the region of the fixed charges for distances $> \lambda$ (electroneutrality): Donnan’s equilibrium.

An electrical double layer is formed at the boundary of the fixed ions region.


The capacitance of the Donnan’s double layer is proportional to the ionic strength ($C_{DON} \propto i_s$).

Overall the gating capacitance $C$ can be described as:

$$C = \left(\frac{1}{C_{\text{fix}}} + \frac{1}{C_{\text{GCDL}}} + \frac{1}{C_{\text{DON}}}\right)^{-1} + C_{\text{par}}$$

The binding adds a new layer that changes the capacitance impacting on the $1/C_{\text{DON}}$

the bio-EGOFET response is governed by a capacitive effect that is independent from the position at which the Donnan's equilibrium is set and therefore does not depend on the Debye's length.
To test this hypothesis the dependence from the ionic strength of the capacitance was studied

\[
\frac{\Delta C}{C_0} = \left( \frac{C_0}{C_{fix}} + \frac{\sqrt{K T}}{e^2 \varepsilon \varepsilon_0 \sqrt{i_s}} + \frac{C_0 g^{-1}}{i_s} \right)^{-1} + \frac{C_{par}}{C_0} - 1
\]

![Diagram showing the relationship between \( I \) and \( \frac{\Delta C}{C_0} \) for different concentrations.]
capacitive tuning of the EGOFET response on gate

CRP in PBS @ fM

Streptavidin-AntiCRP: CRP sensing

$\Delta I/I^0$ vs [CRP] (M)

not-published data
summarizing,

- EGOFET sensors, can probe a protein binding taking place at more than 30 \( \lambda \) far from the transistor channel.

- The mechanism of sensing is mainly capacitive and is due to the formation of Donnan’s equilibria within the protein layer.

- This capacitive tuning of the EGOFET response is virtually insensible to the Debye’s length value.

For details

Adv. Mater. 2015, 27, 911–916
Message to take –home

The mechanism of transduction of the molecular recognition in EG-OFET relies on the electrostatic properties of soft matter.
Financial support

- Laboratorio SISTEMA
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- MERCK
- FLEX Smell
- OrgBIO
- bioEGOFET