BIOSTEC 2016

9TH INTERNATIONAL JOINT CONFERENCE ON BIOMEDICAL ENGINEERING SYSTEMS AND TECHNOLOGIES

21 - 23 FEBRUARY, 2016

ROME, ITALY

BIODEVICES
BIOIMAGING
BIOINFORMATICS
BIOSIGNALS
HEALTHINF

Organic bio-electronic sensors for ultra-sensitive chiral differential detection

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Basilica di San Nicola

Bar

Puglia

The University o
“A.Moro”

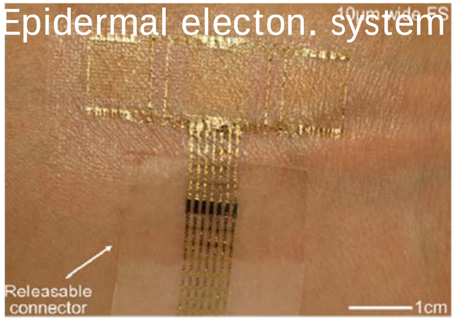
outlook

1. developing and applying new methods for early diagostics / PoC
2. printable bio-electronic field-effect transistors
3. detections down to fM, chiral differential detection with an ESF > 6
4. Odorant Binding and anti-C Reactive Protein as cases of study

printable electronics

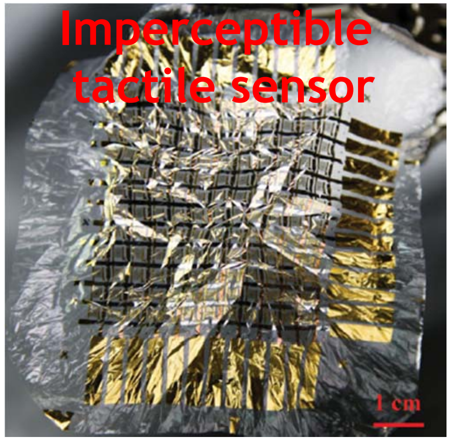
T. Sekitani et al.
Nat. Mater. **2010** , *9* , 1015

Portable sensor
Angew. Chem. Int. Ed. 3/2012, pag. 560



W.-H. Yeo et al. *Adv. Mater.* **2013** , 25 , 2773

e-test strip
http://mobihealthnews.com/23560/smart-diapers-alert-parents-detect-disease/



W.-H. Yeo et al. *Nature* **2013** , *499* , 458

http://www.insideactivitytracking.com/textile-sensors-wearable-smart-garments-will-enable-the-quantified-self/

minority report – Steven Spielberg (2002)

SAMSUNG Flexible AM OLED

https://www.youtube.com/watch?v=-k6r2HQY9Ws

point-of-care biosensors

No sample pretreatment

Neonatal care unit

Early diagnosis

Police checkpoint

Rapid Results

Ambulance & rescue

POC devices

Reduce the frequency of hospital visits

Doctor's office

Real Time Monitoring

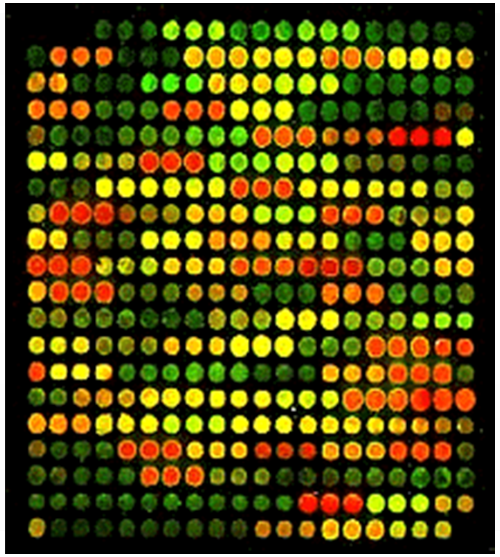
Patient's home

Reduce the medical costs

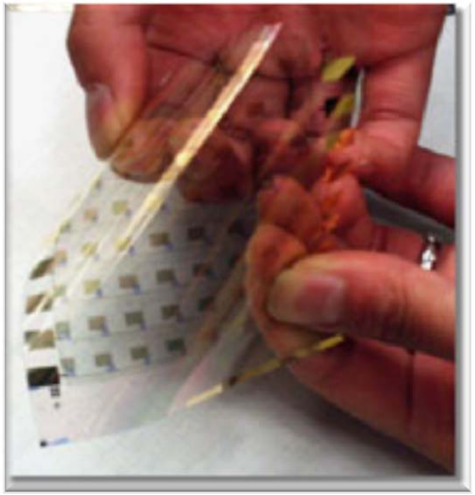
Emergency room

sensing arrays: this is the way to go

Affymax DNA chip



http://bmel.korea.ac.kr/image/intro_fig_5_4.gif



Label-free
Low cost, low power, disposable electronic sensing system
Implemented on flex substrate (plastic, fabric, paper)

OFET BIO-electronic vs.

optical and electrochemical method

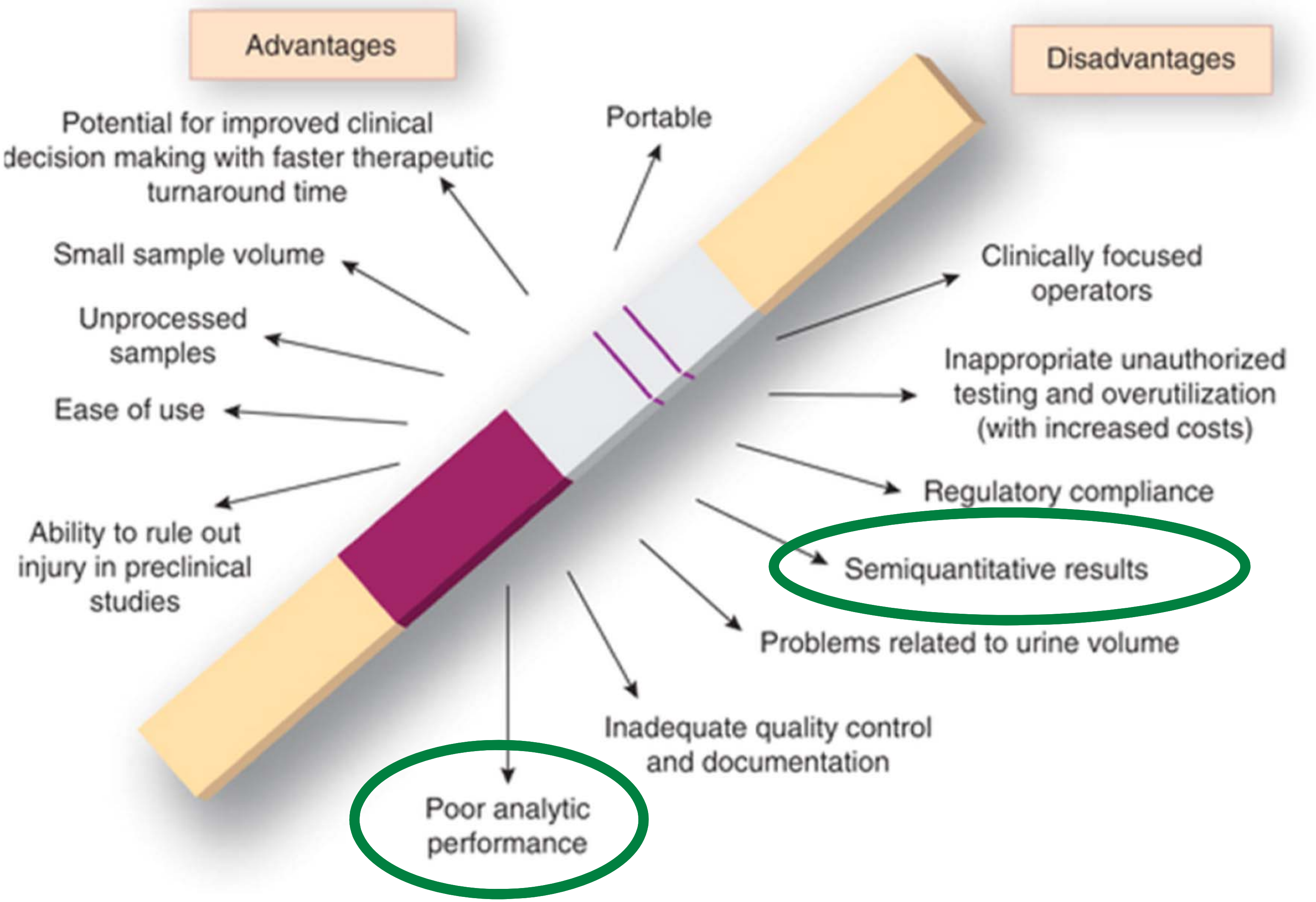
PROS

- *Easy miniaturization*
- *CMOS compatible (no reference electrode)*
- *Label-free*
- *Low cost (printing fab on plastic, fabric, paper)*

CONS

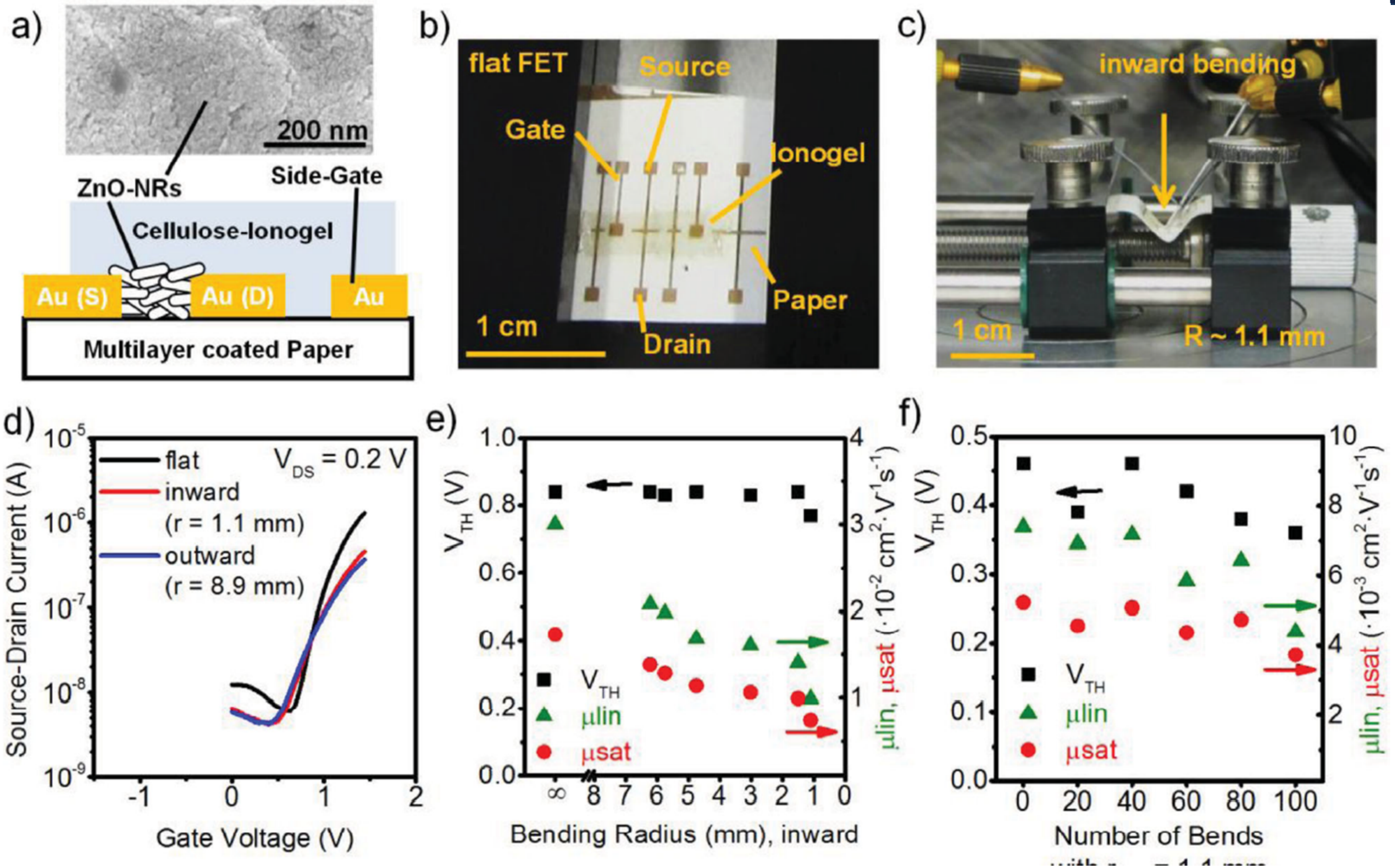
- *Totally novel approach*
- *New production paradigms*
- *Critical is the control of the interfaces*

the search for quantitative stick testing



Schematic drawing of the RenaStick dipstick showing advantages and disadvantages of point-of-care testing in the setting of acute kidney injury. www.nature.com 2014

printed circuits on paper



Thiemann, S. et al. "**Cellulose-Based Ionogels for Paper Electronics**," Adv. Fun. Mater. 2014, 24, 625–634.

electronic OFET bio-sensors @UNIBA

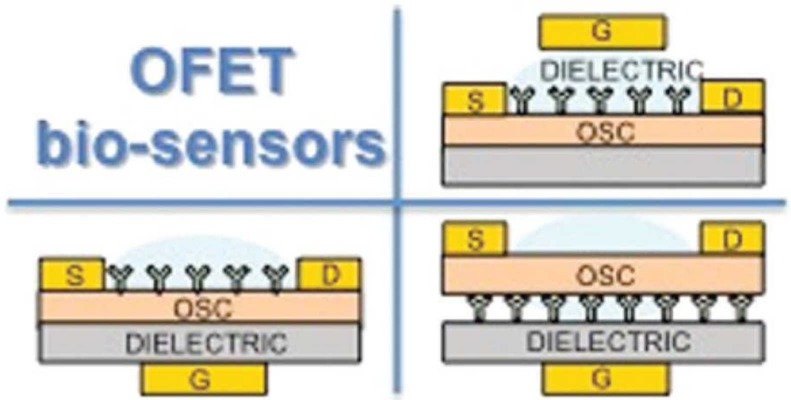
Chem Soc Rev

RSC Publishing

TUTORIAL REVIEW

Chemical Society Reviews

c3cs60127g



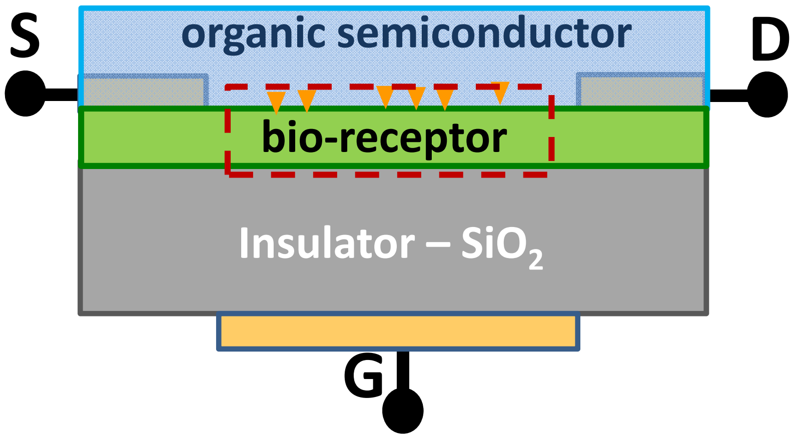
Organic field-effect transistor sensors: a tutorial review

Luisa Torsi,* Maria Magliulo, Kyriaki Manoli and Gerardo Palazzo

Organic thin-film transistors embedding biological recognition elements are successfully employed as ultrasensitive, low-cost, label-free biosensors in several analytical fields.

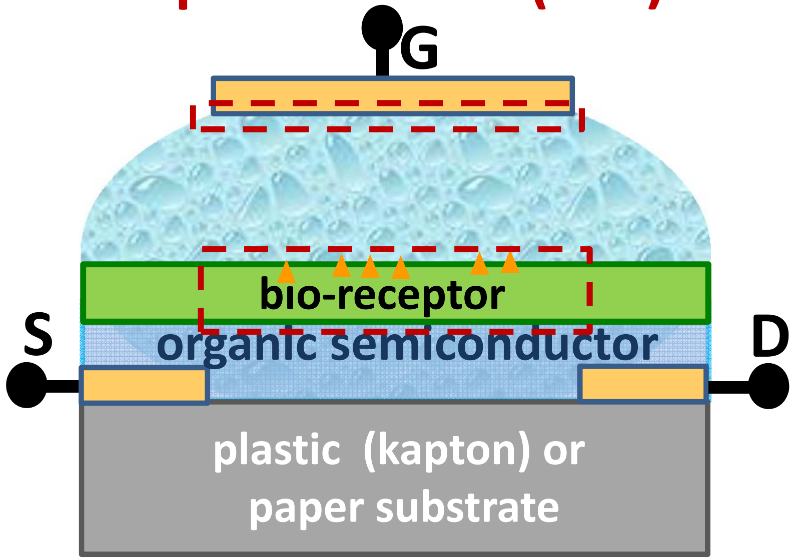
***L. Torsi et al. Chem. Soc. Rev.*, 2013, 42 (22), 8612 - 8628**

impact of a binding event on electronic properties



Bottom Gate OFET (TFT)

Top Gate OFET (TFT)



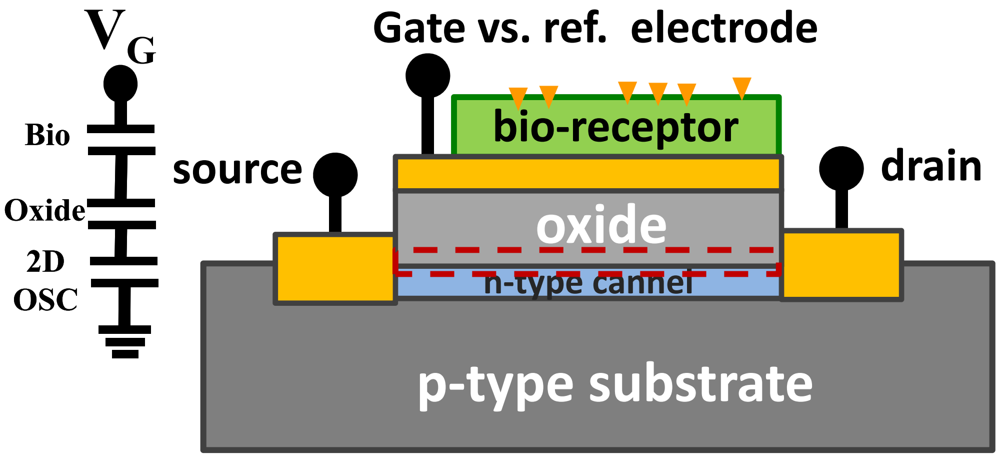
$$\sqrt{I_{DS}} = \sqrt{\frac{W}{2L}\mu_{FET}C_i \cdot (V_G - V_T)}$$

- ❑ *impacts on OSC or gate metal electrochemical potentential →* V_T *changes*
- ❑ *impacts on the OSC transport properties →* μ_{FET} *changes*
- ❑ *Impacts on the gating system capacitance →* C_i *changes*

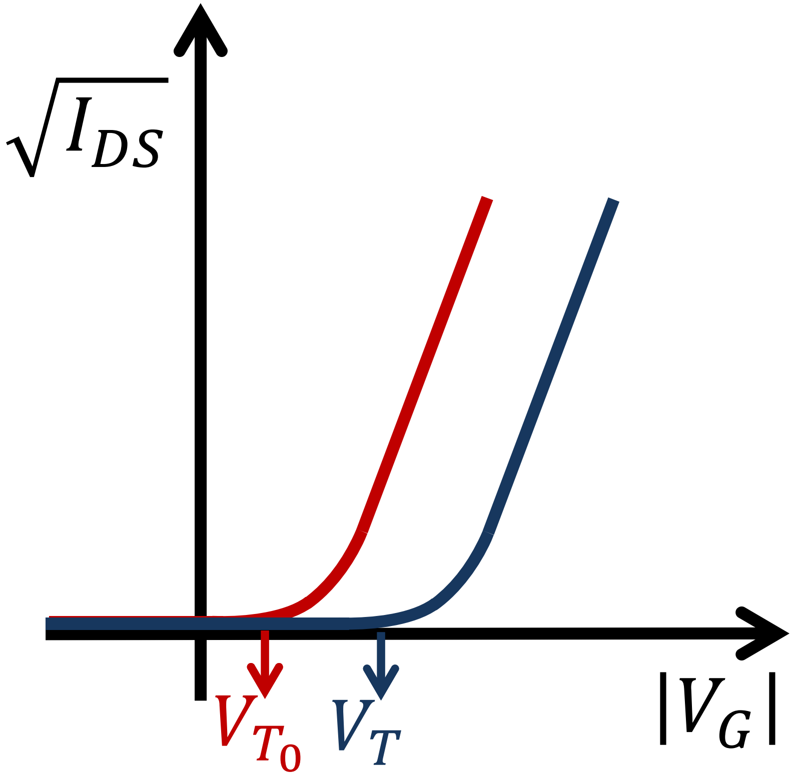
Ion Selective FET (ISFET) like bio-sensor

$$\sqrt{I_{DS}} = \sqrt{\frac{W}{2L}\mu_{FET}C_i} \cdot (V_G - V_T)$$

$$\mu_{FET} = cost$$
$$C_i = cost$$

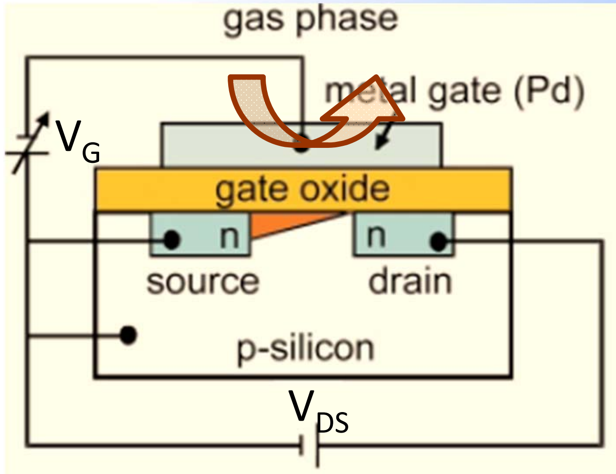


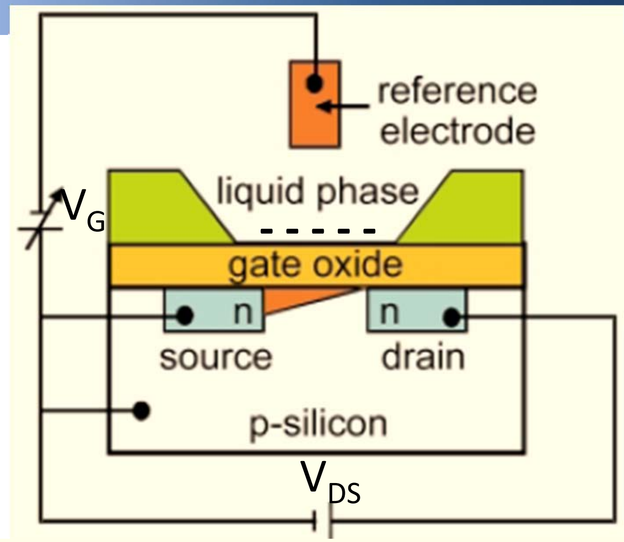
MOSFET

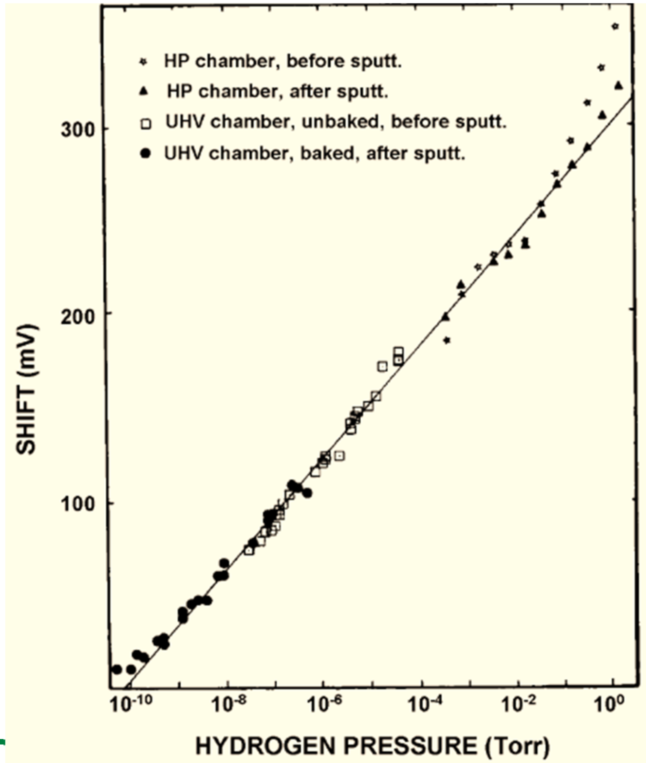


$$\frac{\Delta I}{I} = \frac{2\,\Delta V_T}{(V_G - V_T)}$$

GAS & Ion-Selective FET (ISFET)





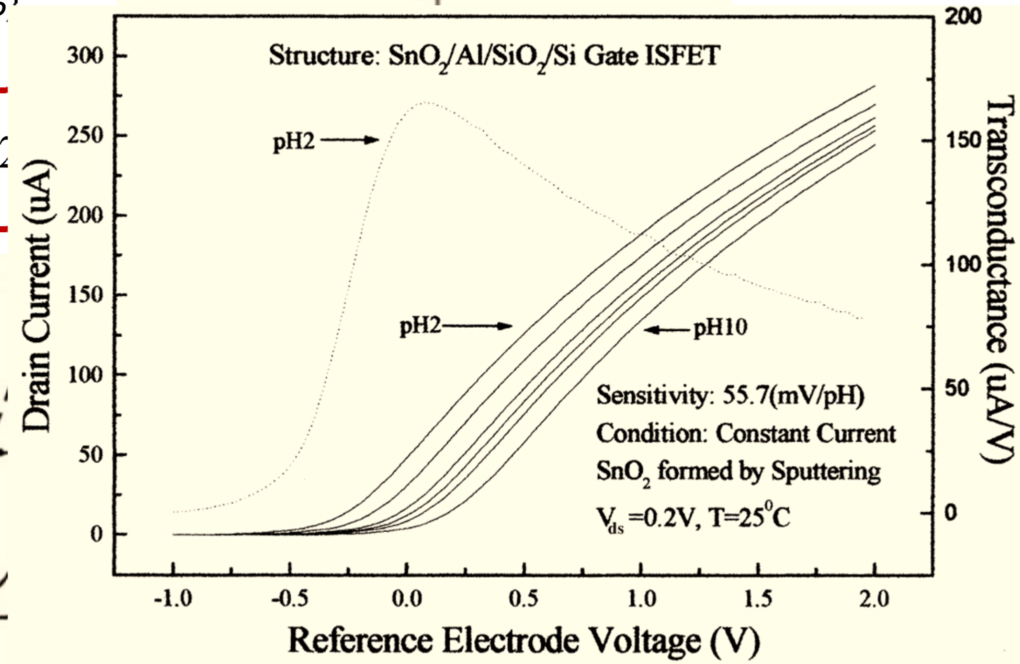


I. Lundström et al. / Sensors and Actuators B 121 (2007) 247–262

55 (1975)

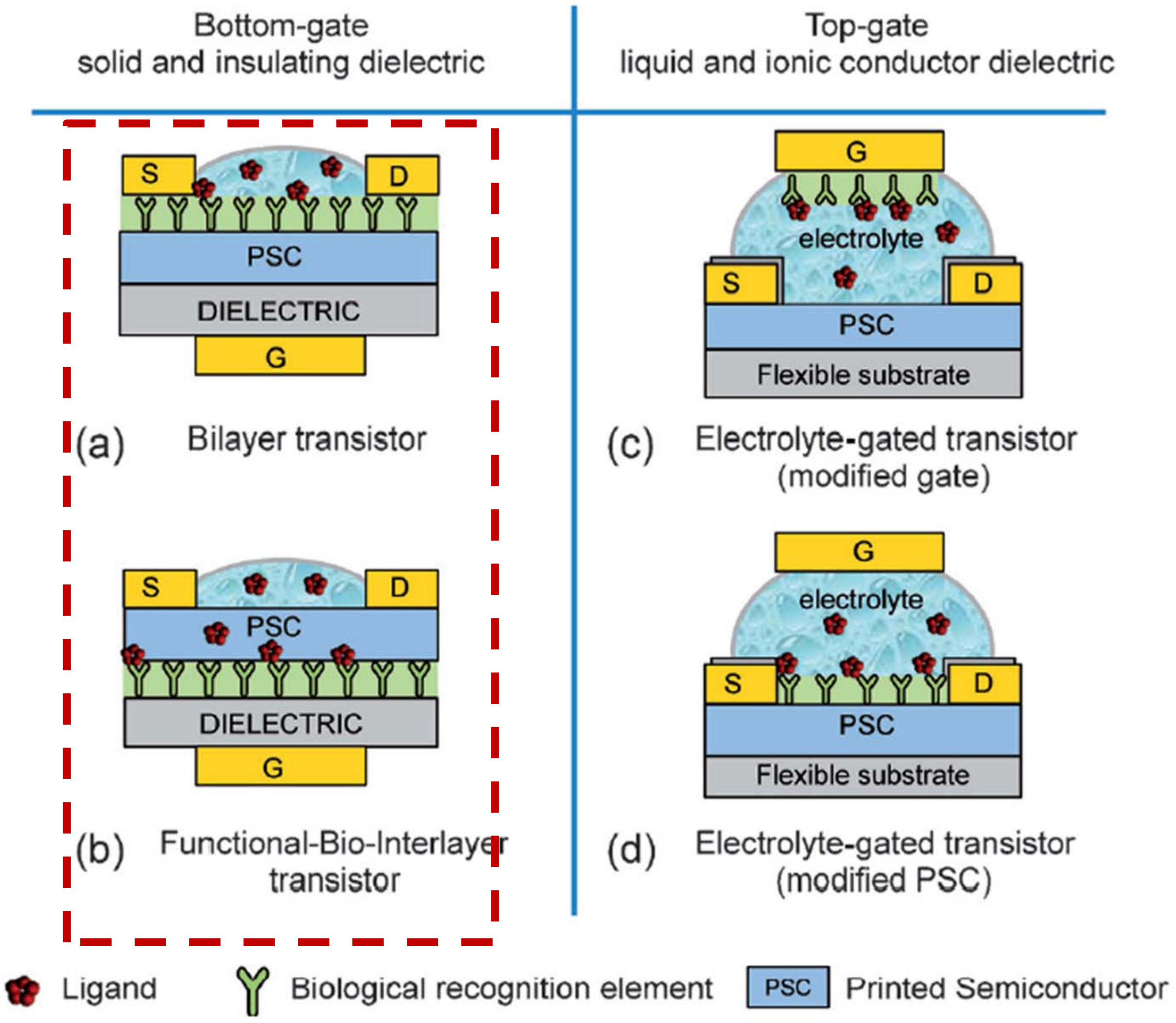
Q_{def} + 2

V_{TO}



C.-L. Wu et al. / Materials Chemistry and Physics 63 (2000) 153–156

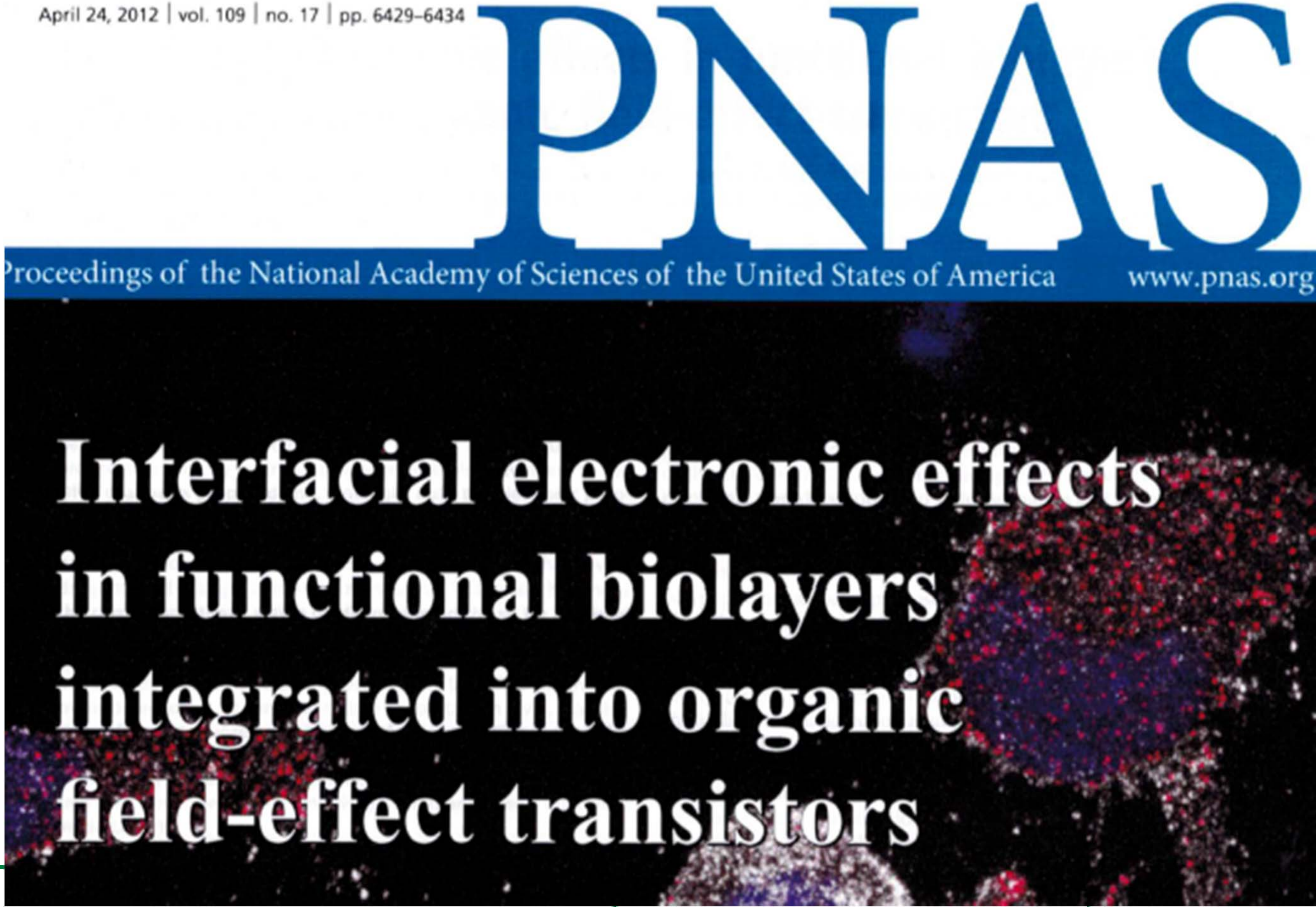
electronic OFET bio-sensors



FBI-OFET

L. Torsi et al *Angew. Chem. Int. Ed.* **2015**, *54*, 12562 – 12576

FBI-OFET sensors



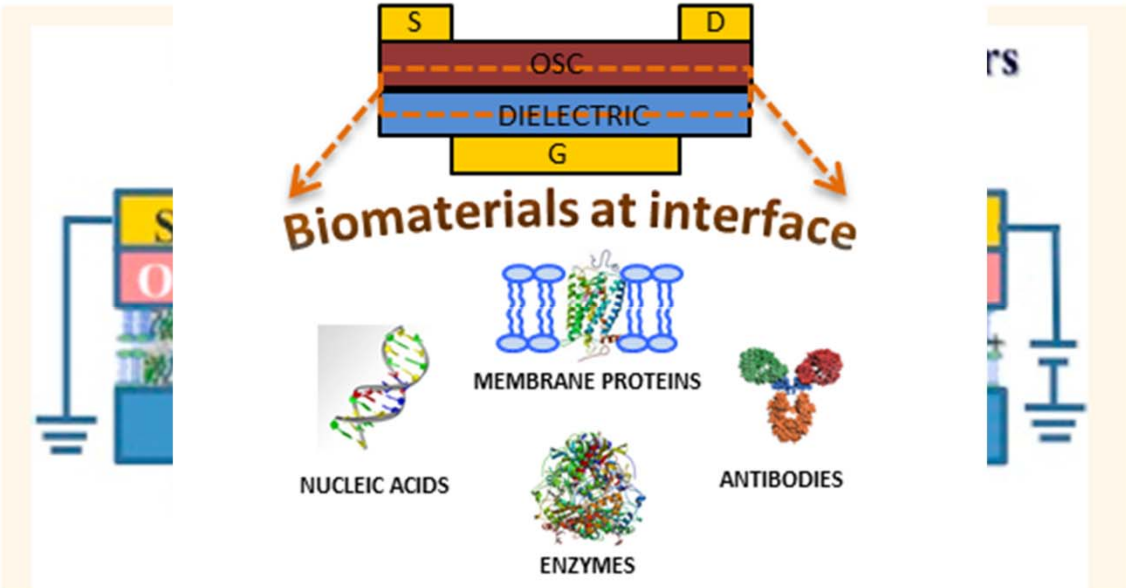
electronic transduction of proton translocation

Materials Views
www.MaterialsViews.com

ADVANCED MATERIALS
www.advmat.de

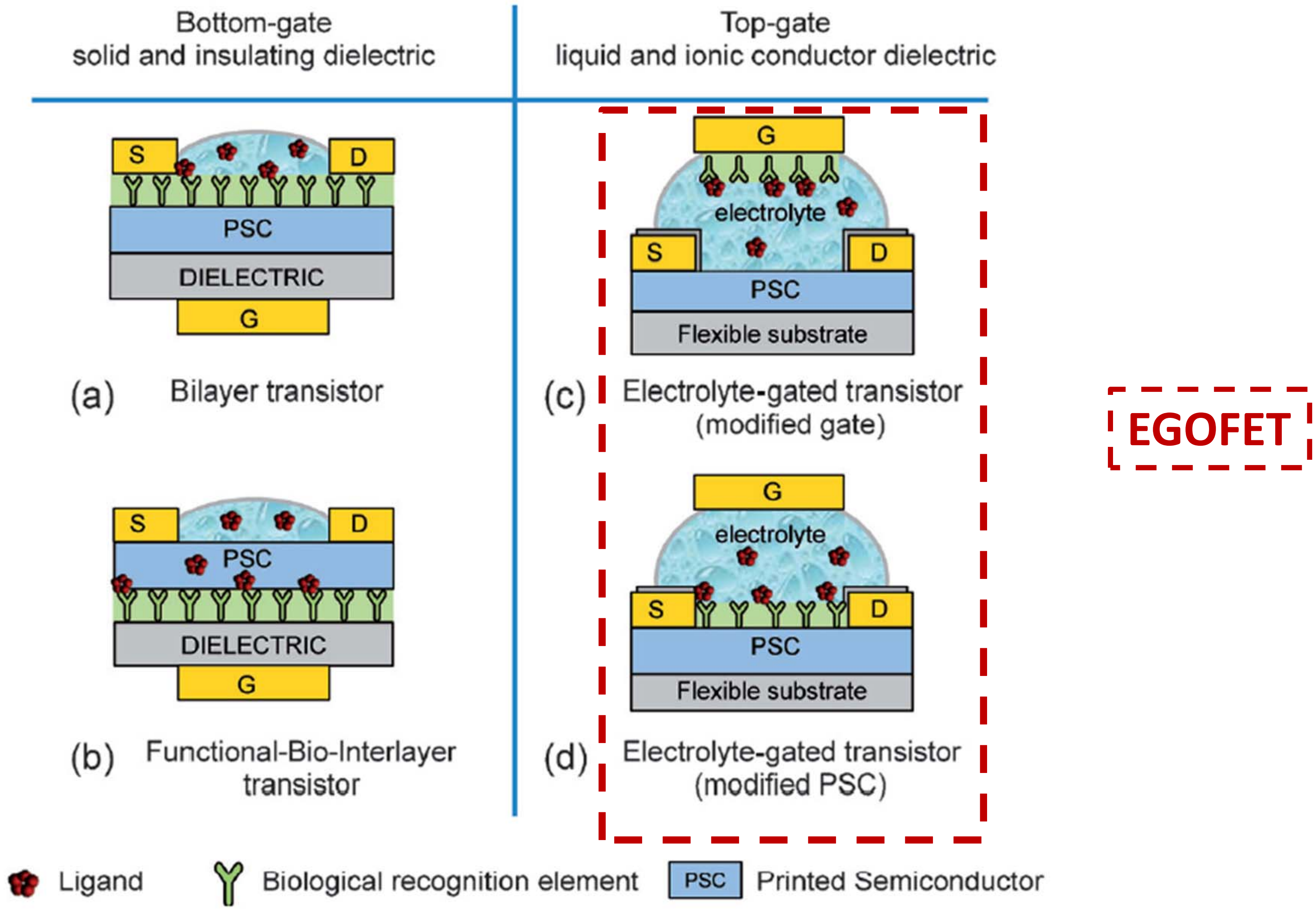
Tailoring Functional Interlayers in Organic Field-Effect Transistor Biosensors

*Maria Magliulo, Kyriaki Manoli, Eleonora Macchia, Gerardo Palazzo, and Luisa Torsi**



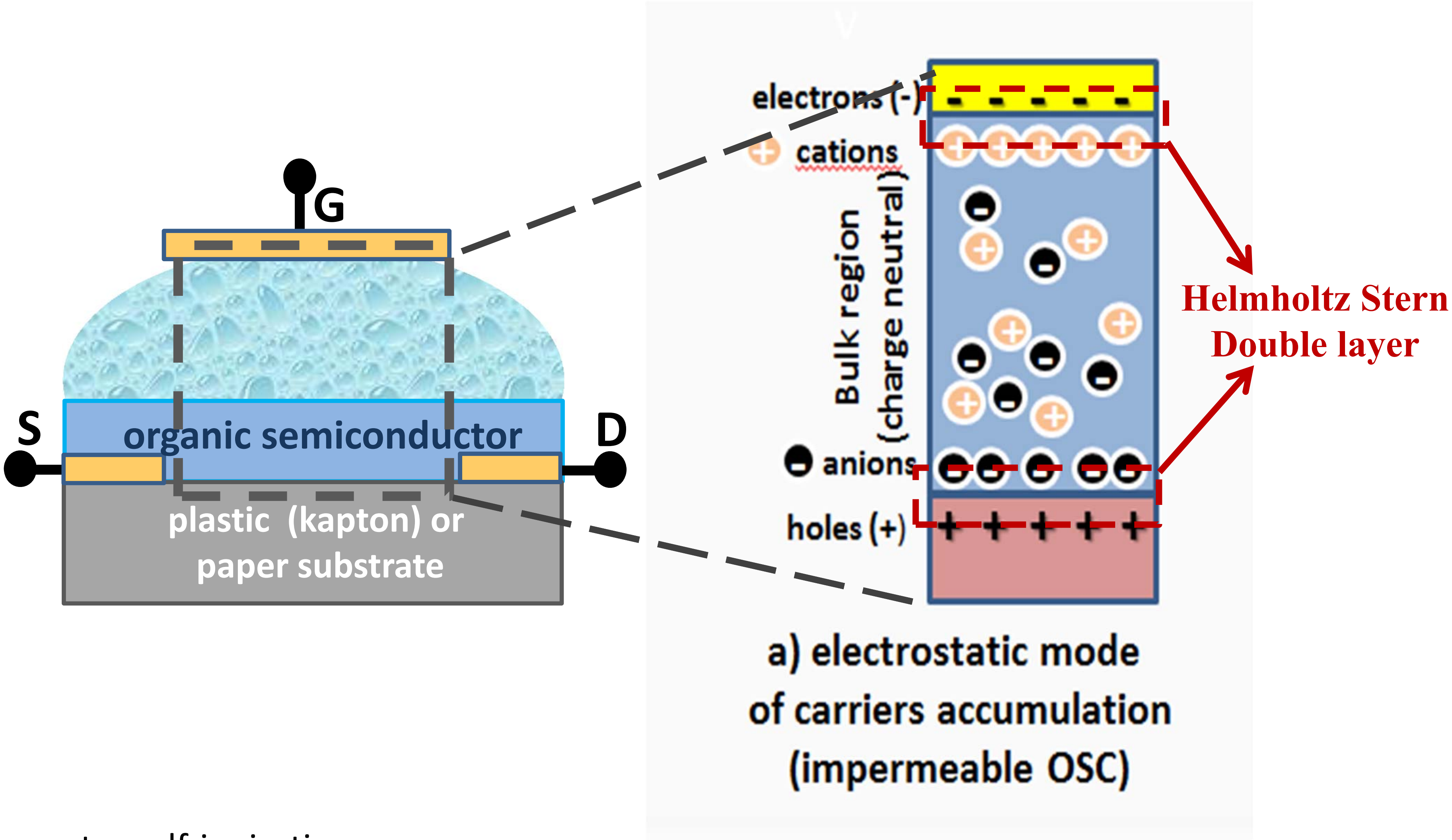
Adv. Mater. **2014**,
DOI: 10.1002/adma.201403477

electronic OFET bio-sensors



L. Torsi et al *Angew. Chem. Int. Ed.* **2015**, *54*, 12562 – 12576

how Electrolyte Gated OFETs work



water self-ionization

H. Klauk, *Organic electronics II: More materials and applications; Wiley-VCH*
S. H. Kim, K. Hong, W. Xie, K. H. Lee, S. Zhang, T. P. Lodge, C. D. Frisbie, Adv. Mater. 2013, 25, 1822-1846;

Polyelectrolytes in EGOFET

ACS APPLIED MATERIALS & INTERFACES

Research Article

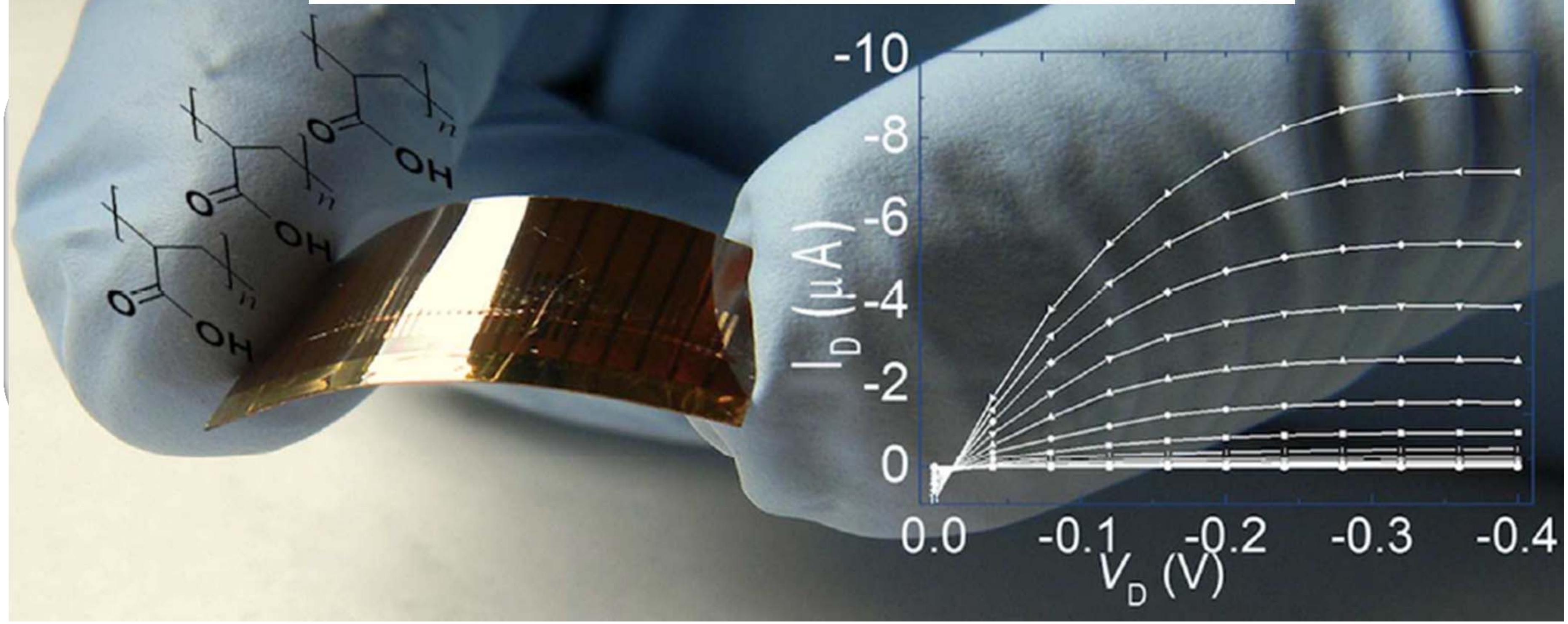
www.acsami.org

Plain Poly(acrylic acid) Gated Organic Field-Effect Transistors on a Flexible Substrate

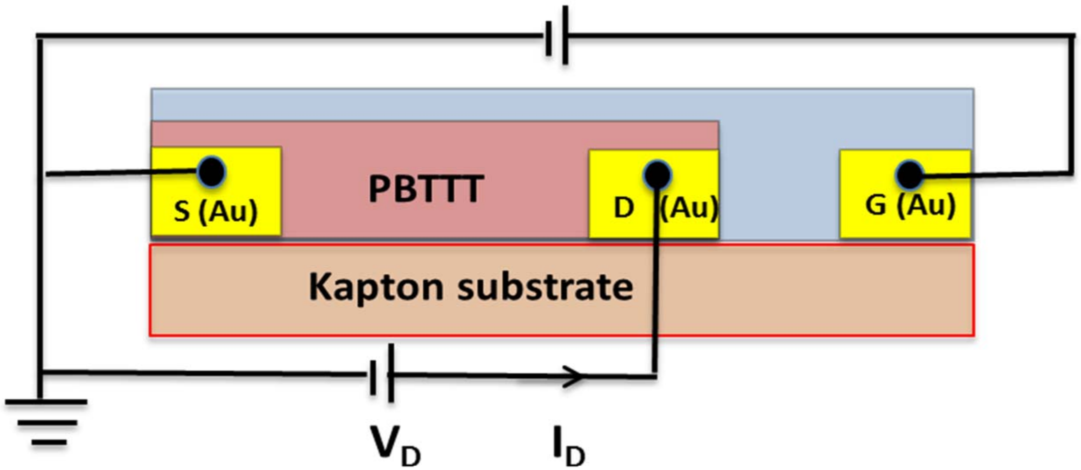
Liviu M. Dumitru, Kyriaki Manoli, Maria Magliulo, Luigia Sabbatini, Gerardo Palazzo, and Luisa Torsi*

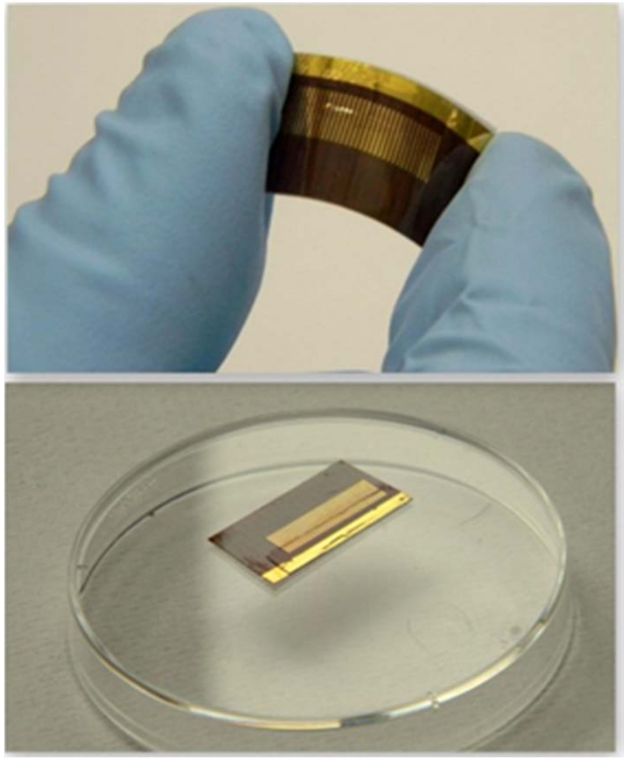
Department of Chemistry, "Aldo Moro" University, Via Orabona 4, Bari 70126, Italy

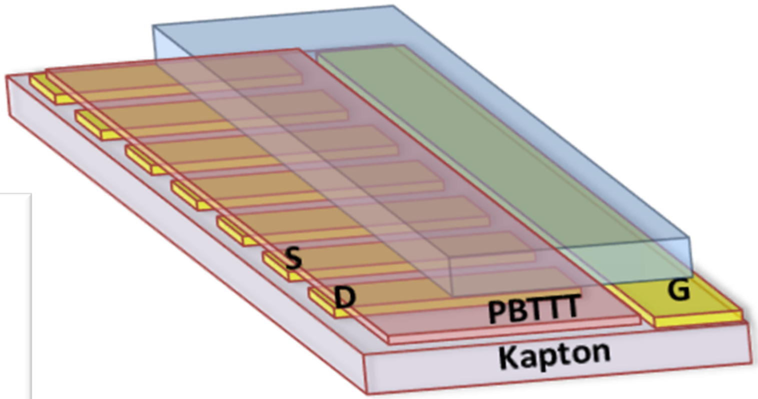
dx.doi.org/10.1021/am403008b | *ACS Appl. Mater. Interfaces* 2013, 5, 10819–10823



EGOFET - architectures





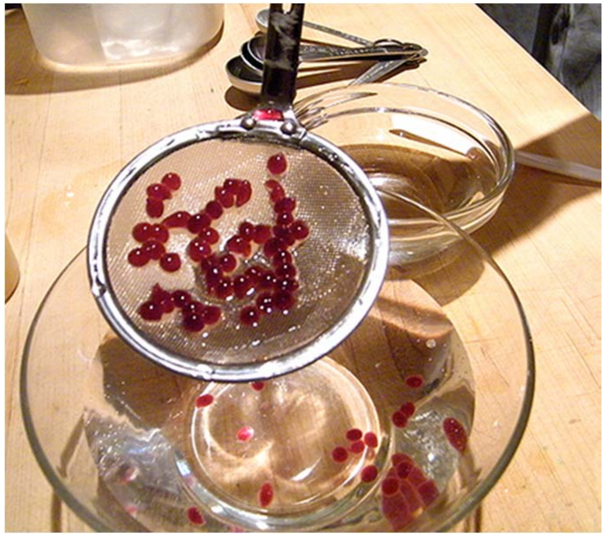


L. Dumitru

Devices channel length *L* = 200 µm
channel width *W* = 4000 µm
Substrates: polyimide (Kapton®)

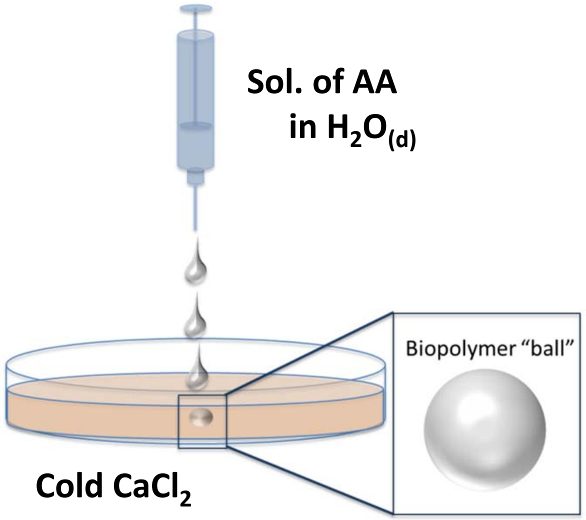
New polyelectrolyte as gating material in OFETs

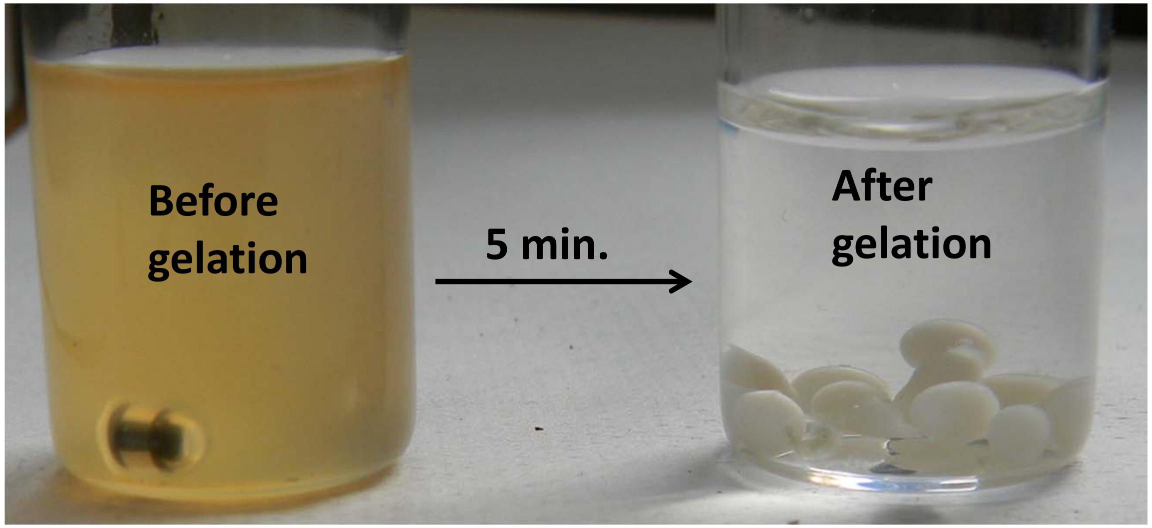


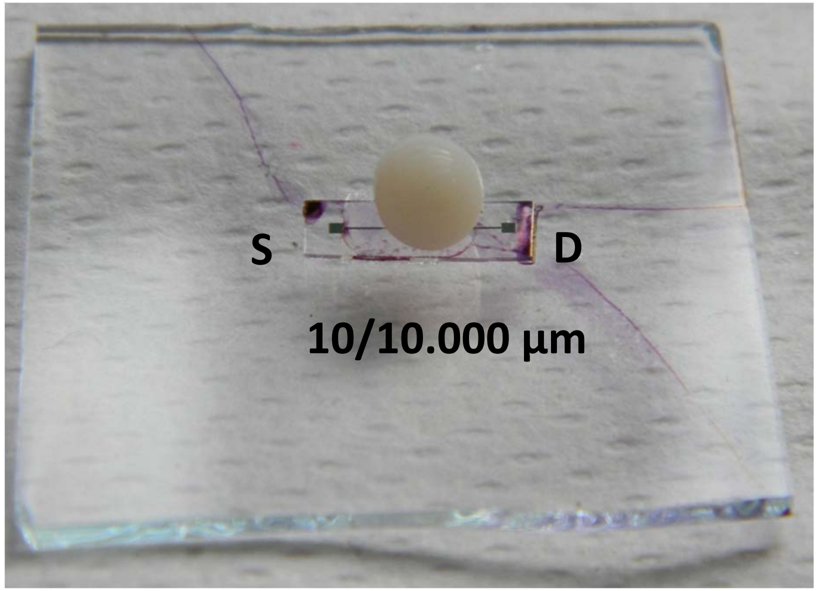


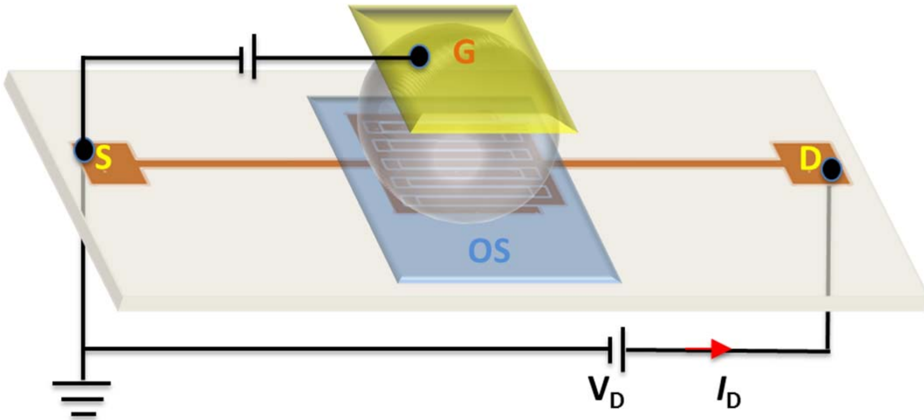
Calcium alginate fruit (blueberry) "caviar"


Alginate capsules

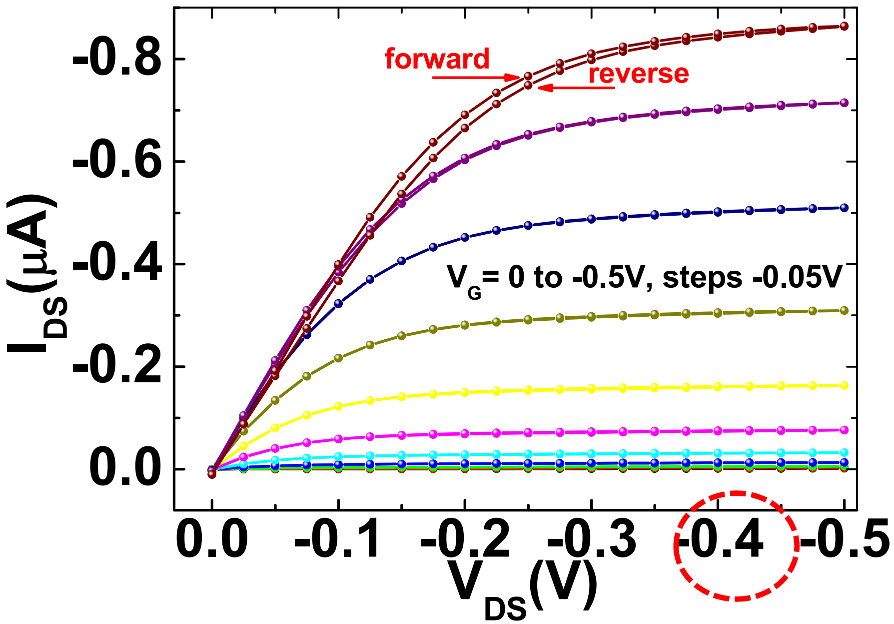


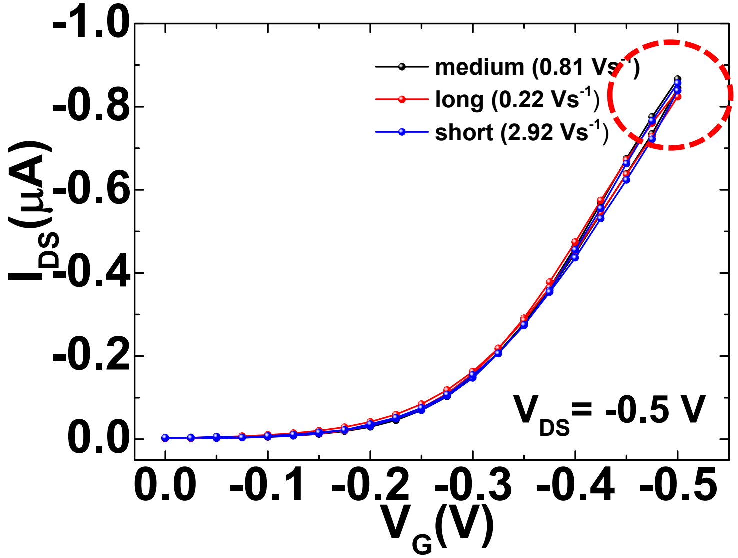






Electrical performance





Capsule based OFET	*Average (n=7)**	*Best*
μ (cm^2 V^{-1} s^{-1})	($1.7 \times 10^{-2} \pm 4 \times 10^{-3}$)	2.3×10^{-2}
V_T (V)	(-0.029 ± 0.019)	-0.004
on/off	(178 ± 158)	438

Green Electronics

Natural materials
or materials inspired by nature
in organic field-effect transistors

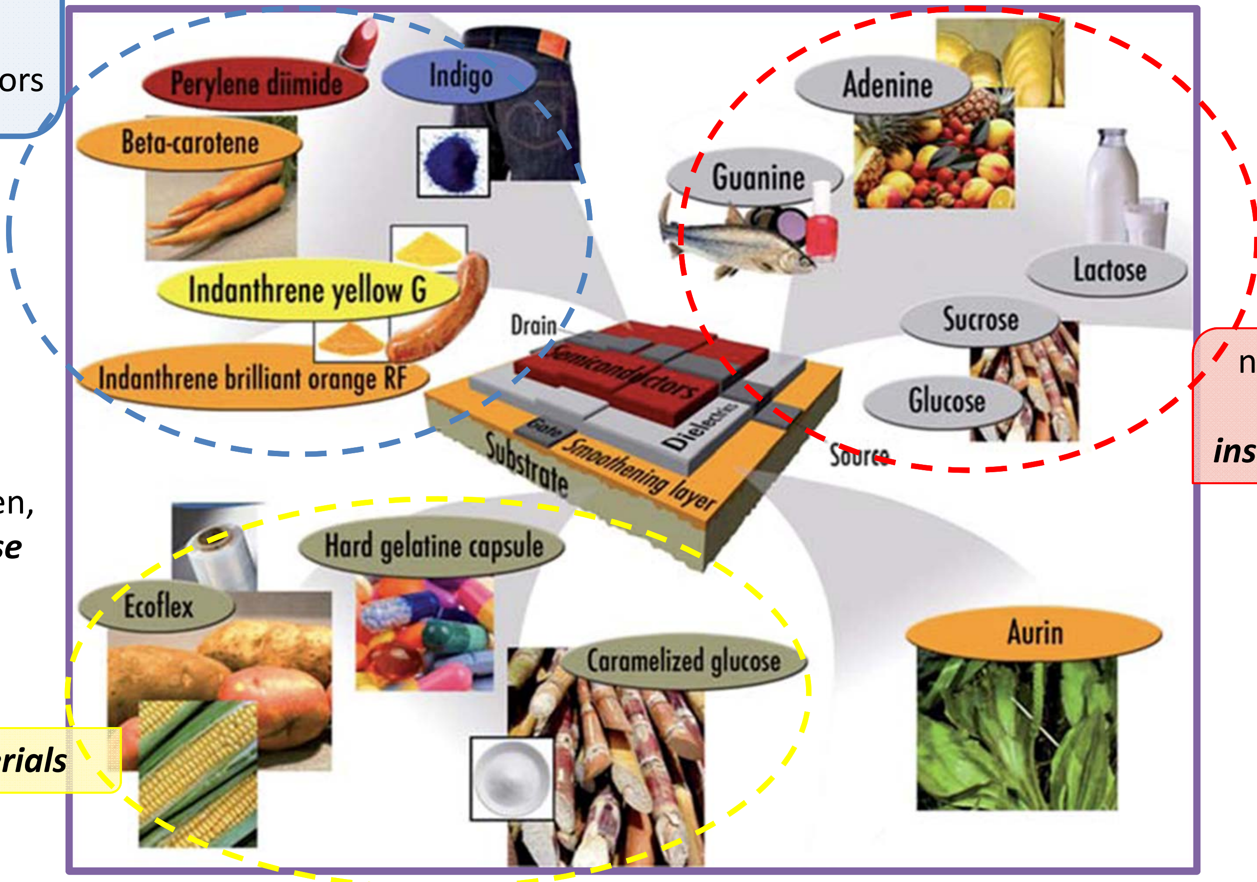
β-carotene and ***indigo***
are natural
p- and n-type
organic semiconductors

sugar molecules or ***nucleobases***

natural dielectrics
with ***good insulating properties***

hard gelatine
produced from collagen,
or ***caramelized glucose***

exotic substrate materials



M. Irimia-Vladu et la. ***Adv. Funct. Mater., 2010, 20***
C. J. Bettinger and Z. Bao , Adv. Mater., 2010 , 22 , 651..

Printing pigments

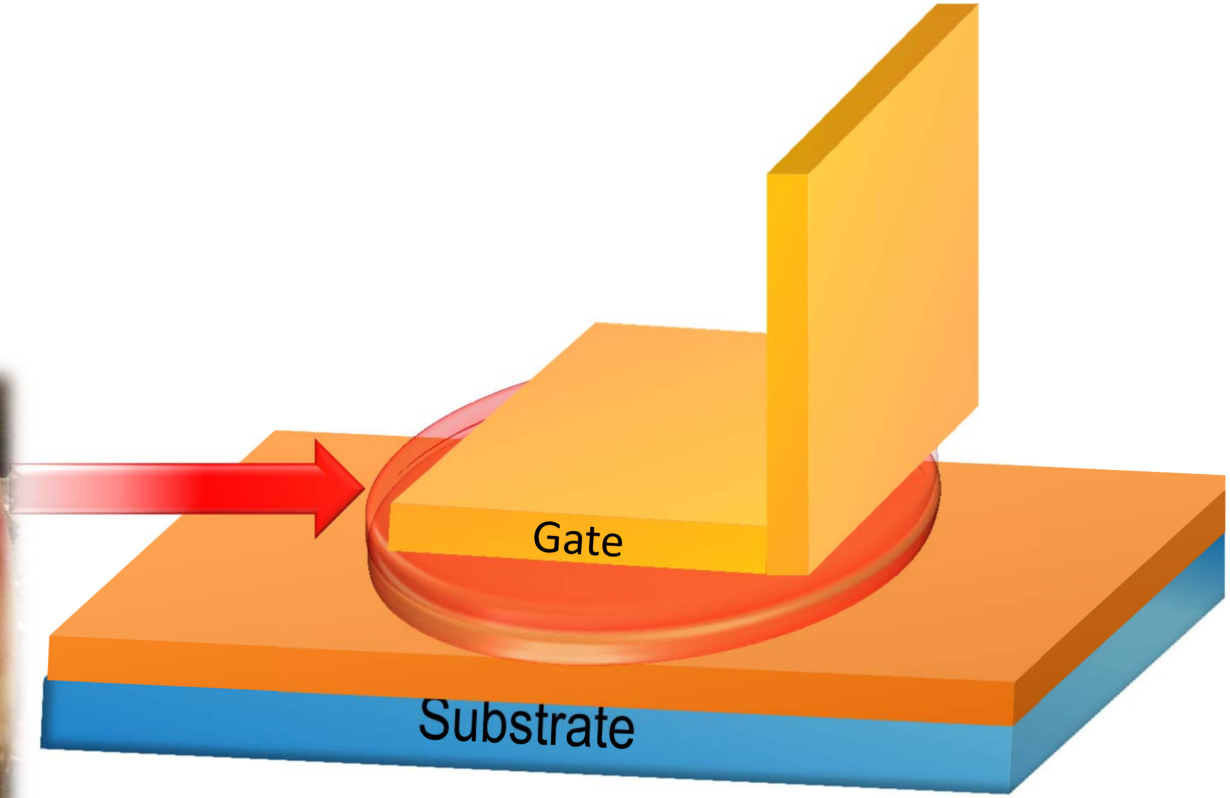
Materials Views
www.MaterialsViews.com
ADVANCED MATERIALS
www.advmat.de

Hydrogen-Bonded Semiconducting Pigments for Air-Stable Field-Effect Transistors

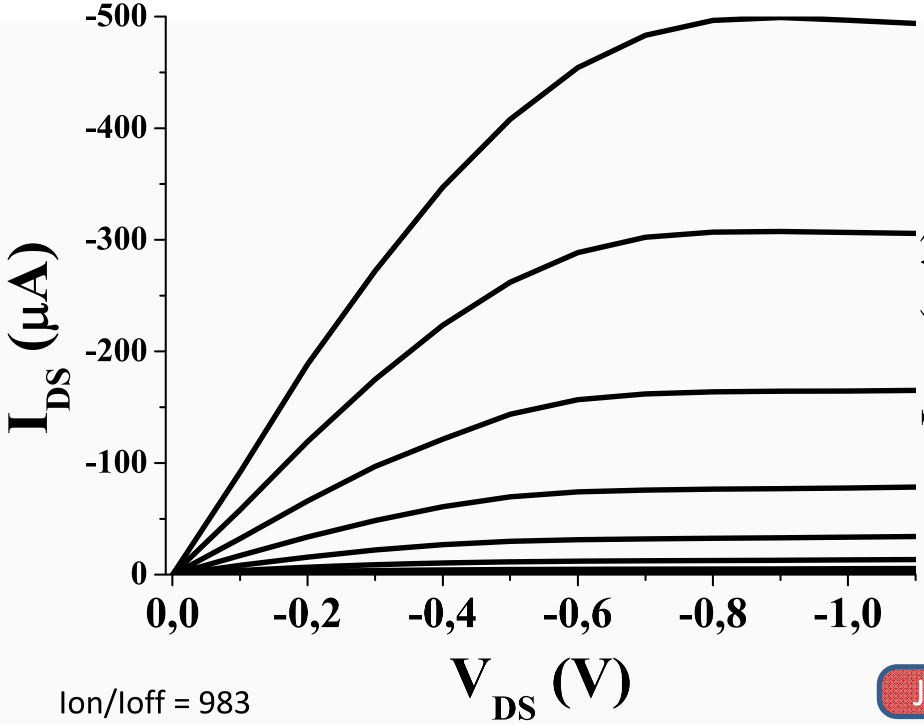
Eric Daniel Głowacki, Mihai Irimia-Vladu, Martin Kaltenbrunner, Jacek Gąsiorowski, Matthew S. White, Uwe Monkowius, Giuseppe Romanazzi, Gian Paolo Suranna, Piero Mastrorilli, Tsuyoshi Sekitani, Siegfried Bauer, Takao Someya, Luisa Torsi, and Niyazi Serdar Sariciftci*

From kitchen to lab: Curiosity driven research

M. Y. Mulla

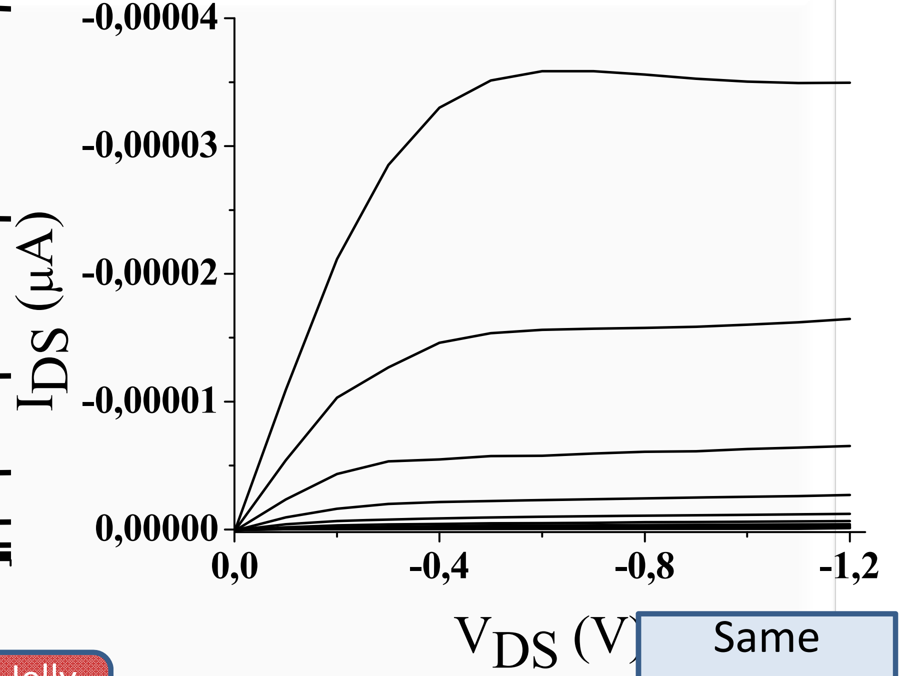


edible Gel di-electric



Jelly

Ion/Ioff = 983
μ [cm2/V.s]= 5.6 E-1
Vt [V]= -0.53
Channel L/W: 10/10000
C = 5 (taken as approximate value because for ion gels literature values are from 5 to 10)

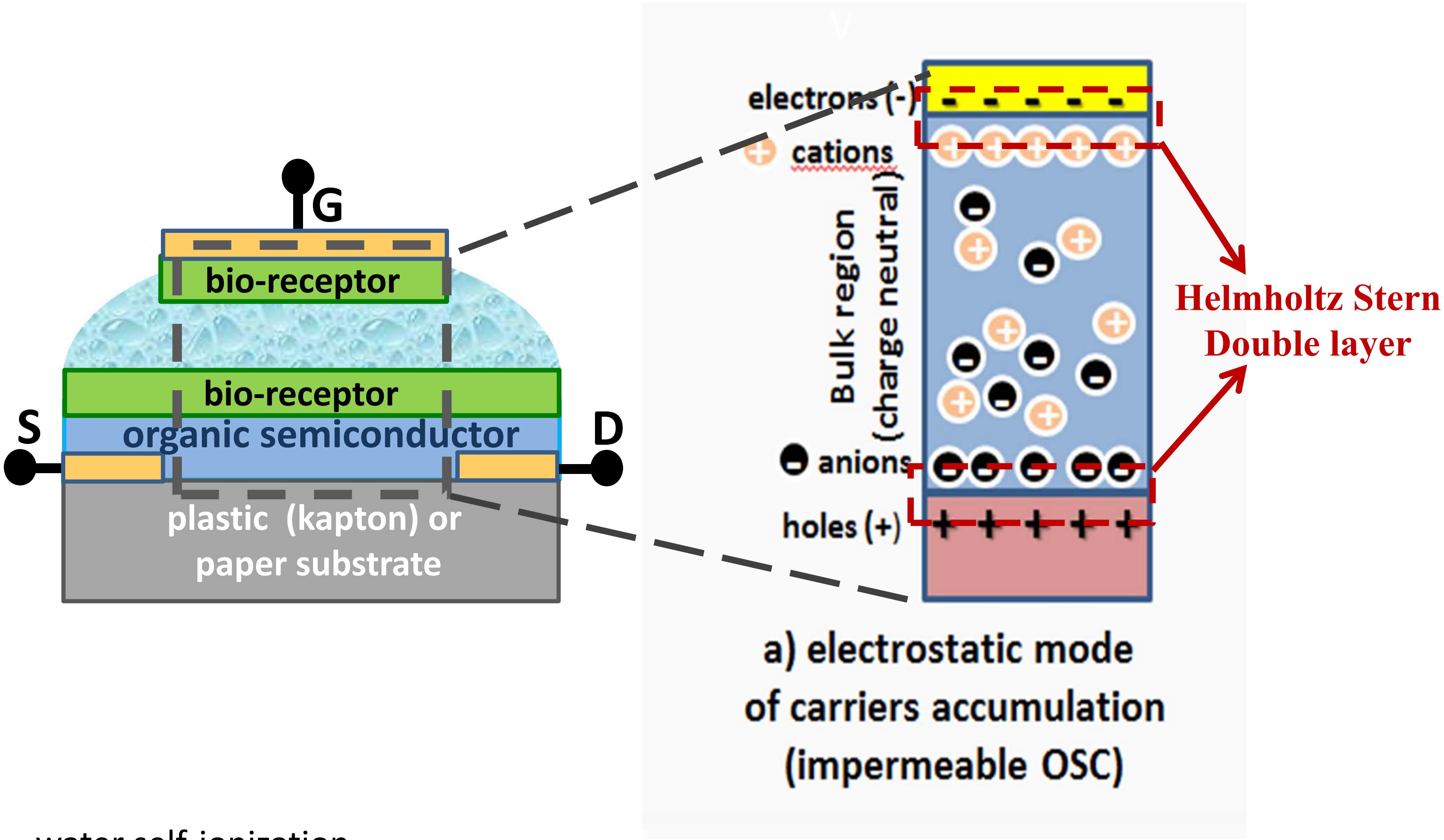


Same device

After 3 days

Ion/Ioff = 302
μ [cm2/V.s]= 5.7 E-2
Vt [V]= -0.74
Channel L/W: 5/10000

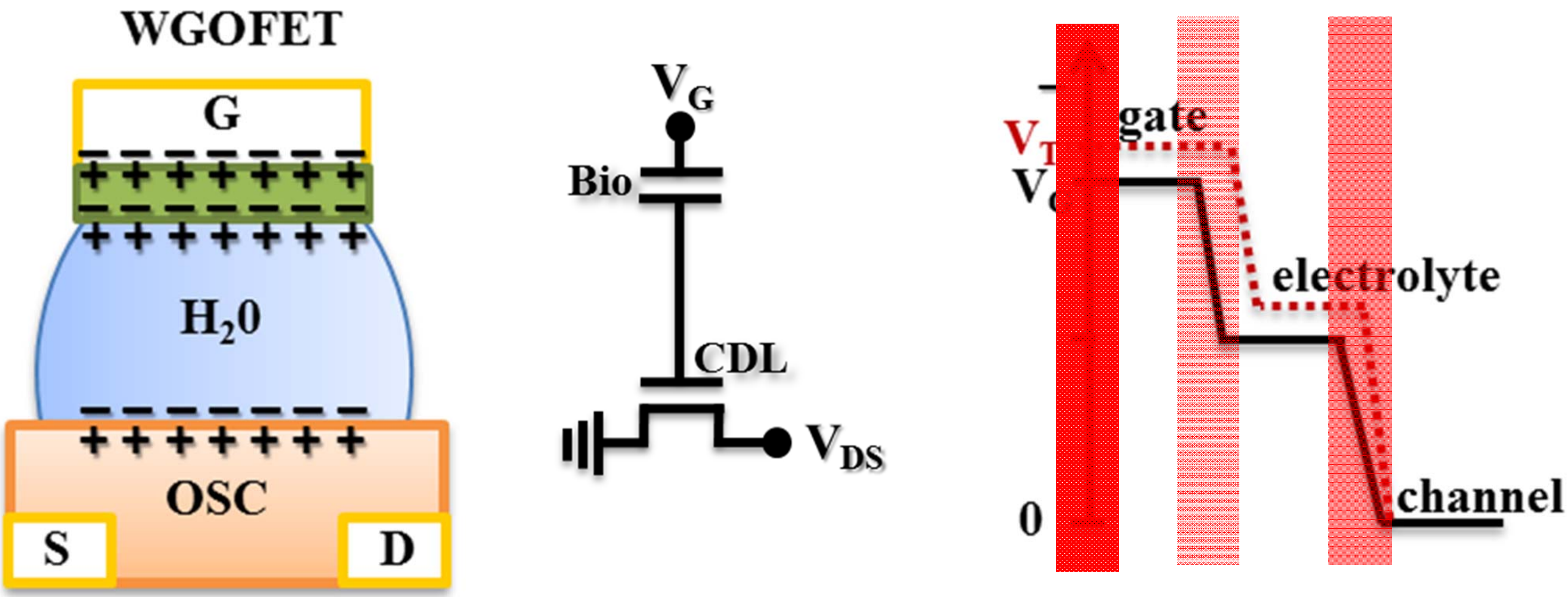
how EGOFETs work



water self-ionization

H. Klauk, *Organic electronics II: More materials and applications; Wiley-VCH*
S. H. Kim, K. Hong, W. Xie, K. H. Lee, S. Zhang, T. P. Lodge, C. D. Frisbie, Adv. Mater. 2013, 25, 1822-1846;

the capacity modulated device



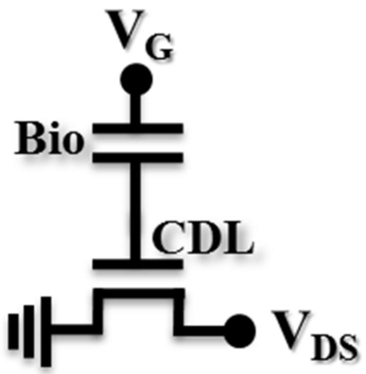
$C_{CDL} \sim 10\text{-}10^2\ \mu F/cm^2$ $C_{BIO} \sim 10^{-1}\ \mu F/cm^2$

$C_{BIO} << C_{CDL}$

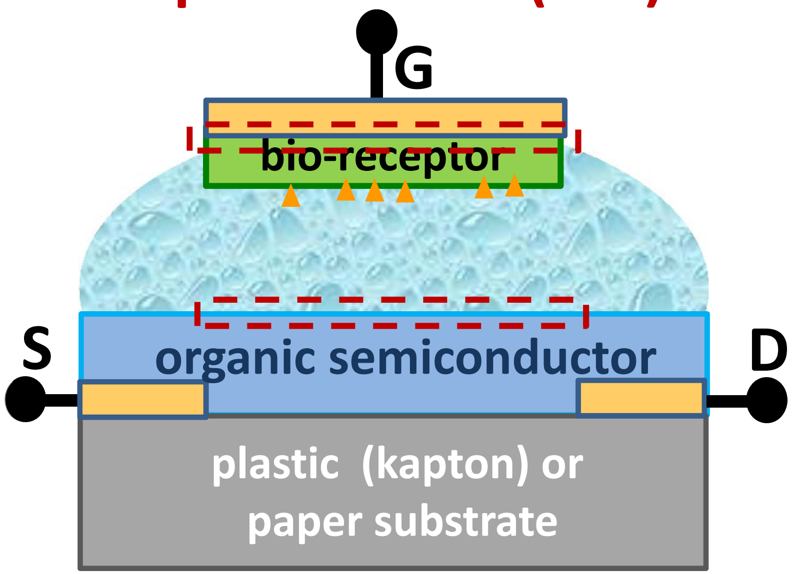
electrolyte gated OFET (EGOFET) sensor

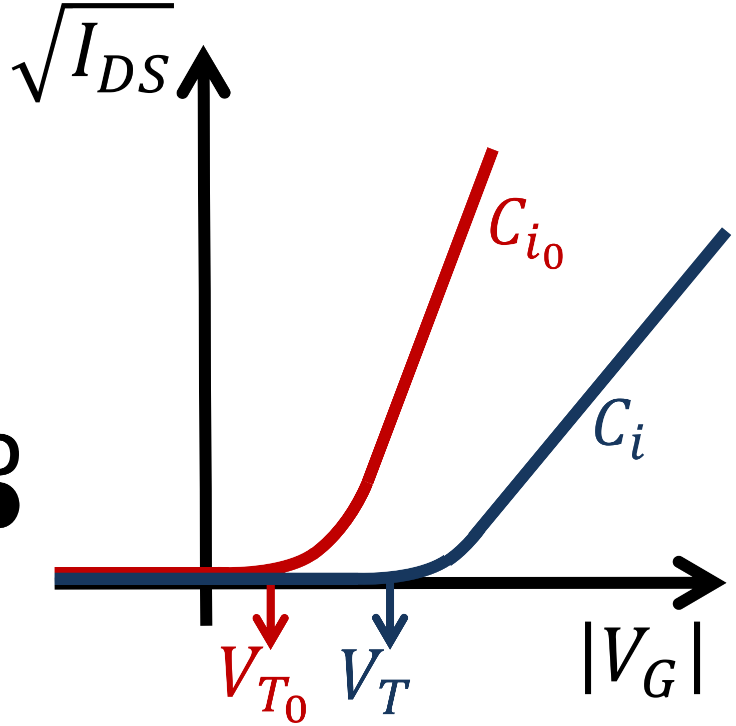
$$\sqrt{I_{DS}} = \sqrt{\frac{W}{2L}\mu_{FET} C_i} \cdot (V_G - V_T)$$

$$\mu_{FET} = cost$$



Top Gate OFET (TFT)





$$\frac{\Delta I}{I} = \frac{\Delta C_i}{C_i} - \frac{2\,\Delta V_T}{(V_G - V_T)}$$

water gated OFET sensors - review

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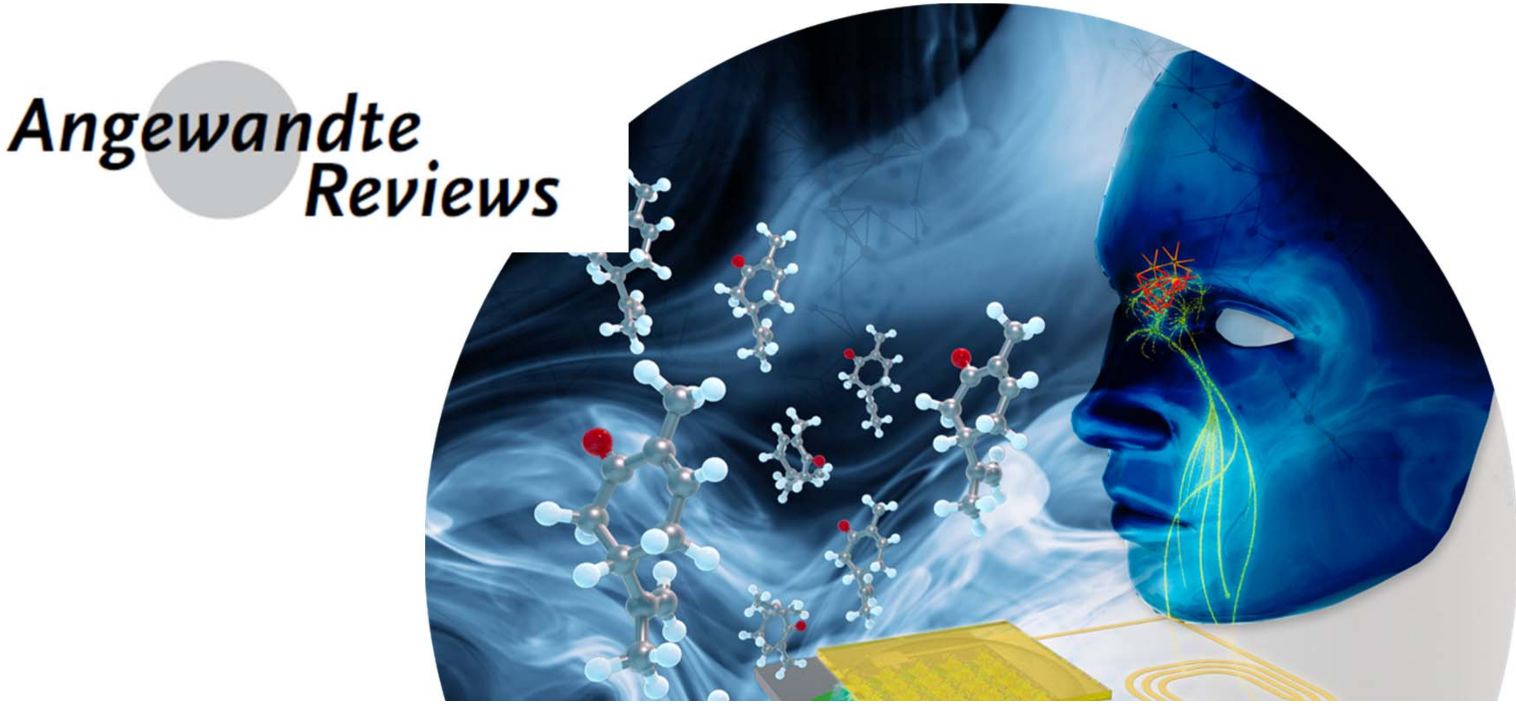

charged species → stronger long-range coulomb interactions (10-100 kJ/mol) → electrochemical potential → ISFET

neutral species (or species carrying a dipole moment) → weaker short-range interactions such as the dipole-dipole or the dispersive ones (2 kJ/mol) → chemical potential → capacity modulated FET

L. Torsi et al *Angew. Chem. Int. Ed.* **2015**, *54*, 12562 – 12576

Odorant Binding Proteins EGOFET sensor

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FlexSmell

nature COMMUNICATIONS

ARTICLE

Received 1 Aug 2014 | Accepted 2 Dec 2014 | Published 16 Jan 2015

DOI: 10.1038/ncomms7010

OPEN

Capacitance-modulated transistor detects odorant binding protein chiral interactions

Mohammad Yusuf Mulla[1], Elena Tuccori[2], Maria Magliulo[1], Gianluca Lattanzi[3], Gerardo Palazzo[1], Krishna Persaud[2] & Luisa Torsi[1]

Mulla, M.Y. *et al. Nature Communications*, 2015, 6, 6010

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EPFL ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

jpc

MANCHESTER 1824

VTT

Holst Centre

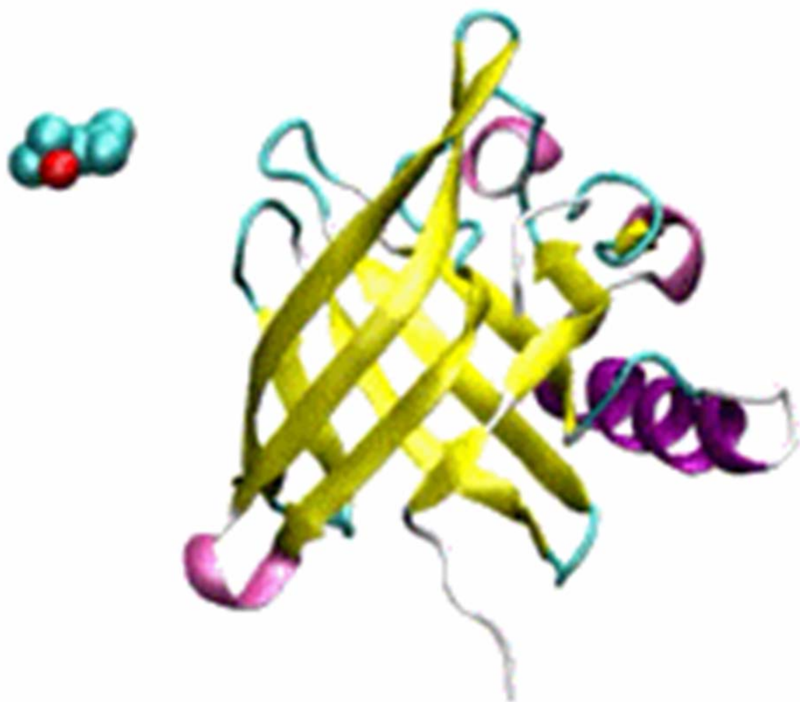
Carton Pack

BIOtest

Odorant Binding Proteins

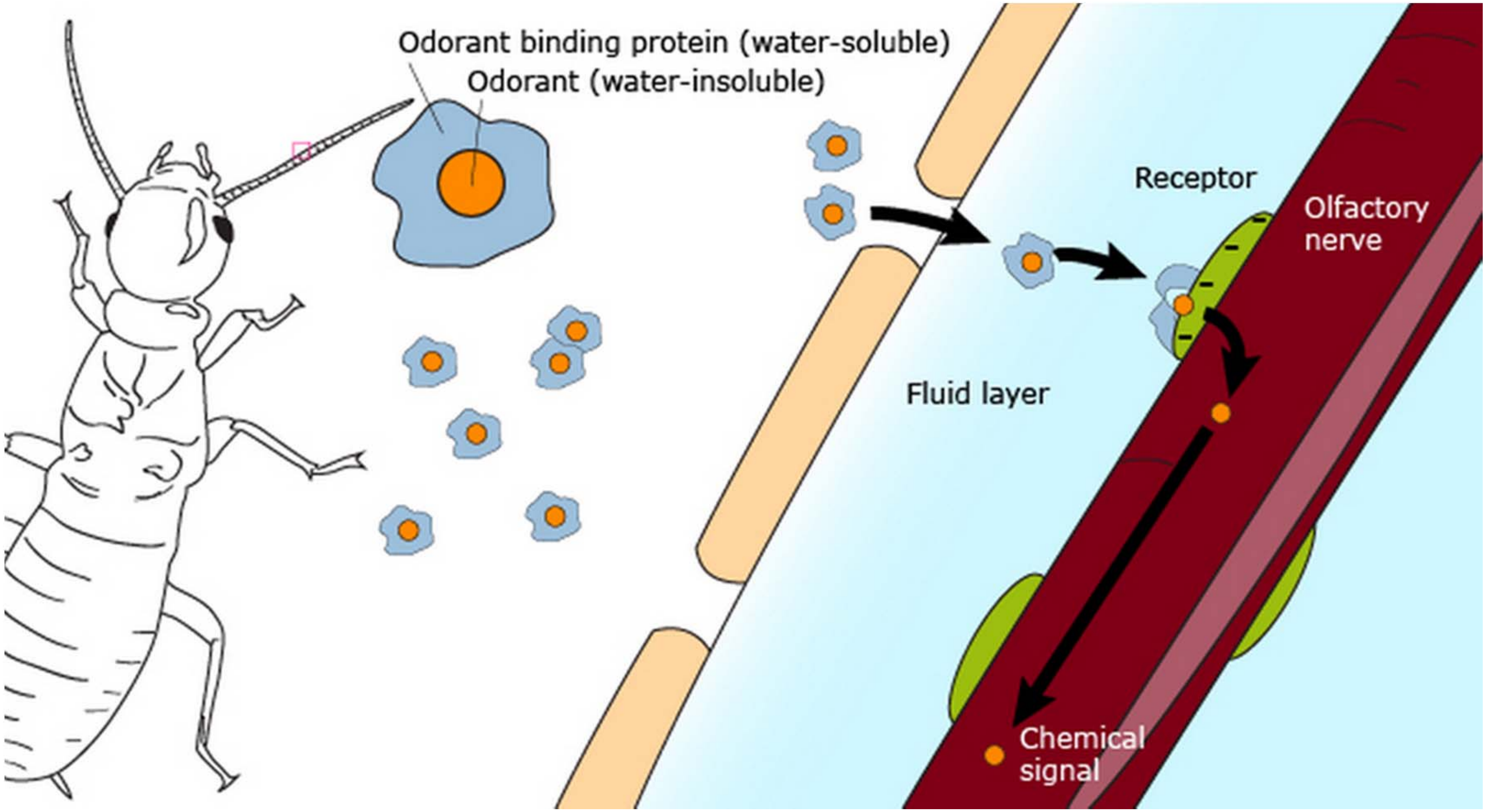
FlexSmell

Krishna Persaud e Elena Tucconi
The University of Manchester,



pOBP is a monomer of 157 amino acid residues (molecular mass of *ca.* 19 kDa) with a height of 38.04 Å and a base of 25.70 Å x 26.40 Å.

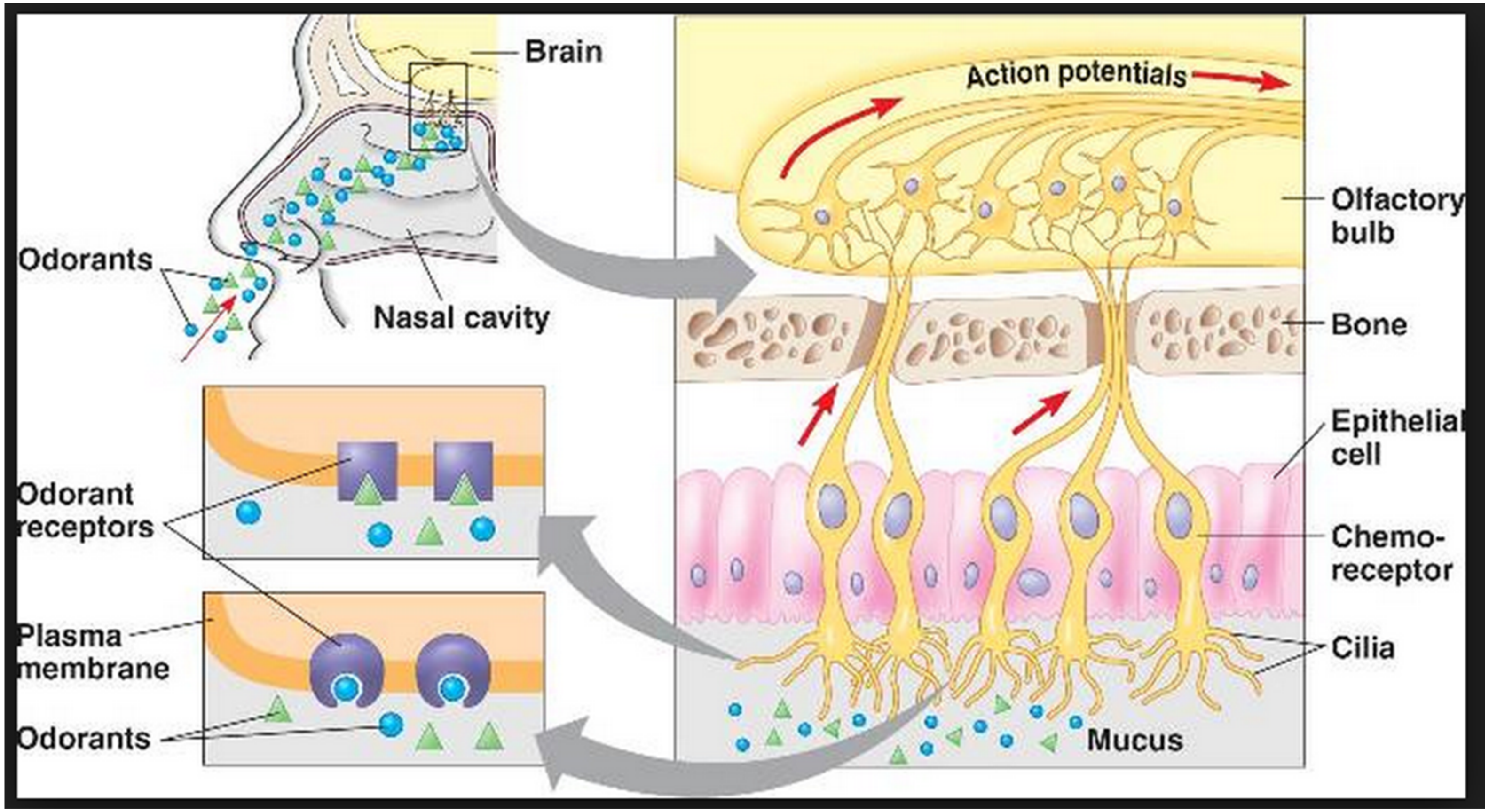
Odorant Binding Proteins



Shuttle odorant molecules
Odorant clearance mechanism

FlexSmell

vertebrate odorant system



FlexSmell

why odorant binding proteins ?

UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

- OBPs are present in high concentrations of mM range in mammalian nose and insects antennae
- Soluble proteins, can be expressed in bacterial systems at low-cost
- Highly stable – in ambient/hot conditions
- Binds reversibly to odorants

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EPFL ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

jpc

MANCHESTER 1824

VTT

Holst Centre

Carton Pack

BiOtest

FlexSmell

pig Odorant Binding Proteins (pOBP)

Pig odorant binding proteins (pOBP)

Poly(A) RNA Binding Protein PABP, PDB 1CVJ

The protein is characterized by a hydrophobic β-barrel cavity,

Differently from other OBPs such as the bovine one, pOBP b-barrel cavity is devoid of naturally occurring bound ligand

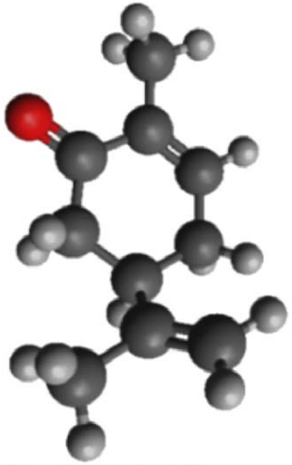
It bears a negative charge

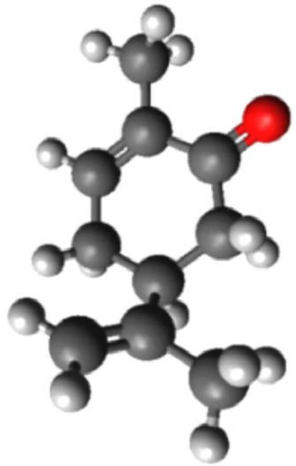
No study on chiral interactions; carvone enantiomers

FlexSmell

chiral ligand molecules

R(-)-Carvone





S(+)-Carvone

Caraway smell

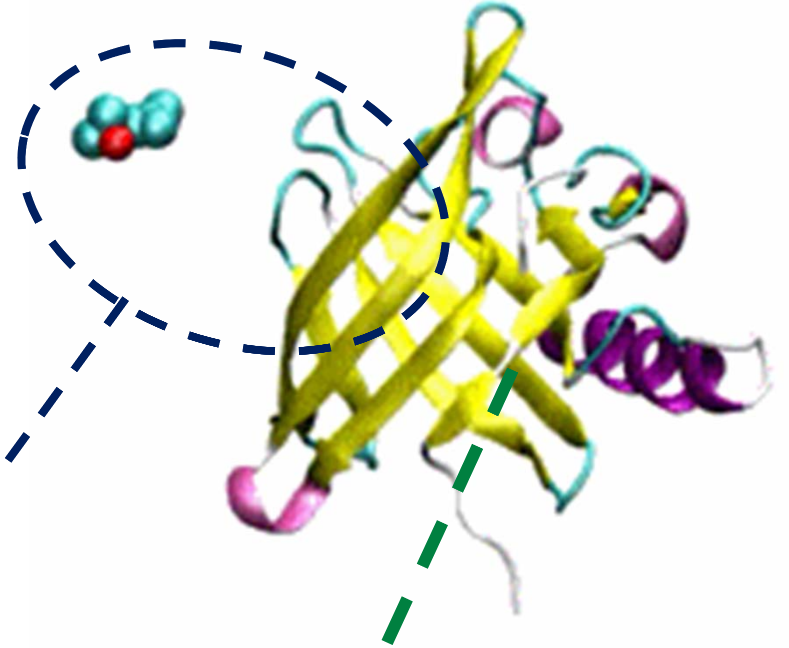
Spearmint Smell

hydrophobic volatile, neutral small molecules are perceived as spearmint or caraway flavours with human threshold for detections of 30 and 420 nM

dipole moment of 3.2-3.6 D associated with the ketone group

The binding process

FlexSmell

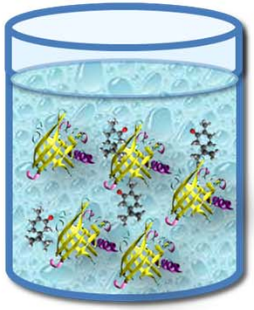


Ligand (L) + **Protein (P)** $\rightleftharpoons$ **Complex P-L**

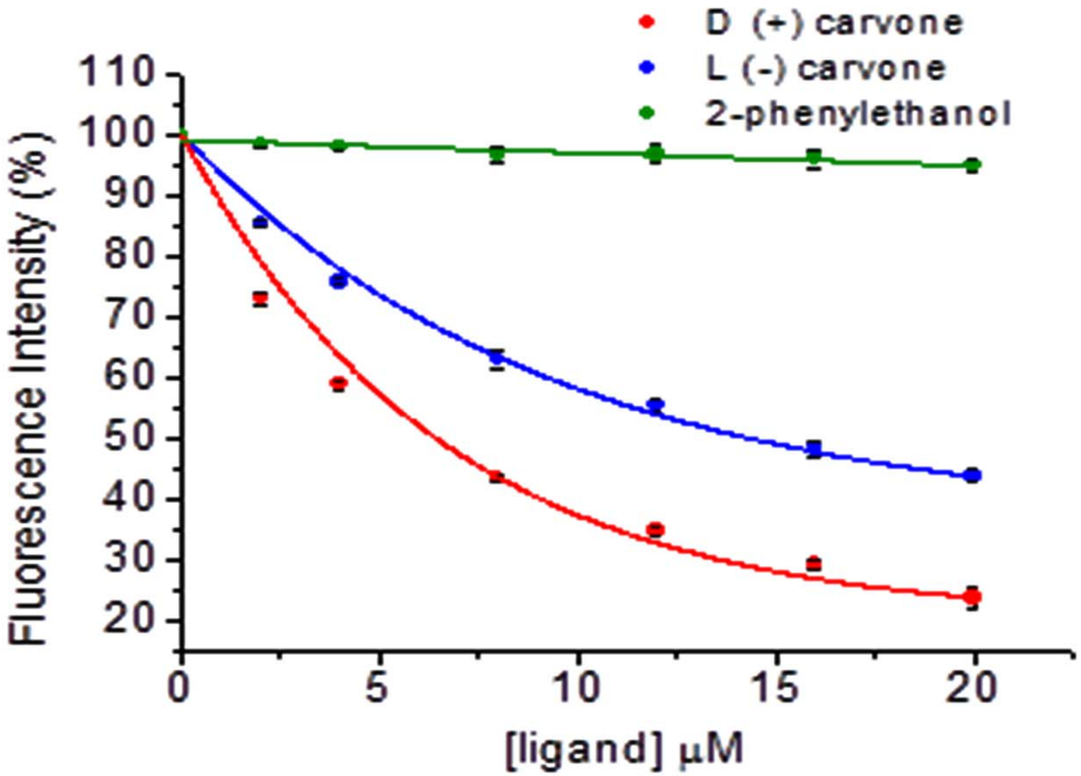
K_D

K_D = [L] @ half occupied protein sites

competitive fluorescent biding assay



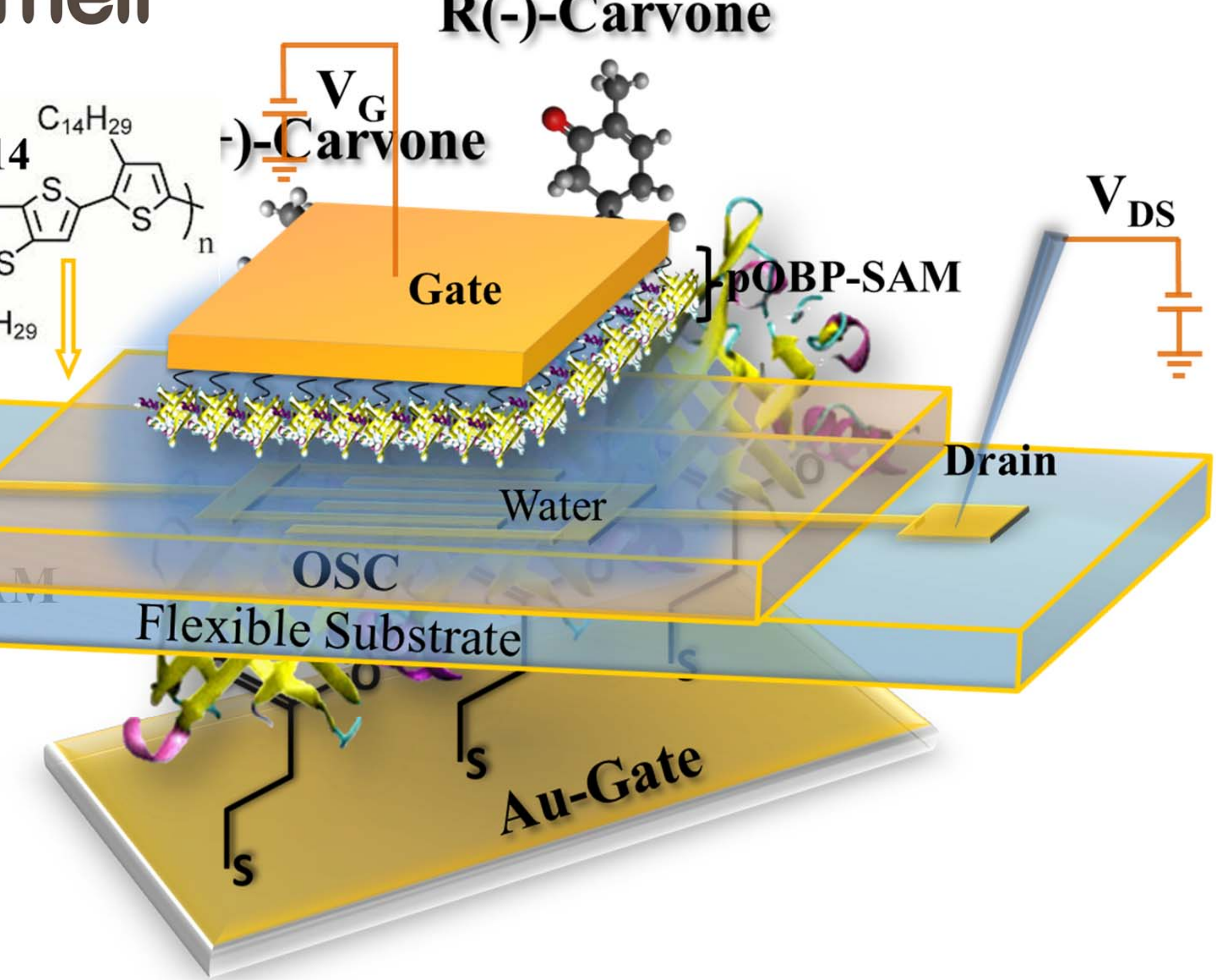
pOBP is chiral active but ESF < 2



$K_{sol}^{(+)} = 0.50 \pm 0.01$ μM and $K_{sol}^{(-)} = 1.22 \pm 0.05$ μM

2-phenylenthanol is shown to binds very weakly to pOBPs (K_D *ca.* 40 mM)

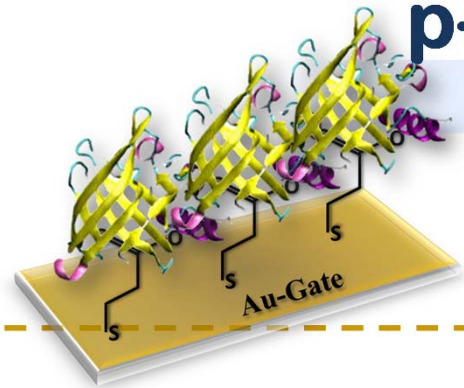
OBP in a water gated OFET sensor

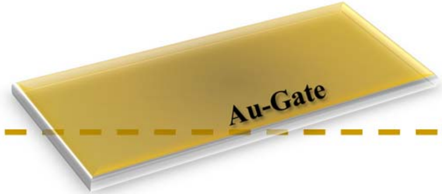


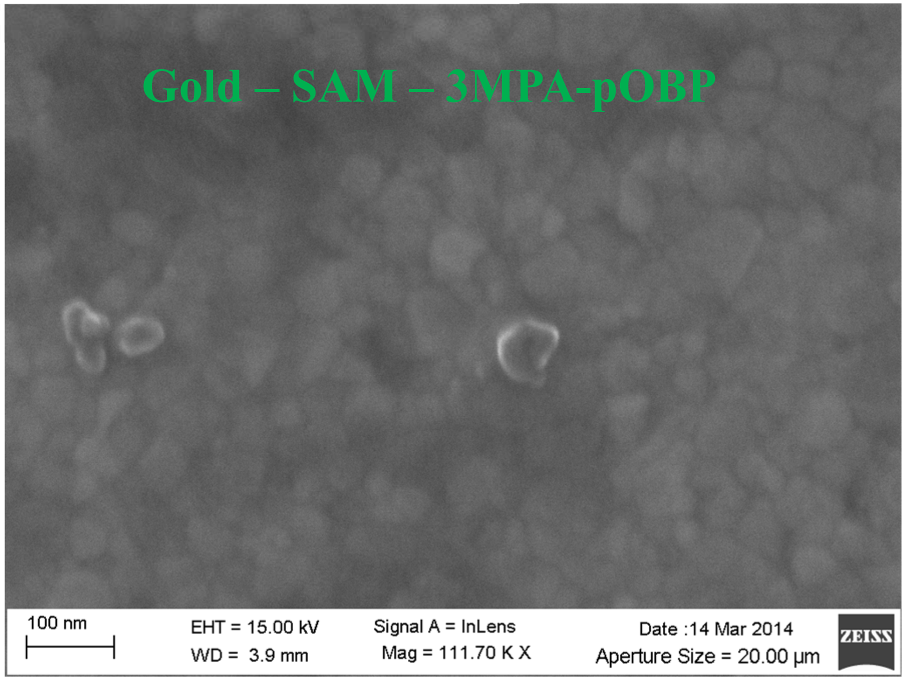
M. Y. Mulla

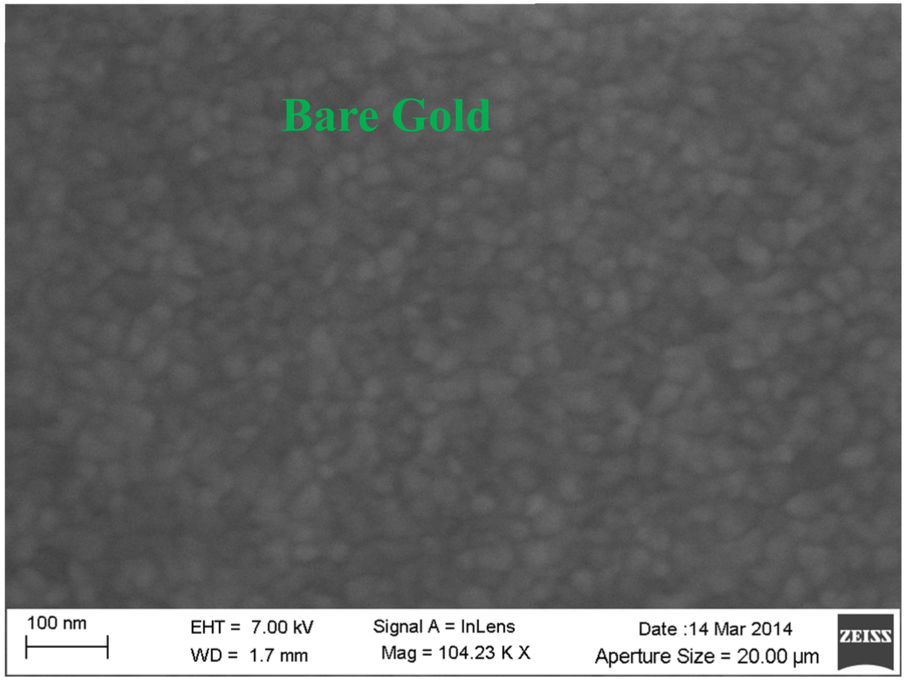
Mulla, M.Y. *et al.* *Nature Communications*, 2015, 6, 6010

p-OBP SAM SEM surface topography





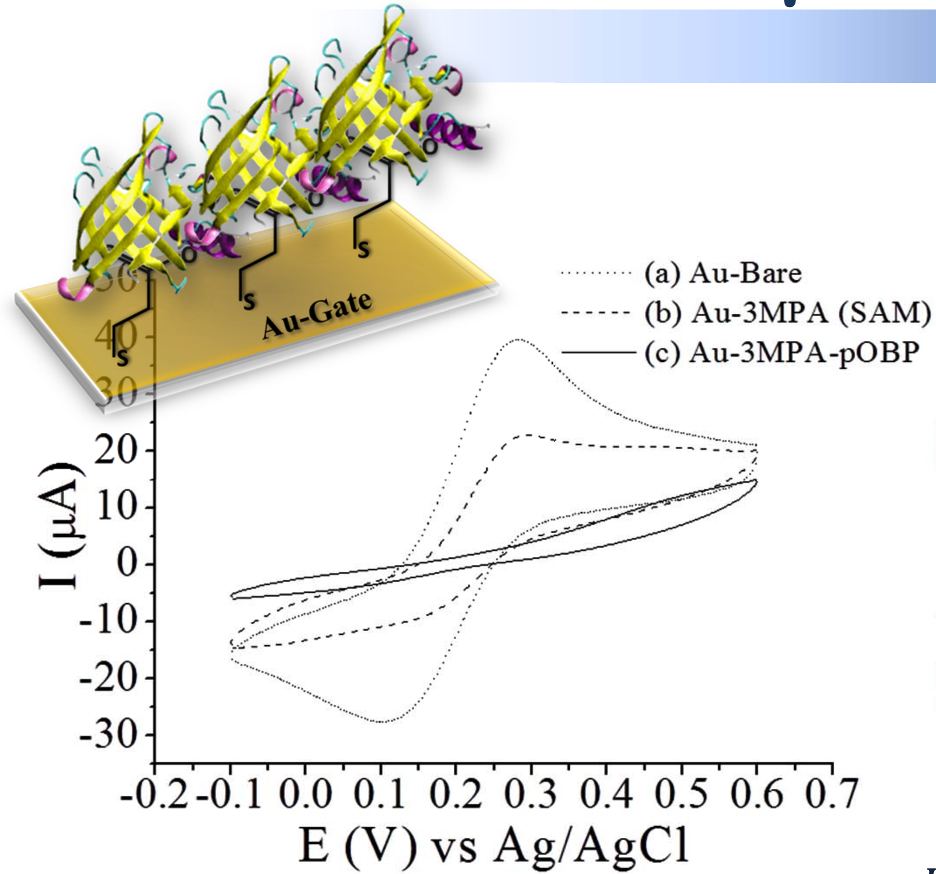


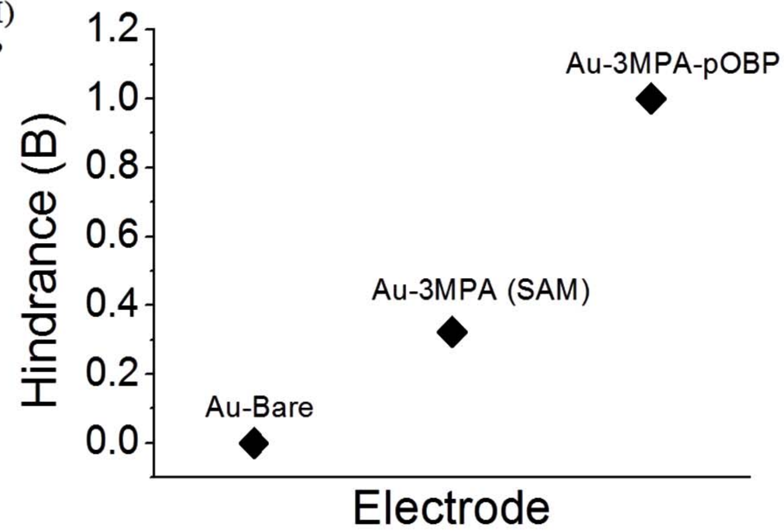


Cinzia Di Franco - CNR - Bari
Maria Vittoria Santacroce and Gaetano Scamarcio - University of Bari

Mulla, M.Y. *et al. Nature Communications*, 2015, 6, 6010

Electrochemical pOBP SAM characterization





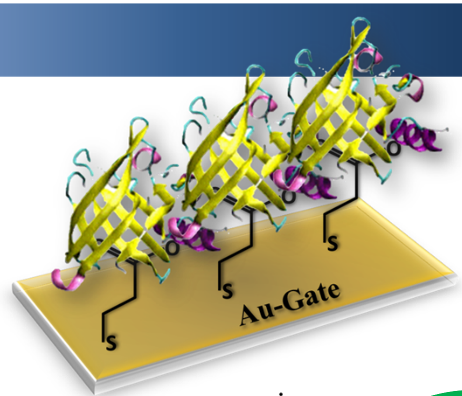
$$B = 1 - \left(I_0^{Fun} / I_0^{Au} \right)$$

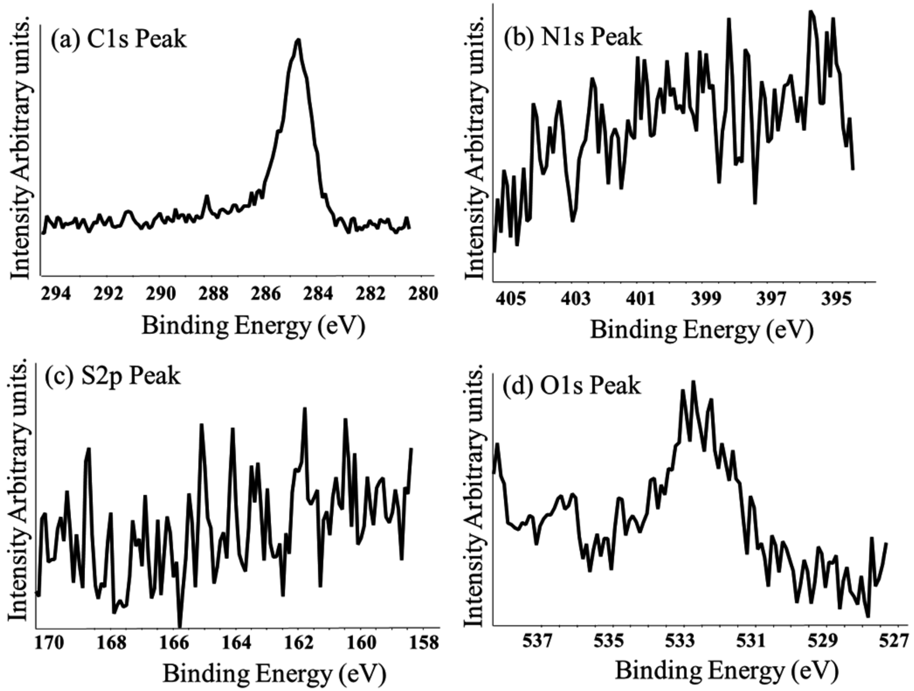
Where, I_0^{Fun} and I_0^{Au} are the oxidative peak currents obtained from the CV curves for functionalized electrode (3MPA alone and 3MPA-pOBP) and the bare Au electrode respectively

$K_4Fe(CN)_6$ electro-active

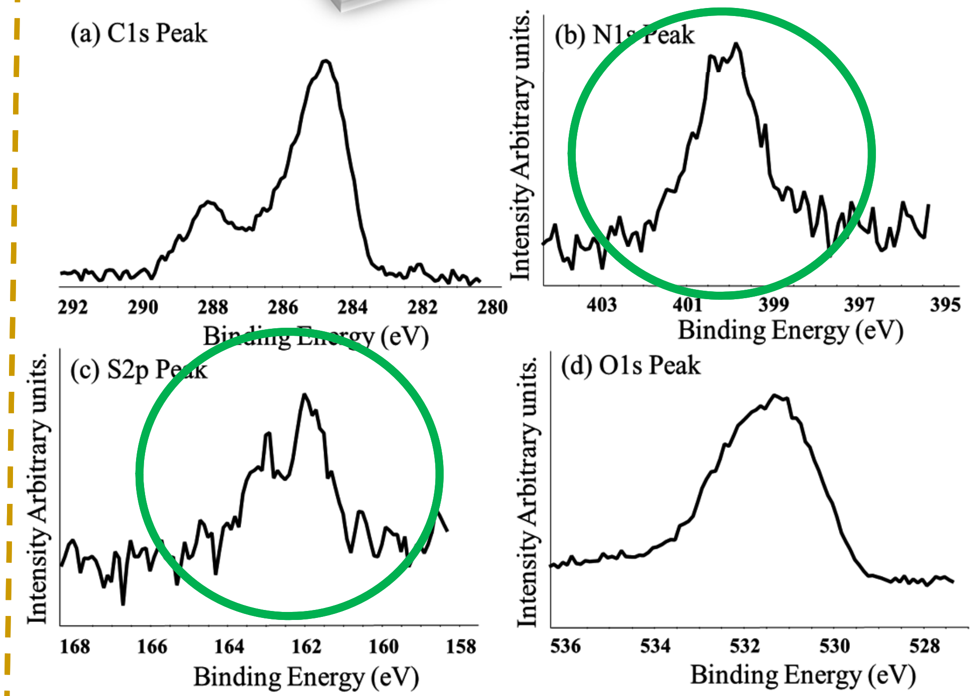
FlexSmell

XPS pOBP SAM characterization





bare gold electrode

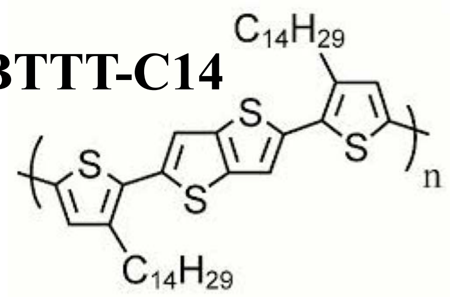


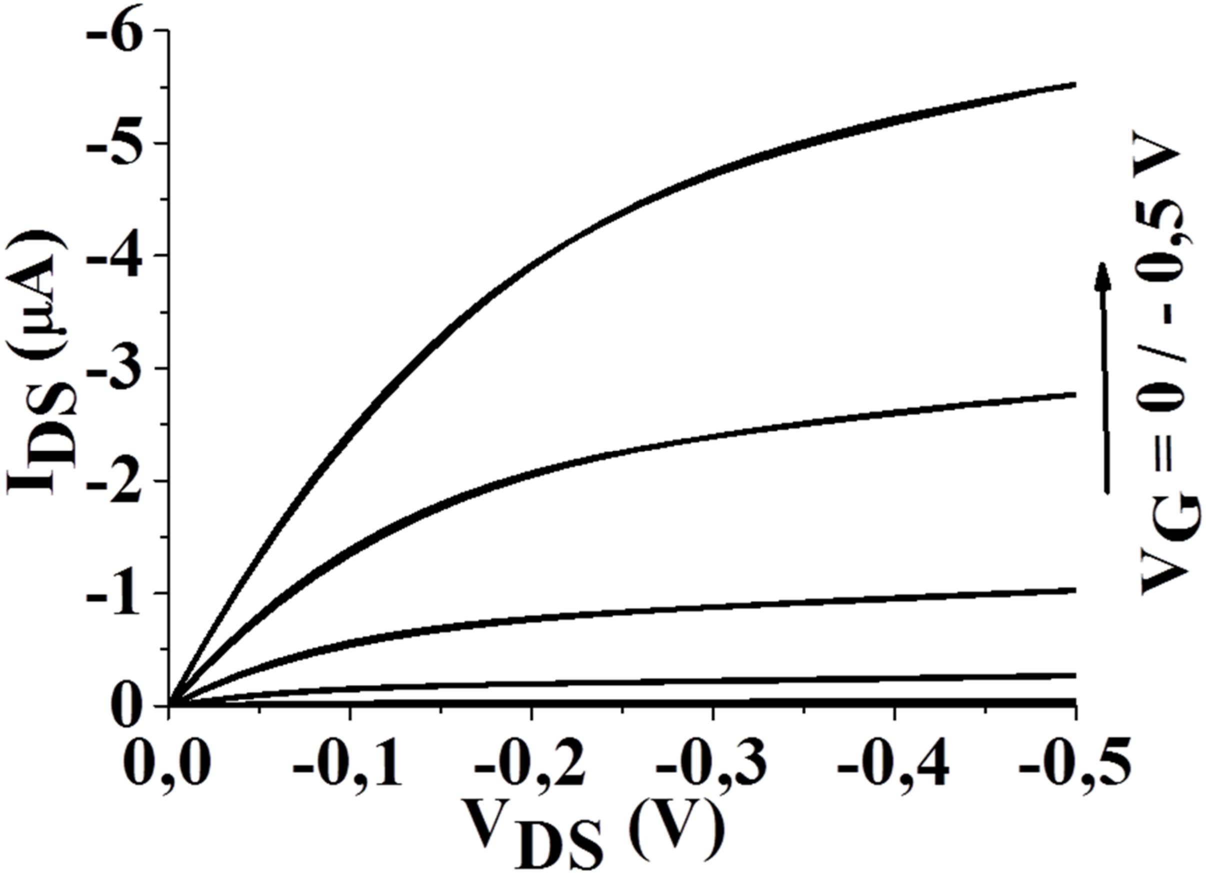
pOBP-SAM functionalized gold electrode confirming presence of (a) carbon 1s, (b) sulfur 2p, (c) oxygen 1s and (d) Nitrogen.

Dr. Nicoletta Di Taranto

I-V Characteristics

PBTTT-C14





V_T = -0.01 ± 0.06 V, *on/off* current ratio of 150 ± 110 and μ_{FET} = 1.1 ± 0.2 10^{-1} cm^2/Vs.

Sensing of tine neutral species with WGOFETs

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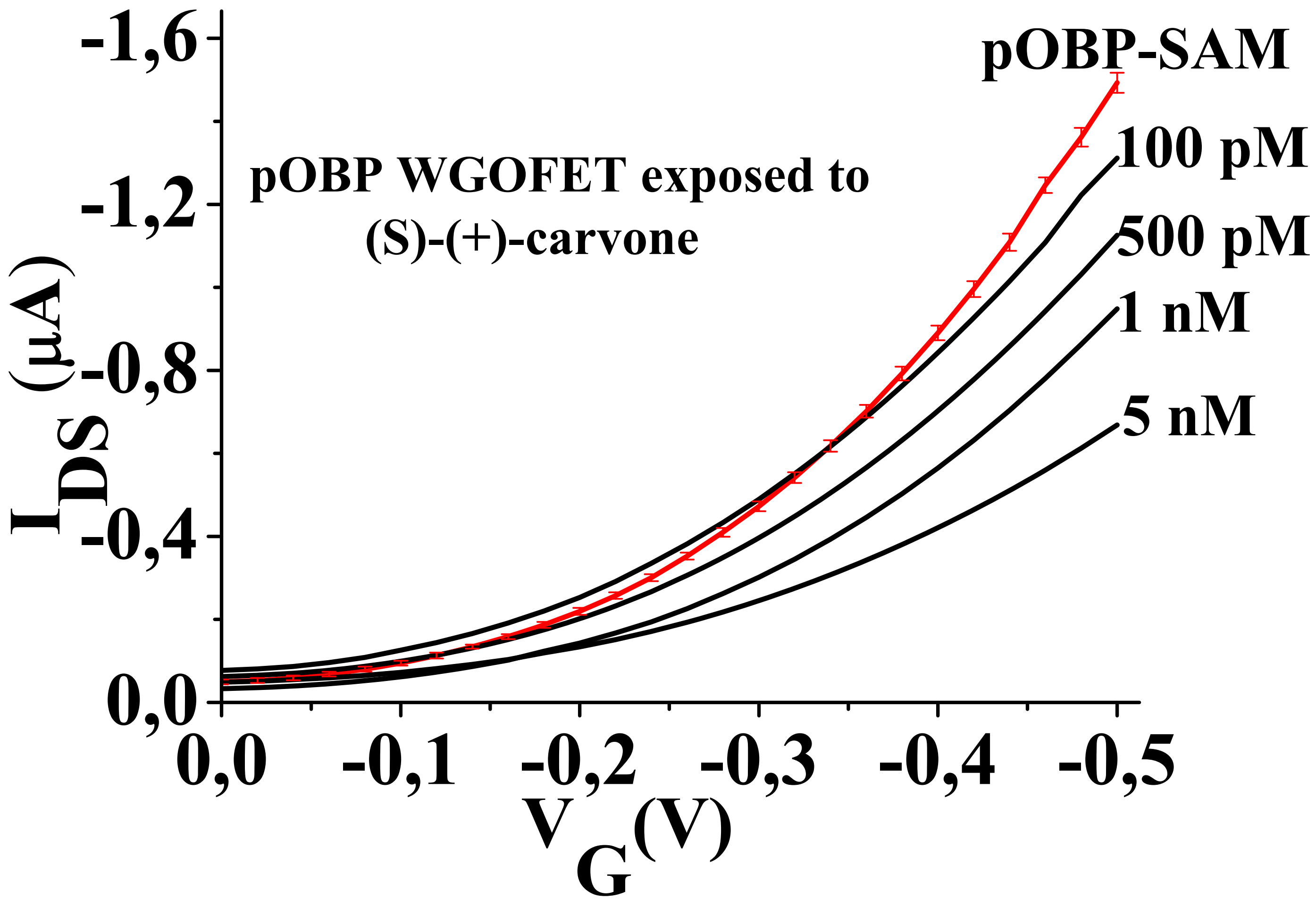

dose-curves with WGOFETs

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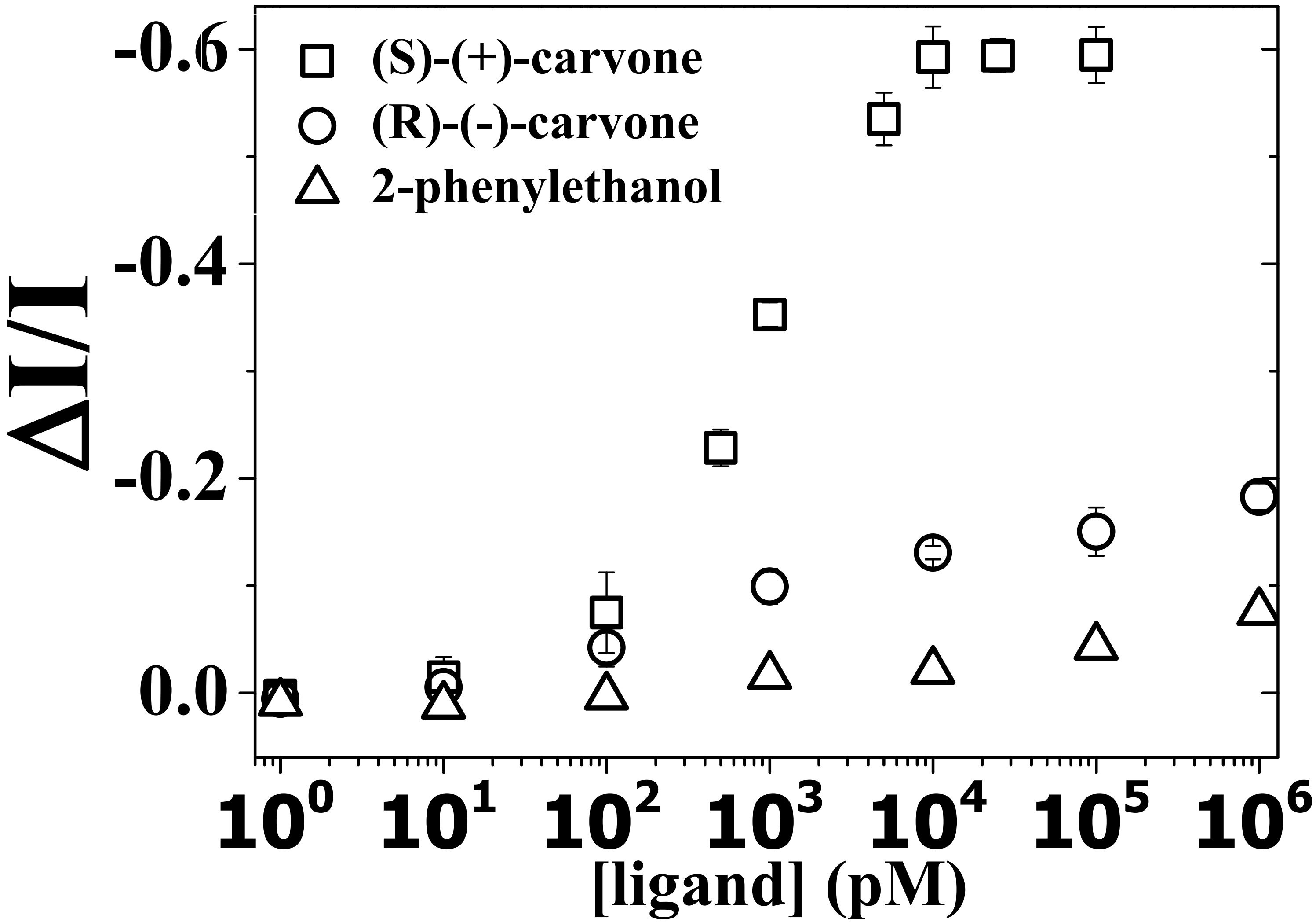
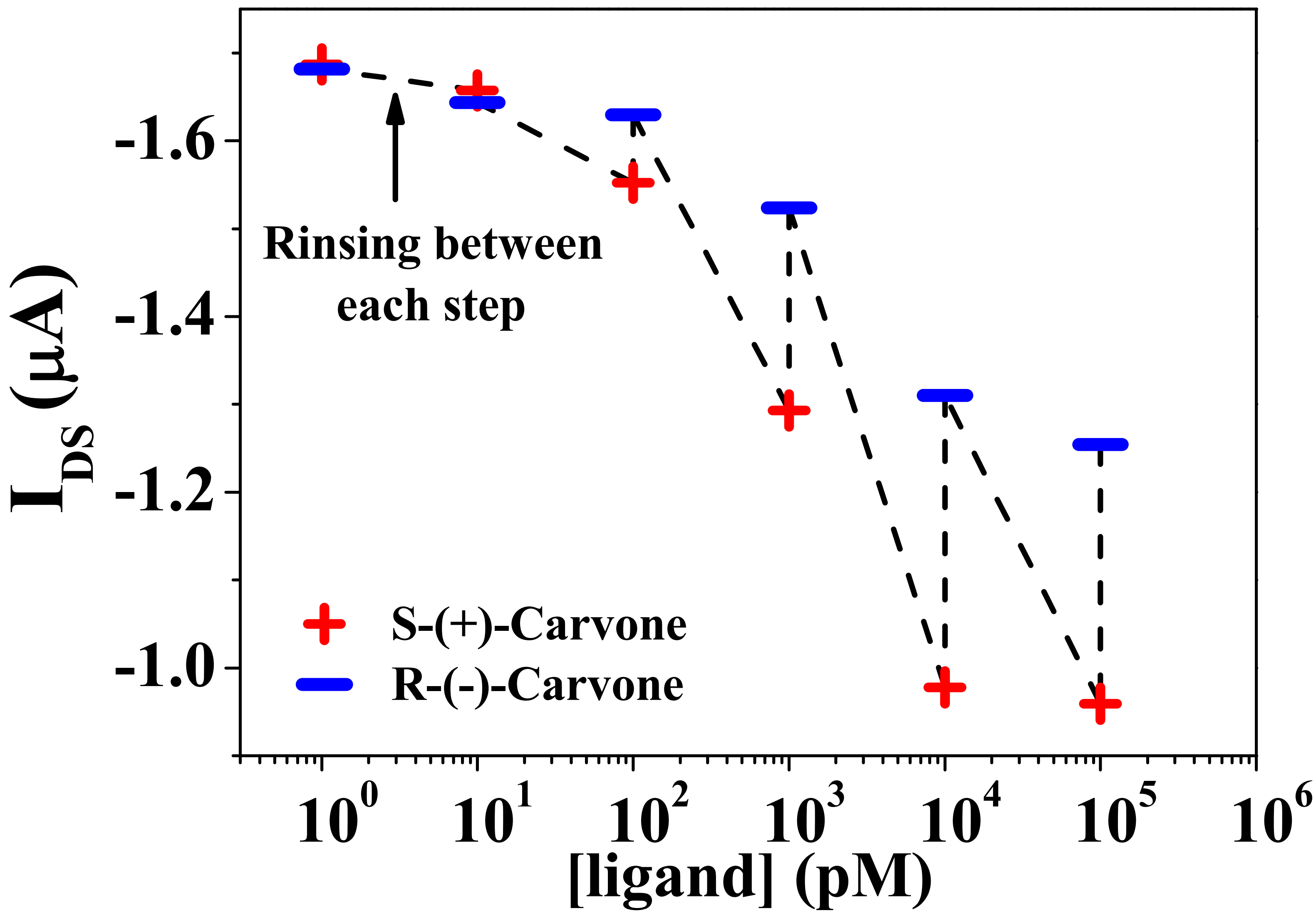
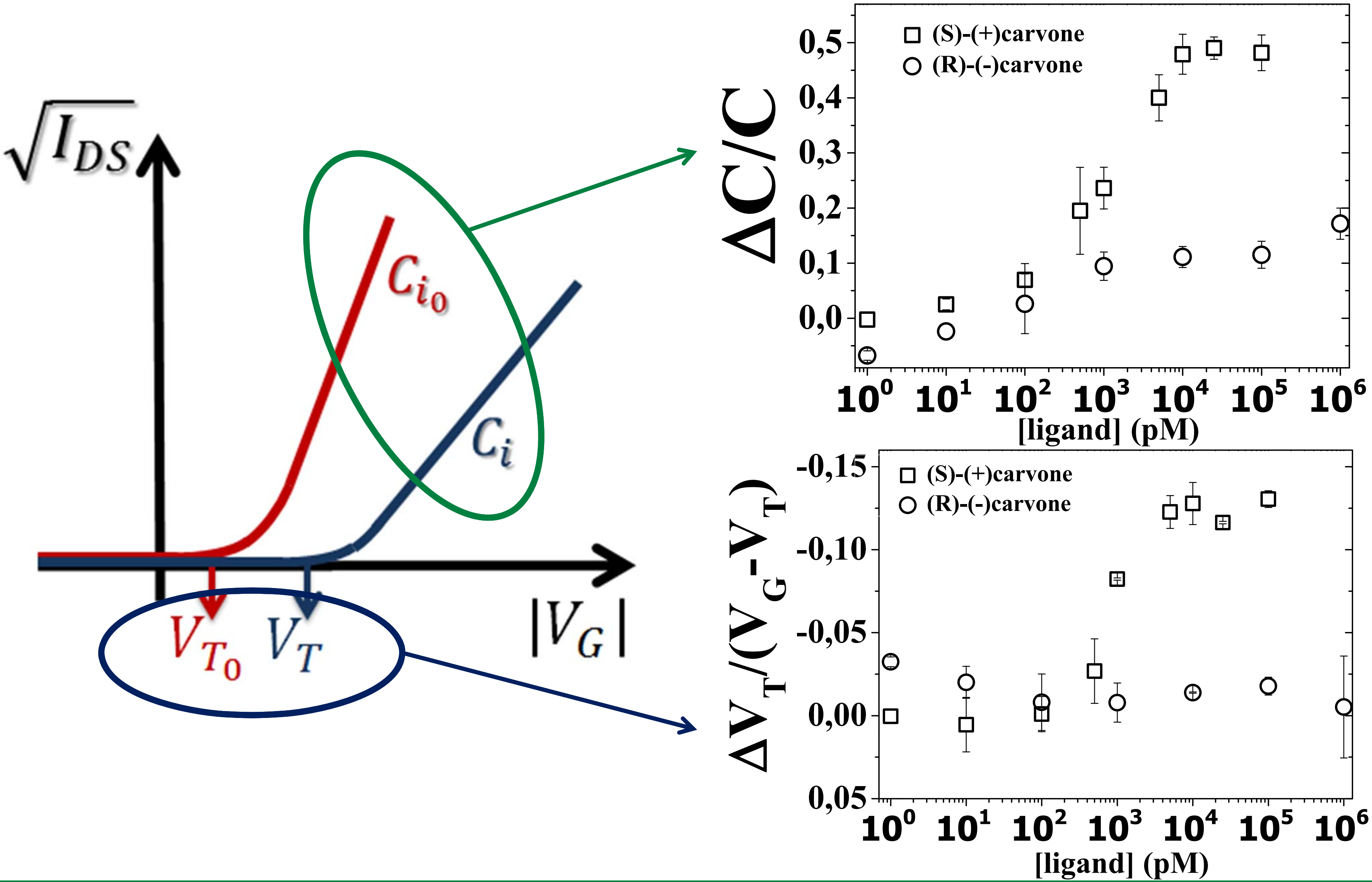


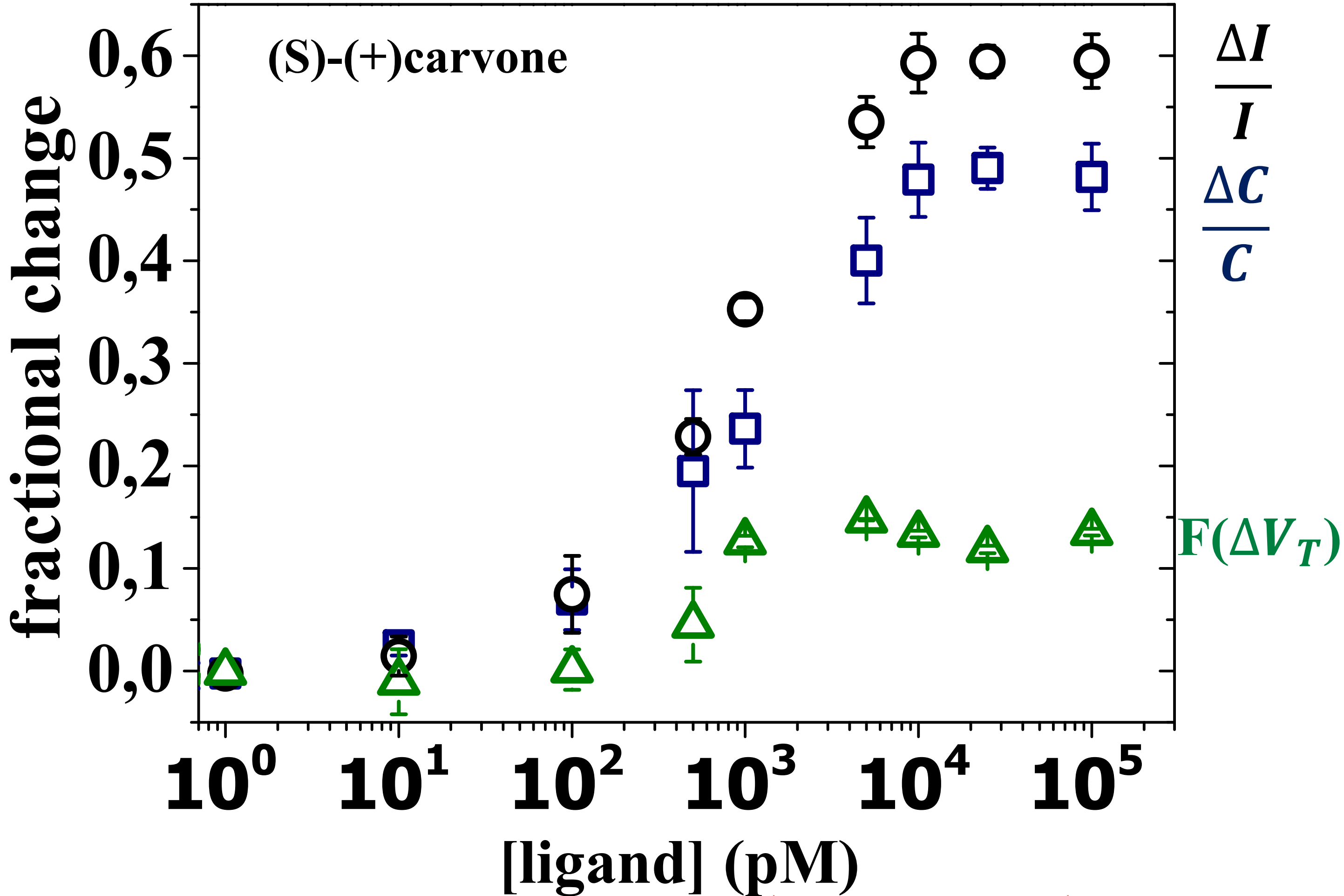
the two enantiomers on the very same gate



Decoupling capacitance and threshold voltage

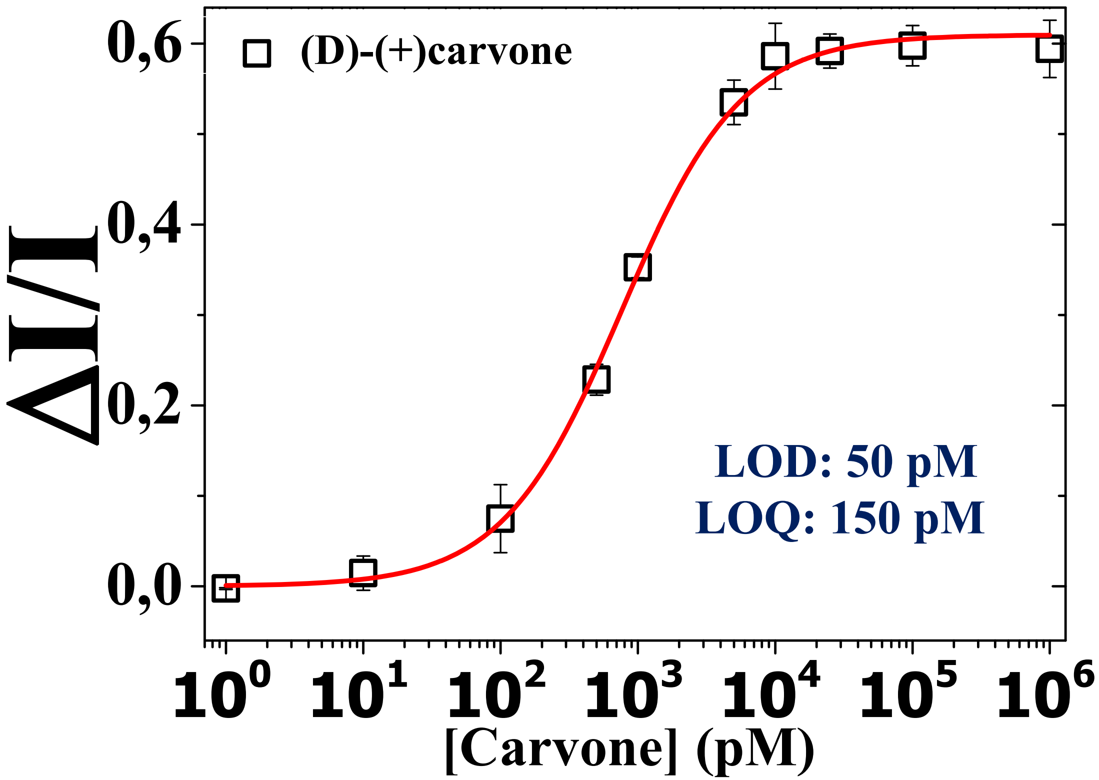


The response is dominated by capacitance



$$\frac{\Delta I}{I} \cong \frac{\Delta C_i}{C_i}$$

(S)-(+)carvone / pOBP complex



single-site Langmuir's isotherm

$$\frac{\Delta I}{I} = b_{MAX}\frac{[carv]}{K_{FET} + [carv]}$$

$K_{FET}^{(+)}$ of 0.81 ± 0.05 nM

$\Delta I/I^{(+)}$ as high as -60%; LOD: 50 pM

electronic OFET Bilayer configuration

A sensitivity-enhanced field-effect chiral sensor

LUISA TORSI[1,2]*, GIANLUCA M. FARINOLA[1], FRANCESCO MARINELLI[1], M. CRISTINA TANESE[1], OMAR HASSAN OMAR[3], LUDOVICO VALLI[4], FRANCESCO BABUDRI[1,3], FRANCESCO PALMISANO[1,2], P. GIORGIO ZAMBONIN[1,2] AND FRANCESCO NASO[1,3]*

[1]Dipartimento di Chimica, Università degli Studi di Bari, 70126, Bari, Italy
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*e-mail: torsi@chimica.uniba.it; f.naso@chimica.uniba.it

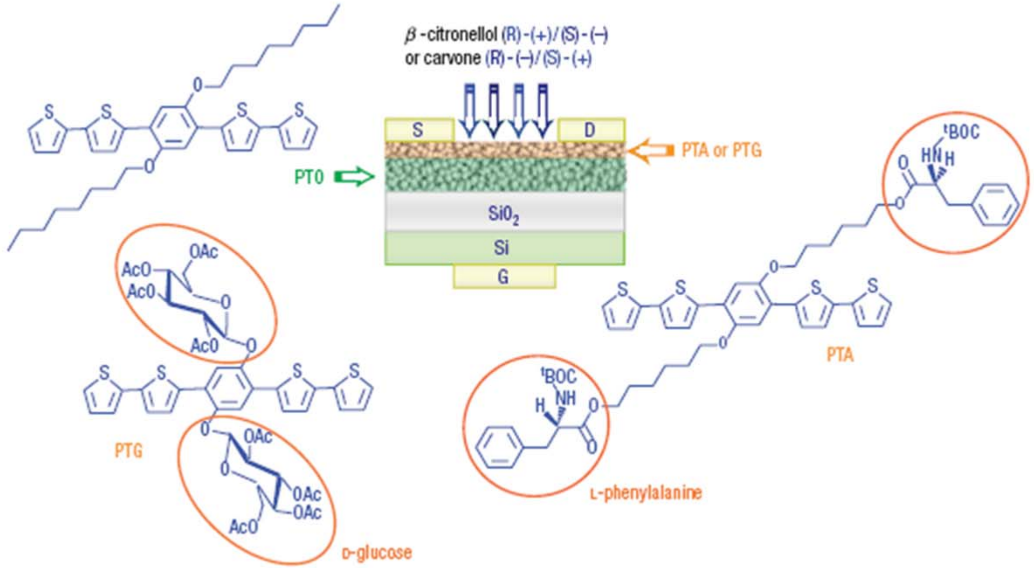
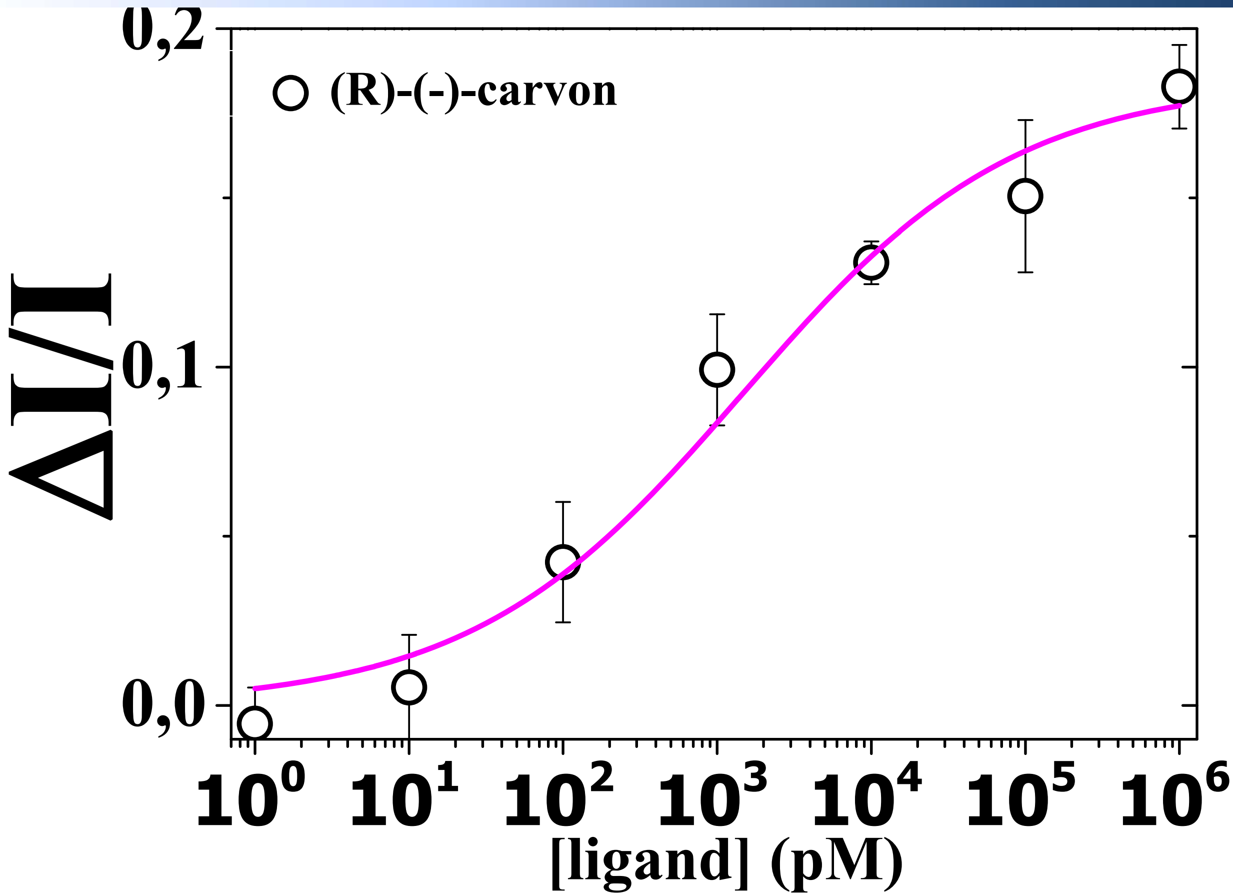


Figure 1 **Bilayer OTFT chiral sensor structure.** The transistor has a bottom-gate device structure that consists of a highly n-doped silicon wafer (resistivity 0.02–1 Ω cm^{-1})

(R)-(-)carvone / pOBP complex



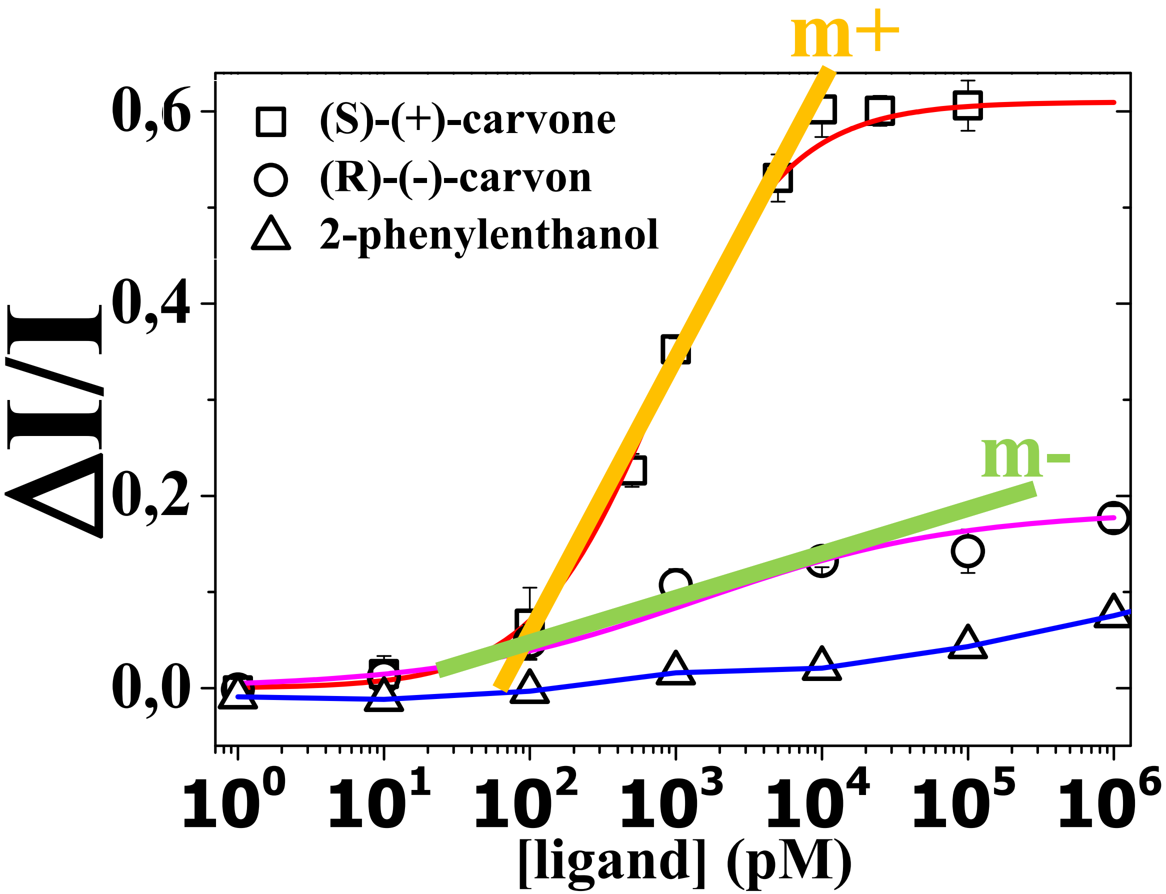
Hill's isotherm
α: level of cooperative

$$\frac{\Delta I}{I} = b_{MAX} \frac{[carv]^{\alpha}}{K_{FET} + [carv]^{\alpha}}$$

$K_{FET}^{(-)}$ of 20 ± 20 nM

$\Delta I/I^{(+)}$ of - 17 % ($\alpha = 0.5$ → non-cooperative binding)

enanthio-selectivity factor > 6



ESF = m+/m- = 6.3

markedly different levels of cooperativity and an exceptionally high ESF

The pOBP capacitance model

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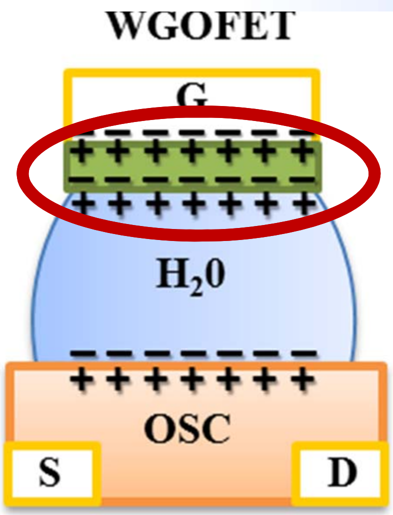
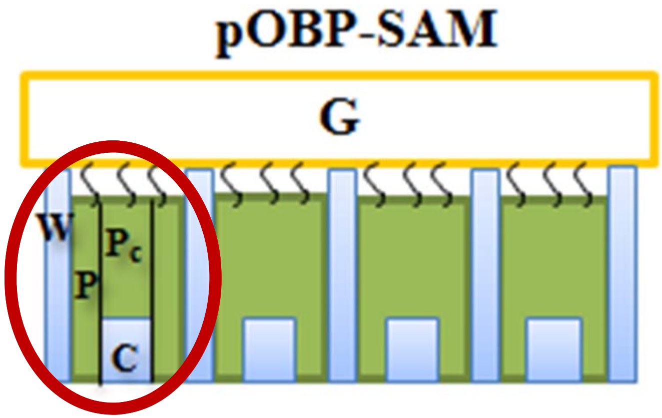
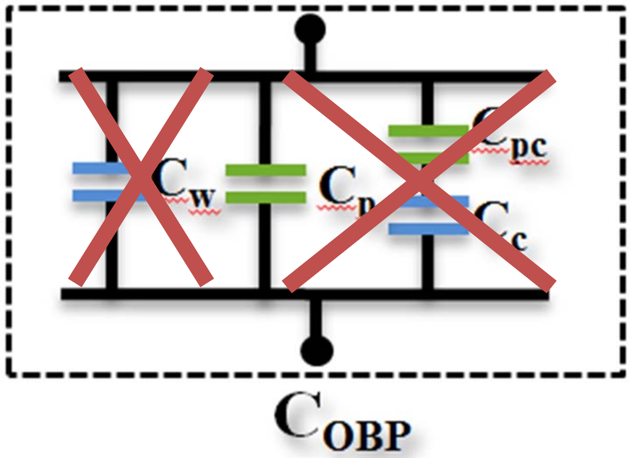






2.4 % of the total surface of the protein exposed to the solvent (~ 7 nm^2) it well accommodate a few water molecules

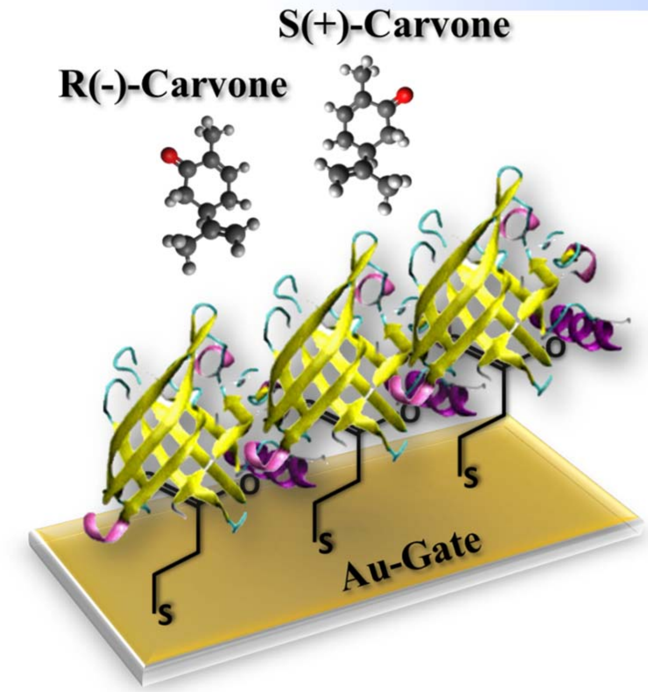
G. Lattanzi

R(-)-Carvone → $C_{OBP} \simeq C_w$

S(+)-Carvone → $C_{OBP} = C_p$

high dielectric percolative path, “water channel”

dissociation constant for 2D receptors



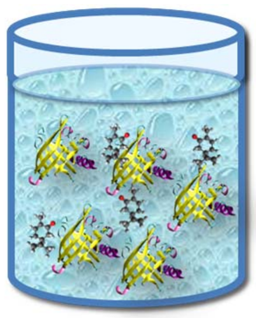
$$\Delta G^{0} = \mathrm{RT}\ln[K_{\mathrm{D}}]$$

Surface segregated OBP

$$\Delta G^{\circ}{}_{FET}{}^{(+)} = -(49.2 \pm 0.1)\ \mathrm{kJ/mol}$$

$$\Delta G^{\circ}{}_{FET}{}^{(-)} = -(41 \pm 2)\ \mathrm{kJ/mol}$$

OBP in solution



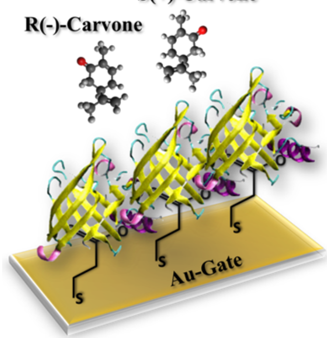
$$\Delta G^{\circ}{}_{sol}{}^{(+)} = -(36.00 \pm 0.05)\ \mathrm{kJ/mol}$$

$$\Delta G^{\circ}{}_{sol}{}^{(-)} = -(33.0 \pm 0.1)\ \mathrm{kJ/mol}$$

FlexSmell

the thermodynamic cycle

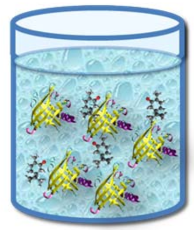
L = carvones P = pOBP e = gate free-electrons P-L=complex



L (sol) + P (gate) P-L(gate) + e(P-L)

– Δ_{imm}G(P) - $\bar{\mu}_e$(...mmG(P-L) + $\bar{\mu}_e$(P-L)

L (sol) + ... P-L (sol)



$$\Delta G^0_{FET} = \Delta G^0_{Sol} + \Delta E_F + W$$

$\Delta E_F = (\bar{\mu}_e(P{-}L) - \bar{\mu}_e(P) = -\ nF\Delta V_T$

W = Δ_{imm}G(P-L) – Δ_{imm}G(P)

binding surface work - surface tension

Financial support

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launching a new journal

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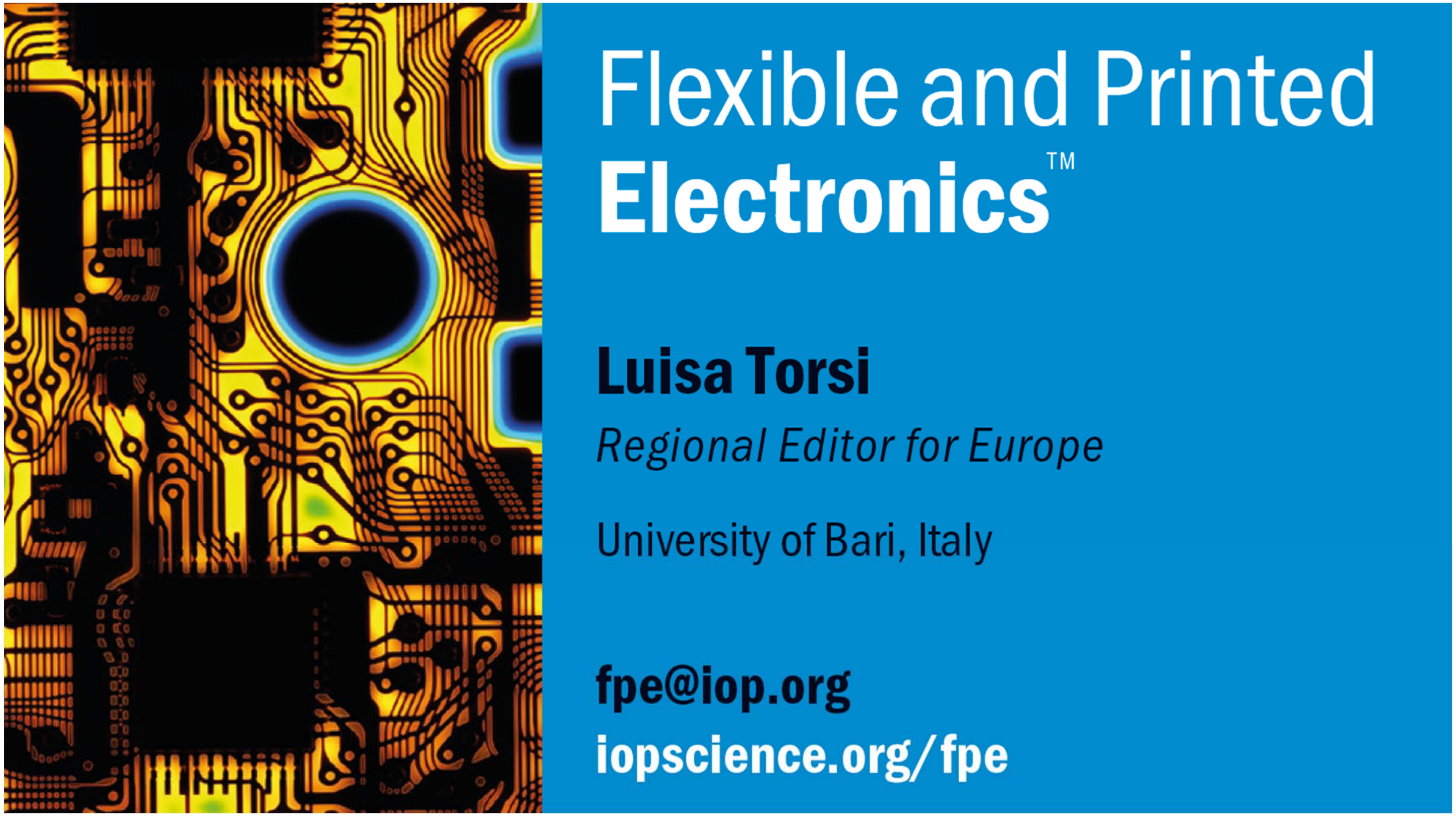

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team & principal collaborations