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Addressing the use of PDIF-CN_2 molecules in the development of n-type organic field-effect transistors for biosensing applications ☆

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ABSTRACT

Background: There is no doubt that future discoveries in the field of biochemistry will depend on the implementation of novel biosensing techniques, able to record biophysiological events with minimal biological interference. In this respect, organic electronics may represent an important new tool for the analysis of structures ranging from single molecules up to cellular events. Specifically, organic field-effect transistors (OFET) are potentially powerful devices for the real-time detection/transduction of bio-signals. Despite this interest, up to date, the experimental data useful to support the development of OFET-based biosensors are still few and, in particular, n-type (electron-transporting) devices, being fundamental to develop highly-performing circuits, have been scarcely investigated.
Methods: Here, films of *N,N′*-1*H*,1*H*-perfluorobutyldicyanoperylene-carboxydi-imide (PDIF-CN_2) molecules, a recently-introduced and very promising n-type semiconductor, have been evaporated on glass and silicon dioxide substrates to test the biocompatibility of this compound and its capability to stay electrically-active even in liquid environments.
Results: We found that PDIF-CN_2 transistors can work steadily in water for several hours. Biocompatibility tests, based on in-vitro cell cultivation, remark the need to functionalize the PDIF-CN_2 hydrophobic surface by extra-coating layers (i.e. poly-L-lysine) to favor the growth of confluent cellular populations.
Conclusions: Our experimental data demonstrate that PDIF-CN_2 compound is an interesting organic semiconductor to develop electronic devices to be used in the biological field.
General significance: This work contributes to define a possible strategy for the fabrication of low-cost and flexible biosensors, based on complex organic complementary metal-oxide-semiconductor (CMOS) circuitry including both p- (hole-transporting) and n-type transistors. This article is part of a Special Issue entitled Organic Bioelectronics—Novel Applications in Biomedicine.

1. Introduction

The structure of an organic field-effect transistor (OFET) is based on the presence of a semiconducting organic channel which is put in direct contact with two conducting electrodes (named source and drain) and is, instead, separated from a third electrode (gate) by a thin dielectric insulating barrier. During the OFET operation, the application of a voltage (V_{GS}) between the gate and the source electrodes allows the accumulation of charges at the organic–dielectric interface by exploiting the equivalent capacitive structure (electrostatic modulation) composed by the gate, the dielectric and the organic semiconductor [1]. In this way, the I_{DS} current flowing between the drain and the source electrodes, as a function of the corresponding drain-source (V_{DS}) voltage, can be largely modulated by varying V_{GS}. OFET are commonly employed as the basic building blocks for the development of complex electronic systems which, thanks to the mechanical and chemical properties of the organic compounds, can be fabricated through low-cost solution techniques even on flexible and large-area substrates.

During the last 10 years, OFET have been receiving an increasing interest also for their possible application in the field of chemical

Abbreviations: OFET, organic field-effect transistors; CMOS, complementary metal-oxide-semiconductor; LUMO, lowest unoccupied molecular orbitals; PDIF-CN_2, *N,N′*-1*H*,1*H*-perfluorobutyldicyanoperylene-carboxydi-imide; PDI8-CN_2, *N,N′*-bis(n-octyl)-1,6-dicyanoperylene-3,4:9,10-bis(dicarboximide); CHO, Chinese hamster ovary; DMEM, Dulbecco's modified medium; SiO_2, silicon dioxide; HMDS, hexamethylsiloxane; FBS, fetal bovine serum; FDA, fluorescein diacetate; PI, propidium iodide; PBS, phosphate buffered saline; MOSFET, metal-oxide-semiconductor field-effect-transistors; LSD, least significant difference; AFM, atomic force microscopy

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and biological sensing. Indeed, it was shown that the active layer of an organic transistor can act both as electrically-active channel and sensitive area [2]. Furthermore, as for other transistor-based sensors, the sensitivity degree of an OFET can be improved by choosing an appropriate working point as a function of the applied V_{DS} and V_{GS}.

However, up to date, the perspective to realize innovative biosensors based on organic transistors has been pursued by various research groups considering only hole-transporting (p-type, where the charge accumulation takes place under the application of negative V_{GS}) compounds, both in form of small molecules (i.e. pentacene) [3–5] or conjugated doped-polymers (i.e. PEDOT-PSS) with intrinsic electronic–ionic hybrid conduction features [6–8].

On the other hand, despite the scarce attention so far received, the identification of electron-transporting (n-type) organic semiconductors, suitable to be applied in the biological sensing and to be combined with the already investigated p-type compounds, is of considerable importance. This, indeed, should open the way to the fabrication of organic bio-sensing devices based on complementary metal oxide semiconductor (CMOS) circuits which show improved performances in terms of higher noise immunity and lower static power consumption in comparison with n-type-only or p-type-only circuits [9]. Moreover, innovative sensing schemes can be achieved by using CMOS circuits instead of discrete transistor sensors [10,11].

To this aim, among the electron-transporting materials synthesized in the last years, perylene carboxylic diimide (PDI) derivatives are an interesting class of compounds, thanks to their capability to combine excellent self-assembling properties with high charge carrier mobility, enhanced electrical stability in air and very effective charge injection achievable using high work function metals (i.e. gold) as electrodes [12,13]. In particular, the robustness of the electrical transport under ambient conditions of these molecules is given by the low-lying values (down to −4.5 eV) of their lowest unoccupied molecular orbital (LUMO) levels, being the energy levels associated to the electron motion [12].

All these features motivated a growing attention by the scientific world toward these materials and a wide number of perylene diimide compounds, obtained by considering different substituent chemical groups (see Fig. 1) in the bay (R_1, R_2) or side (R_3) regions of the basic perylene molecular core, have been analyzed. It is also interesting to remember that perylene molecules have been employed for long time in the pigment industry, with a consolidated tradition in the cosmetics sectors, where the low toxicity of these compounds have made possible their utilization in a vast number of products (lipsticks, hair dyes, etc.) [14]. These applications have consequently demonstrated in a practical way the capability of these compounds to be brought safely in contact with human skin and tissues. In combination with the interesting electrical performances, this last property seems to immediately suggest the possibility that perylene diimide molecules are of real interest for the development of innovative electrically-active devices able to operate as interfacing systems with the living matter.

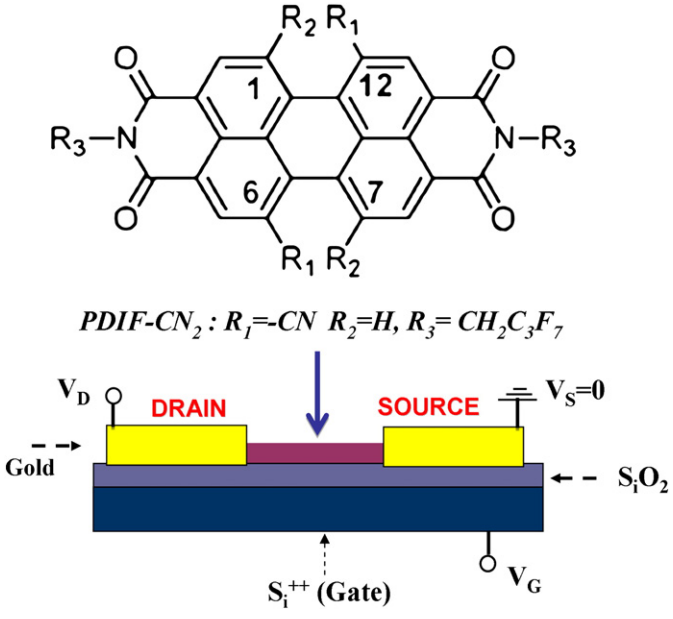

Fig. 1. (Top) Molecular structure of perylene diimide molecules and (bottom) transistor configuration used in this work.

In a previous paper [15], some of the authors of this article have reported, for the first time, on the biocompatibility properties and the electrical operation in aqueous environments of an electron-transporting compound (i.e. *N*,*N*′-bis(n-octyl)-1,6-dicyanoperylene-3,4:9,10-bis(dicarboximide) or PDI8-CN_2), belonging to the family of the perylene diimide derivatives. Here, our work was focused on a different perylene molecule, namely *N*,*N*′-1*H*,1*H*-perfluorobutyldicyanoperylene-carboxydi-imide (PDIF-CN_2), which molecular structure is indicated in Fig. 1, differing from that of PDI8-CN_2 for the presence of fluorinated side chains in spite of simple alkyl groups. Up to date, PDIF-CN_2 is the perylene compound displaying the lowest LUMO level ($E_{LUMO} = -4.5$ eV) and its electrical properties are considerably better than PDI8-CN_2, in reason of the closer molecular packing properties related to the presence of the fluoroalkyl side chains. Charge carrier mobility in PDIF-CN_2 films, indeed, is enhanced by about one order of magnitude in comparison with PDI8-CN_2 [16]. Today, PDIF-CN_2 is one the most interesting compounds for organic electronics application also thanks to the possibility to achieve high quality single crystals [17] and both evaporated [16] and solution-processed [18] films.

In this paper, we have fabricated low-voltage operation field-effect transistors based on evaporated PDIF-CN_2 films, demonstrating that they are able to work in aqueous ambients such as bi-distilled water and Dulbecco's modified medium (DMEM), which is commonly employed for cellular in-vitro cultivations. The main factors affecting the operational lifetime of the investigated devices in these liquids are discussed. The capability of PDIF-CN_2 films to allow the survival and the proliferation of cells on their surface is also assessed by specific experiments involving Chinese hamster ovary (CHO) cells, an immortalized cell line widely employed in the biological field as cellular model.

2. Materials and methods

2.1. PDIF-CN_2 film evaporation and transistor fabrication

PDIF-CN_2 (or ActivInk N1100™) powder was purchased from Polyera Corporation and used without any further purification [19]. For the transistor fabrication, PDIF-CN_2 films were evaporated on 1 cm^2 substrates with a multilayer structure, composed of a thick (500 μm) layer of highly doped Silicon (Si^{++}) working both as gate electrode and substrate, a second layer of thermally grown silicon dioxide SiO_2 dielectric layer with 35 nm of thickness, interdigitated (source and drain) gold electrodes (bottom-gate bottom-contact configuration). In this regard, it should be remembered that the bottom-gate bottom-contact configuration, employing very thin dielectric layers, is presently the most commonly used device structure to assess the operation of organic transistors in aqueous environments [20].

In our devices, the source and drain electrodes were patterned by optical photolithography starting from 100 nm thick gold layers evaporated on thin (~3 nm) chromium films acting as adhesive layer. For all the PDIF-CN_2 devices, the w/L ratio between the width and length of the active channel was about 550, with L being 20 or 40 μm. For all the devices, any single electrode finger in the interdigitated layout was 20 μm wide. More detailed information about the transistor layout can be found