Bio-hybrid Optoelectronic interface for stimulation and characterization of biological tissues and cells

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In the last decades, neural science and engineering, diagnostics, therapy, wearable and implantable devices based on bio-organic electronics are a rapidly growing field. One of the last exciting trends is the electrical characterization of biological systems and the stimulation of cells via organic semiconducting or conducting materials for novel biomedical applications, tissue engineering, regenerative medicine.
Bioelectricity is present in electrically excitable cells such as neurons and in all other cell types in form of electric fields, ionic currents, redox processes and potential differences [1]. Endogenous and non-endogenous bioelectronics signals are responsible for regulating gene transcription and for opening/closing ionic channels in cells. These signalling pathways are involved in different cellular activities such as migrations, differentiations, morphogenesis [2][3]. Moreover, some biomolecules oxidized or reduced by an exchange of electrons are also involved in signalling processes in response to infections or inflammation and have a major role in nutrient metabolism and tissue regeneration [3] [4].
At present, the development of more biocompatible and efficient interfaces between living biological tissues/cells and electronic devices is one of the most challenging tasks for science and technology.
Our focus is the design and realization of a novel bio-hybrid device proposed as a new strategy for the optical-electronic characterization and control of biological tissues and cells. The neo-fabricated device is based on light sensitive organic semiconducting polymers that under light stimulation provide perturbation/excitation of biological cell systems with lower invasiveness respect to electro-mechanical stimulation. It is presented in a form of a sandwich structure (*Fig.1*) where two transparent planar electrodes consisting of poly(3-hexylthiophene) (P3HT) thin film (100nm thickness) spin coated on FTO|Glass (W.E.) and Platinum screen printed on FTO|Glass (C.E.) define an inner chamber for biological tissues deposition and cell cultures. The device is designed for stimulation/recording of biological systems immersed in a physiological solution (DPBS) or culture medium. In particular, we are aiming to study the extracellular potential variation of biological tissues and cells interfaced with organic polymer, before and after light stimulation. Currently, we are focusing on human dental pulp stromal cells (DPSCs) (non-electrically excitable cells) and explanted retinas (electrically excitable tissue).
Preliminary results confirmed the possibility to carry out cell cultures (performed at 37 °C in an atmosphere of 5% CO_2 in air) on the polymer surface without evident alterations in cell viability and morphology, unless an evident delay in the initial phase of cell adhesion on the polymer that can be improved by the use of adhesive molecules (e.g. poly-L-lysine, gelatine, fibronectin). Moreover, the culture conditions contributed to changes in the growth rate of DPSCs seeded on the polymer compared with control cultures. Indeed, the proliferation rate was lower both at 3 and at 7 days of culture, suggesting a slowdown of cell's proliferative capacity on the polymer (*Fig.2)* and, therefore, the need to improve culture microenvironment. On the other hand, it is also known that the growth rate can physiologically decelerate in the presence of extracellular stimuli.

Promising preliminary results were also obtained by analysing the electrical activities of the developed device (photocurrent or photovoltage generated by working in open circuit or short circuit condition, respectively) (*Fig.3)*.
The physical model underlying the photostimulation process (*Fig.4*) is a capacitive mechanism with charges displacement in the polymeric surface and ions redistribution in the electrolyte.
A deeper investigation of the interaction between electrolytic solutions, biological systems and electroactive materials is certainly needed. Moreover, we aim to optimize the protocol of light stimulation and photocurrent generation in order to modulate cell proliferation and differentiation, morphology and cell fate for the creation of customized 3D tissue-like structures for bioelectronics regenerative medicine applications.

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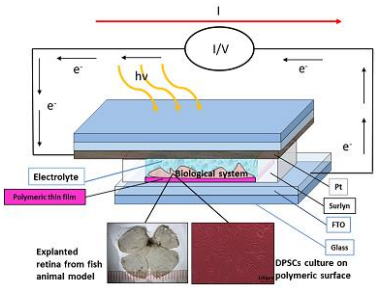

Figure 1. Schematic representation of the light-stimulating/recording device with retinal tissue deposited or cell cultured into it.

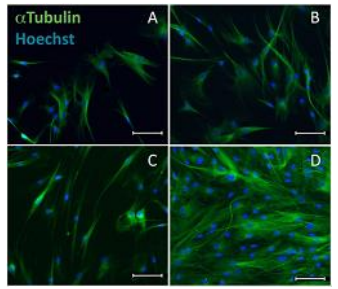

Figure 2. DPSCs stained for αTubulin. Cells cultured on the polymer for 3 and 7 days, respectively (A and B) compared with control cultures at the same time points (C and D).

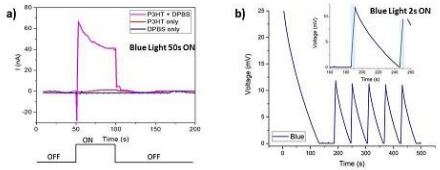

Figure 3. Photocurrent (a) and photovoltage (b) directly recorded by the device following light stimulation.

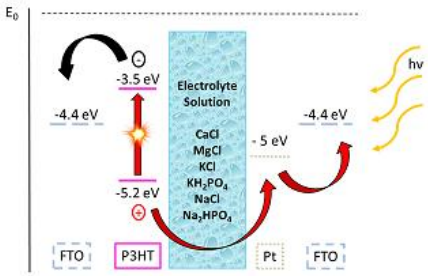

Figure 4. Theoretical model of the working device under light stimulation.