Organic Field Effect Transistors for Neural Stimulation – In Vitro Tests

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Abstract

Pentacene is an organic semiconductor that has the potential to be used as a switching element in active electrode matrices for neural stimulation. In this paper, we demonstrated that Pentacene-based organic field effect transistors (OFETs) can be used to drive stimulation currents of sufficient amplitude through neural electrodes in physiological-like environment. Furthermore, Pentacene was verified in respect to potential affects on cell vitality. The results of these tests indicate that extracts from Pentacene neither inhibit proliferation nor metabolism of the tested mouse fibroblasts. However, some effect on the cell vitality was observed, when cells were in direct contact to Pentacene for 48 h.

1. INTRODUCTION

The potential of organic and polymeric semiconductor molecules to be used in flexible electronic circuits has recently aroused the interest of research. In comparison to traditional field-effect transistors, polymer and organic transistors have advantages like mechanical flexibility and weight reduction. In our latest research work, this capacity is used to create a new generation of flexible neural electrodes using Pentacene as organic semiconductor material for building integrated flexible organic field effect transistors (OFETs) [1]. These can be used as switching element in an active n × m electrode matrix. The main advantage of this method is to reduce the number of lead wire in a n × m electrodes matrix, that means instead of $n \times m$ interconnects, only $n + m$ interconnects are required to drive a stimulation current through the individual contacts of the matrix. In matrix design, the source contact of an OFET is used as nerve electrode, through which the drain-source current enters the excitable tissue. In the here presented work we investigate the capability of the OFET to work as a voltage-controlled current source that copes with complex electrode impedance in vitro. Additionally, we do the first steps towards an assessment of the biocompatibility of Pentacene by investigating its potential cytotoxic properties on the mouse fibroblast cell line L 929.

2. METHODS

2.1. Organic Transistor Technology

In our work presented here, the OFETs have been made using pentacene as active layer. Pentacene has been chosen because of its relatively easy deposition technology [2] and high charge carrier mobility [3].

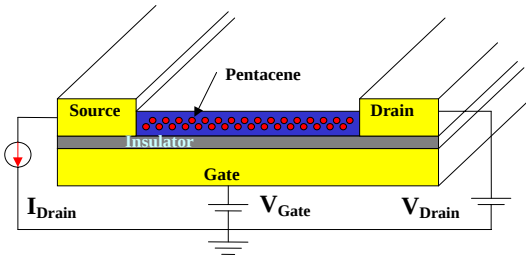

Figure 1: Cross section of the OFET.

Figure 1 shows the cross sectional structure of the OFET used. The OFET had a channel length of 20 µm and a channel width of 72 mm. The insulator layers were 300 nm SiO_2. 300 nm thick gold layers constituted the drain and source contacts and a n-doped silicon wafer was used as gate contact. In some investigations – for better electrical properties – surface modification process [4] like plasma activation and self-assembled monolayer (SAM) were applied.

2.2. Cytotoxicity Test

The cytotoxicity of pentacene was tested in vitro according to ISO 10993 on L 929 mouse fibroblasts cells. For the so-called direct contact test, the cells were brought into direct contact with the Pentacene layer and incubated for 48 h. The vitality of the cells were then evaluated by according to their morphology and death rate. Further more, so-called extract tests were carried out as follows:
The cell metabolic activity was investigated via the reduction of tetrazolium salts (WTS-1 test kit, Boehringer Mannheim, Mannheim, Germany) and generation of formazan. Also, the cell proliferativ ability was tested by the BrdU test, based on the measurement of 5-Bromo-2'-deoxyuridin (BrdU) incorporation during DNA synthesis in proliferating cells, and by chemiluminescence's detection by means of an ELISA reader (Cell Proliferation ELISA BrdU (colorimetric), Boehringer Mannheim, Mannheim).

2.3. Measurement Setup

In these investigations a 12 polar cuff microelectrode array was used, having disc-shaped platinum contacts with a diameter of 300 µm (impedance in saline: 8.5 kΩ, 46 ° at 1 kHz sine). OFETs were used to drive the stimulation current pulse through the cuff electrode by applying symmetrical voltage pulses of 20 Vpp to 50 Vpp to the drain contact (pulse generator: HP3245, Universal Source). The gate voltage is switched from 0 to –50 V. All measurements in this experiment were carried out using a digital oscilloscope (Tektronix, THS730A). The stimulation current was determined by measuring the voltage drop across Rm=1 kΩ, connected between cuff electrodes and ground potential (Figure 2).

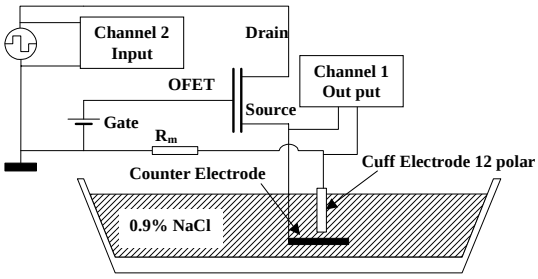

Figure 2: Setup to measure the switching effect of OFET in physiological environment.

3. RESULTS

3.1. Cytotoxicity Test of Pentacene

The extract tests with the tetrazolium salts WST-1 and the BrdU test showed that the extract of the pentacene samples did not impair the vitality and DNA synthesis of L 929-cells.
The direct contact test showed that the cells, which are incubated with pentacene layer, have a reduced number of green coloured cells, which reveals the vitality of the cells (figure 3). The morphology test showed that adherence between the cells and the pentacene layer is weak.

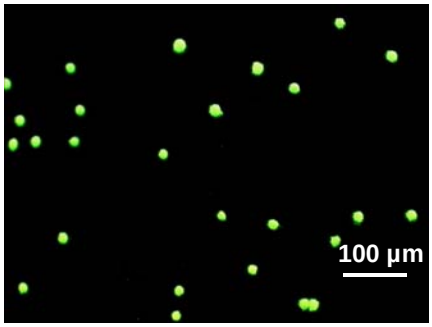

Figure 3: Fluorescence staining green colour showing the vitality of the cells

3.2. Current Injectiction into Physiological Environment

The measurement shows that the amplitude of the current flowing through the physiological environment (saline solution) can be controlled by the gate voltage. The maximum current amplitude driven by the OFET was about 300 µA (Figure 4). To achieve this current, the drain potential was set to 50 Vpp pulse and the gate potential was set to –50 V. In the next step, the drain potential of the OFET was kept at 20 Vpp pulses while the potential of the gate was switched from 0 V to -50 V. The OFET was connected to the cuff electrode as shown in Figure 2. The voltage drop across the electrode interface and electroltye was measured. At low gate voltage – the organic transistor is in "off"-state – no voltage signal was detected (Figure 5). After increasing the gate voltage – "on"-state of OFET – the electrode voltage increases and stays constant in the saturation regime of the OFET (Figure 6).

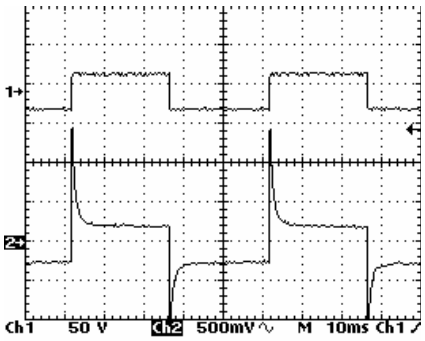

Figure 4: Channel 1 shows ±25 V drain potential pulses. Channel 2 recorded a 600 mV voltage drop across R_m=1 kΩ.

4. DISCUSSION AND CONCLUSIONS

The extract-based cytotoxicity tests of Pentacene showed promising results, while the direct contact seemed to be rather critical to the cells. Integration of OFETs into polyimid-based microelectrode arrays will lead to a completly sealed Pentacene layer, which protects cells from direct contact with the semiconductor. The good results from the extract tests are very important because soluble particles from the Pentacene (as contained in the extract) could potentially diffuse through sealing layers and reach cells.

Thanks to a high channel width to length ratio, and surface modification techniques we obtained a maximum drain-source current in the range of 300 µA, at relatively high gate-source and drain-source voltages. But these voltages are in the range that can be supplied by a telemetry system. According to Margalit, a current amplitude of about 150 µA at 300 µs pulse width is sufficient to excite retinal cells [5]. This data encourage us to propose the apoplication of active matrix electrode arrays using Pentacene OFETs for retina stimulation. It could be shown that the stimulation current intensity can be controlled by changing the gate potential. The idea of using organic field effect transistor (OFET) for switching electrical excitation of nervous tissues is completely new and no data and experience are available in the literature. In vitro tests have proved the feasibility of using OFETs, which can be integrated in already existing polymer microelectrode array as active switching elements and voltage-to-current converters.

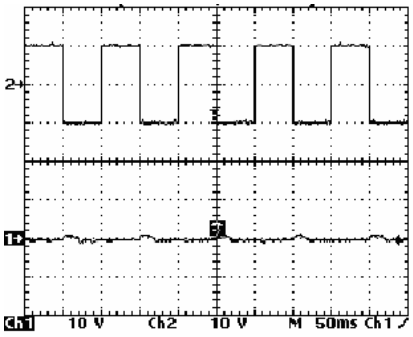

Figure 5: Channel 2 shows ±10 V pulses of the drain potential. Channel 1 displays the voltage drop across the electrode and electrolyte for a gate potential of 0 V.

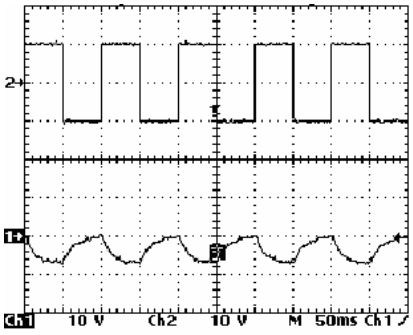

Figure 6: Channel 2 shows ±10 V pulses of the drain potential. Channel 1 displays the voltage drop across the electrode and electrolyte for a gate potential of –50 V.

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