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Silicon and reduced graphene oxide device concepts for electronically interfacing individual cells in culture

Sven Ingebrandt[1], Xuan-Thang Vu[1,2], Lotta Delle[1], Ruben, Lanche, Felix Hempel[1], Achim Müller[1], Jessica Ka-Yan Law[1], and Vivek Pachauri[1]

[1] University of Applied Sciences Kaiserslautern, Department of Informatics and Microsystem Technology, Amerikastr. 1, 66482 Zweibruecken, Germany
[2] present address: RWTH Aachen University, Department of Physics, Otto-Blumenthal Street, 52074 Aachen, Germany
*Corresponding author : sven.ingebrandt@fh-kl.de

Abstract

For the *in vitro* recording from cell cultures, different device concepts are used. Most of the time highly-sensitive, low-noise devices are needed to record from electrogenic cells in culture such as neurons and heart muscle cells. The two main concepts for such applications are microelectrode arrays (MEA) and field-effect transistor (FET) arrays. The classical configuration is the MEA chip on glass substrates and the FET chip – as a highly integrated version – on silicon fabricated in a CMOS process. Both device types can meanwhile be found in different commercially available instrumentations. For *in vitro* electrochemical recording of cell secretes, amperometric or impedimetric readout principles can be used. However, so far – apart from the Electrical Cell-substrate Impedance Sensing (ECIS) concept – electrochemical readout isn't used a lot in this field. In recent years, graphene as an emerging material class has attracted a lot of attention in the scientific community with high prospects especially for the electrochemical readout concepts. In addition the field-effect transistor devices were downscaled to nano dimensions as silicon nanowire arrays, which can offer improved signal-to-noise ratio due to an increased sealing between cellular membranes and active device structures. Our group is developing various device concepts and readout principles in this framework, which will be discussed in this presentation.

1. Introduction

The electronic coupling of electrogenic cells such as neurons or muscle cells to readout devices embedded inside of a classical petri dish has attracted a lot of researchers over the past three decades. In early works researchers used metal lines out of gold covered by a protection layer and de-protected the inner part of the sensing electrodes for electronically interfacing with cells [1]. Over the years the technique was commercialized and several different systems are available nowadays. In parallel, but with a somewhat later start, similar systems based on field-effect transistor arrays were developed and refined over the years [2]. A lot of effort was put into the understanding of the signal shapes and in optimization of the technique in terms of signal-to-noise ratio [3,4]. The group of P. Fromherz in Munich, Germany, contributed quite a number of pioneering articles to the field. This group introduced in cooperation with Infineon Technologies the first industry realization of an FET sensor chip with a huge number of readout channels [5]. Meanwhile this technique is mature and also this CMOS approach is close to commercialization [6,7].

Apart from these developments towards commercial applications, researchers came up with more exotic designs of using silicon nanowire (SiNW) arrays to interface with neuronal cells [8]. The downscaling of the structures in contact with the cell membrane leads to an increased sealing of the cellular membrane and by this to increased signal-to-noise ratios. If the structures are small enough, an engulfment of the sensor into the cell can be observed and sensors detect then the intracellular signal shape of the action potentials [9].

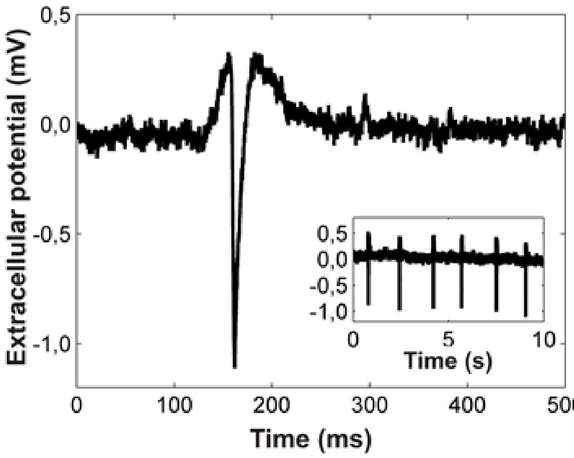

Fig. 1 Action potential shape recorded from a cardiac myocyte culture on a SiNW sensor array.

In the past 10 years a new boom of using graphene as transducer material has started and is ongoing. Graphene represents a new concept since these devices are neither classical field-effect sensors nor metal electrode sensors. Graphene devices have demonstrated that they can be used to detect action potential activities as well as amperometric signal parts for electrochemical detection of neurotransmitters [10]. Lieber et al. demonstrated the parallel usage of SiNW and Graphene sensors at one cell and compared the recorded signals [11].

2. Results

SiNW sensor devices

Our group has developed a process for top-down fabrication of SiNW devices, which results in robust and reusable devices with electronically identical characteristics from sensor to sensor [12]. We mainly used them for electronic detection of biomolecules, but signals from cardiac myocyte cultures were successfully detected as well [13] (Fig. 1). The recorded signals show identical signal shape compared to the more classical approaches with FET and MEA sensors.

Reduced graphene oxide devices

In addition, we developed devices based on reduced graphene oxide (rGO) in a bottom-up and in a top-down approach. We used these devices for impedance sensing of cell-substrate adhesion as a cheap alternative to commercial ECIS systems [13] (Fig. 2). With this platform we were able to measure the adhesion strength of individual cells in a pure electronic approach. We aim to optimize the fabrication procedure of these devices and to use them in amperometric readout assays to detect cellular secretion as well.

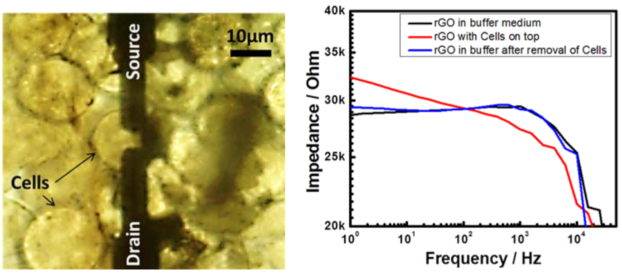

Fig. 2 ECIS-type of sensor approach using a reduced graphene oxide sensor platform. The adhesion of the individual cells to the FET-like sensors can be detected by impedance sensing.

Generally, when using new transducer materials and device concepts, experimental data need to be tested and compared to the classical models and established readout systems. In particular the combination of potentiometric and amperometric recording hold great promise for future device concepts. In nature, the communication in the brain is not only of electronic nature. In parallel biochemical communication plays a huge role and is with the classical platforms so far not available to researchers.

3. Summary and Outlook

In the past our group developed several different device concepts for interfacing living cells in culture based on the two classical approaches MEA and FET arrays. In recent years there is a trend of using new material classes as transducer for such devices. The most prominent one is graphene, which adds in the form of reduced graphene oxide the possibility to combine amperometric sensing of cell secretes with potentiometric sensing of action potentials. By such approaches one can expect in future a new class of device types, which might be able to uncover the biochemical communication in cell cultures as well.

Acknowledgements

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