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Pharmacological Active Cell Sensor Array

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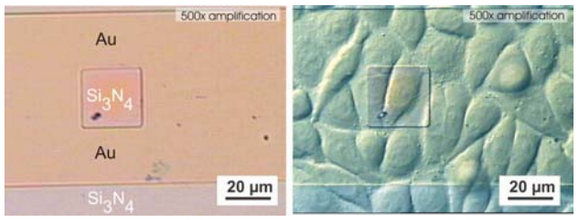
The complexity of chemical analytes in life science demands a high level of selectivity from chemical sensors. Biological systems have developed this desired selectivity as key feature for their metabolism. Hence, biological systems can provide the sensitive and selective transducer for a sensor array. To benefit from this selective recognition a cell culture has been integrated into a microelectronic sensor array.

This approach allows an accurate characterization of physiological reaction patterns of cells that is crucial for solving cell biological, pharmacological and medical problems. Standard devices such as dye test kits usually disregard the dynamics of cellular reactions and only evaluate a final result so that valuable information is usually lost. Apart from this, in most cases only a single parameter may be measured, although cellular reactions express themselves in a variety of different aspects. The strength of microelectronic sensor systems is based in the non-invasive procedure and the continuous signal analysis so that microsensor systems are well suited for the acquisition and analysis of cell-based biosignals derived from cultured cells and tissue preparations. Such cell-based biosensors allow to characterize the function of cells such as the contraction of single cardiac muscle cells or the resorption through a intestinal ephitel cells. For reliable interpretation of chemical sensing several 1000 cells have to be measured to asses biological parameters. For this purpose, a fully automated device capable of detecting and recognizing individual cells is desired.

This work describes the device fabrication, experimental setup, procedure, and some preliminary results of monitoring of cell signals including impedance and equivalent circuit parameters. As cell culture colon carcinoma cells were chosen as they provide an excellent model for the intestinal ephitel tissue responsible for the incorporation of orally delivered pharmaceuticals. The microfabricated device consists of either silicon or glass substrates containing multiple extracellular electrodes that interface with the CaCo-2 cells. These electrodes can be used for general single electrode extracellular stimulation/recording studies. The electrodes were designed in an array format for parallel analyses. This microelectrode array allows to determine changes in conductivity and impedance a range from 40.0 Hz to 1.0 MHz. The potential for rapid analysis of cell response to various drug was investigated. Depending on their detection principle these microelectronic biosensor are applicable in numerous fields of biomedical and cell biological research.



(a) (b)

Fig. 1 Microelectronic electrode configuration with silicon nitride dielectric and gold electrode after fabrication (a) and with a cell culture of CaCo-2 tissue (b) on the same microelectronic substrate.