A Single-Cell Electronic Sensor of Toxins

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Abstract. Here we propose a simple label-free bio-electronic toxin detector based on non-destructive impedance spectroscopy (IS) method with a single living cell as a sensing element. The toxins distort cell membrane, which significantly affects on the impedance level of an electrode, which covered by a cell. This effect could be used for toxin detection. We believe that our bio-sensor will open a new roadmap in water purity purposes and will save many a one lives.

1. Introduction
Research of living matter has become a hot topic in experimental physics in the resent years. Numerous efforts are being made to develop the new nondestructive and label-free methods for cell diagnostics in vitro. The impedance spectroscopy is one of the promising methods for this [1]. The developed by Ivar Giaever electrical cell-substrate impedance sensing technology have become practical in the areas of cancer research, wound healing research, pharmacology, etc [2, 3]. Here we show a possibility of the usage IS based bio-sensor as selective detector, which a priory reacts on any bio-active toxiferous substances.

2. Theory
According to the Giaever-Keese theory [2], the cell on the electrode acts as an added serial active resistance $R_s$ in the impedance, because current flow not only through electrochemical impedance $Z_{e/c}$ (electrode located in phosphate buffered saline), but also through seal between cell and electrode (figure 1). If electrode is not covered by cell or if cell-membrane is distorted, the value of added resistance $R_s$ decrease. The total impedance $Z_{total}$ of the electrode/cell/electrolyte interface reads as

$$Z_{total} = Z_{e/c} + R_{sol} + R_s,$$

where $R_{sol}$ is active bulk resistance of the electrolyte. The action of a toxin on a cell leads to the distortion of the cell membrane. Therefore, after the action of a toxin $R_s$ value should become much lower than $Z_{e/c} + R_{sol}$. Accordingly, the impedance spectrum of a cell-contained electrode becomes similar to the impedance spectrum of the empty electrode. This phenomenon can be used for a selective toxin detection.
3. Materials and methods
We have used multielectrode array MEA 200/30 (Multi Channel Systems GmbH, Germany, 30 μm electrode diameter) covered by HeLa cells in 0.5 ml of the phosphate buffered saline (Biolot, Russia) with 7.5 μl propidium iodide in vitro under microscope study and home-made advanced device and processing for impedance measurements [4, 5]. Triton X-100 (Union Carbide, USA) was used as model toxin. HeLa cells were obtained from the Bank of Cell Cultures of the Institute of Cytology of the Russian Academy of Sciences. Impedance spectra were measured between large rectangle reference electrode (50 μm × 250 μm, not presented on photographs) and empty (control) electrode (50 μm diameter, not presented on photographs), and between reference electrode and electrode covered by a single cell [see figures 1(b,e,h)]. Photographs were made by Leica DM4000 microscope (Leica, Germany).

During the IS measurement 2.5 μl of the toxin were added into matrix Petri dish. The final concentration of the toxin was 2.5 μl per 1 ml of the phosphate buffered saline.

4. Results and discussion
The results are shown on figure 2. This data indicate, that impedance of the covered by cell electrode is higher (by magnitude) than impedance of empty electrode before adding toxin and close to empty control electrode after adding toxin. This is result of the significant cells’ membrane distortion, what additionally justified by the fluorescence of the propidium iodide.

So, criteria of the close equality between impedance spectra of the cell-contained and empty electrode could be used as danger alarm. We believe that our bio-sensor will open a new roadmap in water purity purposes and will save many a one lives.
Figure 2. Toxin effect on the impedance (color on-line). Photographs of the electrode with cell (in green circle), magnified image of the electrode with cell, and impedance spectra: (a), (b), (c) – before adding toxin; (d), (e), (f) – 1 minute after adding toxin, arising propidium iodide fluoresce; (g), (h), (i) – 2.5 minutes after adding toxin, cell membrane distorted. Green solid lines corresponds to covered by cell electrode, red dashed line corresponds to control (empty) electrode (not presented on photographs).

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