

Technology Offer

Detection of adhesion resistance in cells or lipid membranes by noise analysis

Ref.-No.: 0204-3316-WT

Background

The function of brain tissue is based on the dynamics of numerous nerve cells and their synaptic interaction. Direct electrical interfacing of semiconductors and nerve cells is the physical basis for a systematic development of hybrid neuroelectronic devices, such as neurocomputers and neuroprostheses. Excited nerve cells and field-effect transistors are coupled by a dissipative mechanism: ionic current through the adherent cell membrane flows along the electrical resistance of a narrow layer of electrolyte between cell and chip and gives rise to an extracellular voltage on the open gate oxide of the transistor. The resistance in the area of cell adhesion determines the amplitude of the recorded extracellular voltage. That resistance, however, is also an intrinsic source of thermal voltage noise.

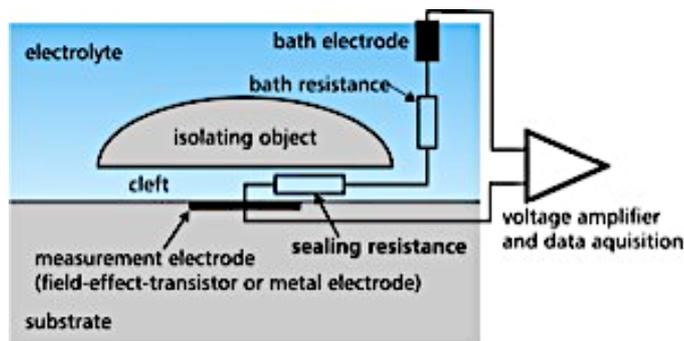


Figure 1: The electrolyte-filled cleft between an isolating object and an electrode forms the sealing resistance. By measuring the Nyquist noise of this resistance one can determine the properties of the sealing, such as its extension, the cleft width and its change over time.

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The voltage fluctuations in the adhesion area of nerve cells from rat brain, which are cultured on oxidized silicon. As a probe, an electrolyte oxide-silicon field-effect transistor is used as sketched in Fig. 2(b). It consists of an open gate between source and drain contacts and is insulated from the electrolyte by 10 nm silicon dioxide. A local change of voltage in the electrolyte layer between cell and chip gives rise to a modulation of source-drain current. Because of a buried channel configuration, the transistor has a particularly low $1/f$ noise. The gate with a dimension of $6\mu\text{m} \times 7\mu\text{m}$ is small enough to be completely covered by a mammalian nerve cell, but large enough to avoid a dominance of the $1/f$ noise that increases with decreasing gate area.

Advantages

This method allows the direct electrical interfacing of a semiconductor device to an individual mammalian nerve cell. The firing neuron directly controls the source-drain current of a buried channel electrolyte-oxide-silicon (EOS) field-effect transistor. Experiments demonstrate the feasibility of noninvasive monitoring of neuronal systems by semiconductor chips at the level of individual cells and lay the foundation for applications of very large scale integration technology in neuroscience and pharmacology.

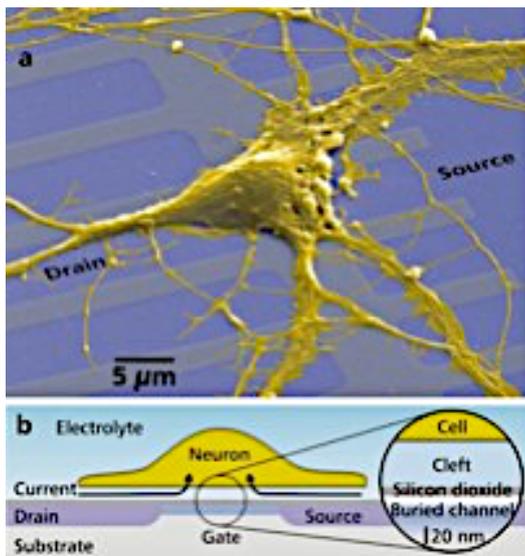


Figure 2: Rat neuron on electrolyte-oxide-silicon (EOS) field-effect transistor. (a) Electron-micrograph (colorized) of hippocampal neuron on silicon chip with linear array of p-type buried channel transistors after eight days in culture. Between source and drain leads are the open voltage-sensitive gates. The surface of the chip is chemically and structurally homogeneous consisting of silica with a surface profile below 20 nm. (b) Schematic cross section of a neuron on a buried-channel field-effect transistor with blow-up (drawn to scale) of the contact area. During an action potential, current flows through the adhering cell membrane and along the resistance of the cleft between chip and cell. The resulting extracellular voltage in the cleft modulates the source-drain current.

The recording and analysis of voltage noise can be applied not only for cell adhesion, but also for other contacts of organic films and solids in electrolyte, such as supported lipid membranes without or with membrane proteins.

Experiments demonstrate that thermal noise can be used as a probe for the electrical properties of cell adhesion. In comparison to other methods, this approach does not require a perturbation of the cells, e.g., staining with a dye or contacting with a pipette, nor any external stimulation. This novel technique is non-invasive, does not rely on molecular probes and does not require any intra or extracellular stimulation.

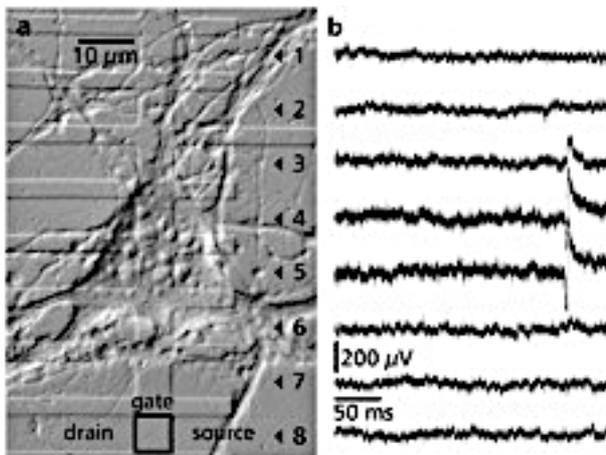


Figure 3: Noise of extracellular voltage due to cell adhesion. (a) Differential interference contrast micrograph of nerve cell from rat on linear array of electrolyte-oxide-silicon field-effect transistors. The elements of a selected transistor are indicated at the bottom. The cell body completely covers the transistors No. 4 and 5. (b) Extracellular voltage recorded by the transistors within a bandwidth of 1 Hz to 10 kHz. The transistors beneath the cell body exhibit an enhanced noise. Near the end of the traces, the transistors No. 3, 4, and 5 record spontaneous neuronal excitation.

In addition to the observation of cell adhesion, the adhesion noise has a general relevance for extracellular recording; as for frequencies above 1.5 kHz the observed adhesion noise is larger than all other noise sources combined, which means that the thermodynamic limit of extracellular recording has been reached.

Modern semiconductor technology could provide suitable tools for massive parallel monitoring of neuronal activity at high spatial and temporal resolution.

Patent Information

Patent DE 102005019191, Priority Date April 4, 2005.

Literature

1. M. Voelker and P. Fromherz. *Nyquist noise of cell adhesion detected in a neuron-silicon transistor*. Phys. Rev. Lett. 96, 228102 (2006)
2. M. Voelker and P. Fromherz. *Signal transmission from individual mammalian nerve cell to field-effect transistor*. Small 1, 206-210 (2005)

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