Introduction
Microelectrode arrays (MEAs) have become essential for monitoring neural cells. They provide a significant tool for measuring neural activity of cells cultured in vitro. However, one of the main limitations of MEAs is related to their low spatial resolution. Commercial MEAs usually contain approximately 60 electrodes, with electrode sizes ranging from 10 to 50 \( \mu \)m, and inter-electrode spacing ranging up to 100 \( \mu \)m. These dimensions are much larger than the 5-20 \( \mu \)m typical size of vertebrate neurons used during electrophysiological experiments, and therefore constitute a limitation in terms of spatial resolution. However recently, a new generation of CMOS-based MEAs containing a high-density of sensors has emerged. These new devices take advantage of CMOS electronics, which offers on-chip multiplexing, amplification, and filtering, for handling a large number of closely spaced electrodes. Thus, these new devices have a pitch dimension as low as 7.8 \( \mu \)m with a diameter of 4.5 \( \mu \)m [1], enabling electrophysiological experiments at subcellular resolution.

The design of these novel CMOS-based MEAs demands accurate compact electrical models of the cell-electrode interface in a format enabling co-simulation with the CMOS circuits. Thus the electrical characteristics, such as noise or power consumption, of MEAs could be modelled and simulated as a whole system including the cell-electrode interface and the electronics. In this scope, an electrical model of the cell-electrode interface for recording neural activity from high-density MEAs has been developed. This model, the area-contact model, takes into account the spatial distribution of the cell-electrode interface are not modelled.

Thus, an area-contact model, where spatial distributions are taken into account, is needed.

Area-Contact Model [2]
Area-contact model of the attached cell membrane, where \( V_{R,off} \) is the intracellular potential, and \( V_{G(j0)} \) is the potential at the cell-electrode interface at a distance \( r \) from the center of the cell.

\[
\frac{\partial V_i(r,s)}{\partial r} + 2arV_i(r,s) = 2arV_i(s)
\]

\[
V_i(r,s) = V_{G(j0)}(s) e^{2a(r_c-r)} - 1
\]

\[
a = \frac{sP_{c,m} \left( C_{e,m} + sC_{c,m} \right)}{2d \left( g_{c,m} + sC_{c,m} + \mu L \right)}
\]

\( H_{R,off} \) versus the distance from the center of the cell for different frequencies of \( V_{G(j0)} \).

Area-contact model of the electrode with the load impedance (\( R_{spread} \) is neglected).

\[
V_i(s) = Z_{load} \int_0^r V_i(r,s) - V_i(s) \frac{1}{Z_i(r,s)}
\]

Amplitude of \( H(j\omega) \) versus the electrode radius for (a) different cell-electrode distances and (b) different frequencies of \( V_{G(j0)} \). A typical cell diameter of 10 \( \mu \)m is considered. Moreover, a frequency of 1 kHz is used in (a) and a cell-electrode distance of 70 nm is considered in (b).

The load impedance is a 10 pF capacitance. It represents the typical input impedance of the first amplification stage of CMOS-based MEAs.

→ Optimum electrode radius for a 10 \( \mu \)m neural cell = 3.5 - 4 \( \mu \)m.

Noise Model [3]
For Pt electrodes, thermal noise has been empirically shown to be the dominant noise source [4]. Thus, the electrode is considered to be nonfaradaic and the nonequilibrium excess noise caused by charge transfer processes produced by electrochemical interactions at the electrode surface is not taken into account.

\[
V_{R,noise} = \frac{4kT R_{seal}}{V_{R}} \quad R_{seal} \rightarrow \text{Equivalent noise resistance}
\]

\[
V_{local,noise} = \frac{4kT R_{local}}{V_{R}} \quad R_{local} = \text{Real part of } Z_{local}
\]

In order to be able to compare the electrode and electrolyte solution noise with the noise of the CMOS circuitry, the equivalent noise of the cell-electrode interface at node \( V_e \) needs to be calculated. Thus, for the case where a cell lies on top of the electrode, the noise spectral density at node \( V_e \) is expressed as:

\[
V_{R,noise} = \frac{Z_{load} + R_{local} + Z_{load}}{4kT \left( R_{local} + R_{local} \right)} \left( \frac{V}{\sqrt{Hz}} \right)
\]

Usually, \( V_{input,amp} \leq 10 \mu V_{R,noise} \)
Thus, the electrode noise can be the largest noise source of the whole system. If the electrode diameter is smaller than 10 \( \mu \)m, Pt-black electrodes have a smaller equivalent noise at node \( V_e \) compared with Pt electrodes.


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