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Computer simulation for electrochemical impedance of living cell adhered on the inter-digitated electrode sensors.

Pooja Kenchetty P[1], Taiki Miura[1] and Shigeyasu Uno[1]

[1] Department of Electrical and Electronic Engineering, Faculty of Science and Engineering, Ritsumeikan University
1-1-1, Noji-Higashi, Kusatsu, Shiga 525-8577, Japan
E-mail : gr0340if@ed.ritsumei.ac.jp, suno@fc.ritsumei.ac.jp

Abstract

We examined the sensitivity of inter-digitated electrode (IDE) impedance sensor for adherent cells by simulation. The higher cell density, larger cell size and smaller electrode geometry resulted in higher sensitivity. It was found, for the first time, that IDE gives better sensitivity than facing electrode configuration for adherent cell sensing.

1. Introduction

The monitoring of living cells by impedance measurements through electrochemical sensors are suitable for point-of-care diagnostics due to fast, simple, label-free, non-invasive and real-time characteristics [1]. Especially, the impedance methods are more widely used for its non-invasive and sensitive nature. The impedance sensing methods and the different electrodes have been reviewed [2]. The inter-digitated electrodes (IDEs) were found to be the suitable sensing elements due to the electric field and current density concentration in the vicinity of the electrodes to achieve higher sensitivities [3]. The simulation works on geometrical optimization of IDE were discussed in the absence of living cells [4,5]. Many experimental works on living cell monitoring using IDE are available for floating cells [6,7], where the sensitivity of facing electrode (FE) configuration is higher than IDE-like coplanar electrode [8]. However, for adherent cells, there are no works available that discuss the sensitivity of IDE and its geometrical optimization. In this work, the 3D simulations were done to study the sensitivity of IDE for cell size, cell density and different electrode geometries. Our results will benefit experimentalists in selecting the highly sensitive electrode configurations and geometries.

2. Simulation Model and Methods

The simulation model of IDE in Fig.1(a) represents a unit domain which encloses the working electrode (WE) and counter electrode (CE). The electrode width, W, is kept equal to the spacing, S, between the electrodes. The diameter of the adherent cell was chosen to be 10μm [9] with the gap of 100nm above the electrode surface. The equivalent circuit model representing the different components in the presence of cell is shown in Fig. 1(b), where R_{sol}: solution resistance, C_{sol}: solution capacitance, R_{gap}: extra-cellular gap resistance, C_{dl}: double layer capacitance, C_{mem}: membrane capacitance, R_{cell}: cytoplasm resistance. Fig.1(c) gives the parameters used for solving the Maxwell's equations using finite element method (FEM) for impedance simulation as in Fig.1(d). The unit domain is regarded to be repeated infinite times for a given IDE structure because of the periodic boundary condition.

3. Results and Discussion

Fig.2(a) shows the different cell positions considered to study the impact on impedance due to cell position. Fig.2(b) represents the Bode plot where the impedance due to C_{dl} is significant below 10^5 Hz and the changes in impedance in the presence of cell is observed in the R_{sol} region above 10^5 Hz. The maximum impedance was achieved when the cell is at the electrode edges. This is because of the current density concentration along the edges of IDE as shown in Fig.2(c). As the cell position cannot be controlled in actual experiments, it is necessary to take the average for all the possible cell positions. Considering the symmetry, it is sufficient to take the average from the center of the electrode to that of the unit domain. Thus, such average was taken in further results. Fig.3 shows the average sensitivity, r, for various cell densities, which is in fact represented by varying the domain depth, Ly. Apparently, higher cell density (smaller Ly) results in higher sensitivity. Likewise, Fig.4 shows that the larger cell size leads to higher sensitivity. Fig.5 shows the different electrode geometries possible for Lx = 120μm. The higher sensitivity was achieved for smaller W and S, which is due to occurrence of many electrode edges and hence larger current density in the vicinity of sensor surface. Finally, the IDE was compared to FE with same cell density as shown in Fig. 6, showing that the sensitivity of IDE is always higher than FE in the presence of adherent cell. This is because the current density is maximum in the vicinity of IDE and the area occupied by the cell is greater than FE.

5. Conclusions

The sensitivity of IDE impedance sensor was examined for adherent cells. The higher cell density, larger cell size and smaller electrode geometry resulted in higher sensitivity. It is important to note that the IDE showed better sensitivity than FE in contrast to that of floating cells [8]. This makes IDE as the suitable choice of electrode for experimentalists working on adherent cell studies.

References

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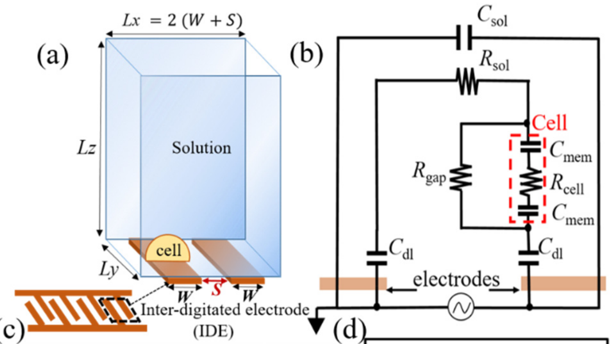

(c)

Parameter	Value
Solution relative permittivity	78
Solution conductivity [S/m]	1.5
Membrane relative permittivity	3.0
Membrane thickness [nm]	5.0
Cytoplasm relative permittivity	78
Cytoplasm conductivity [S/m]	1.0

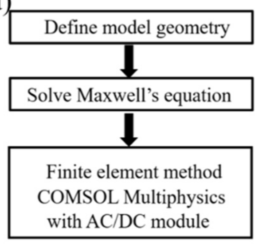

Fig. 1: (a) Simulation model (b) Equivalent circuit model (c) Parameters used (d) Simulation flow for impedance values.

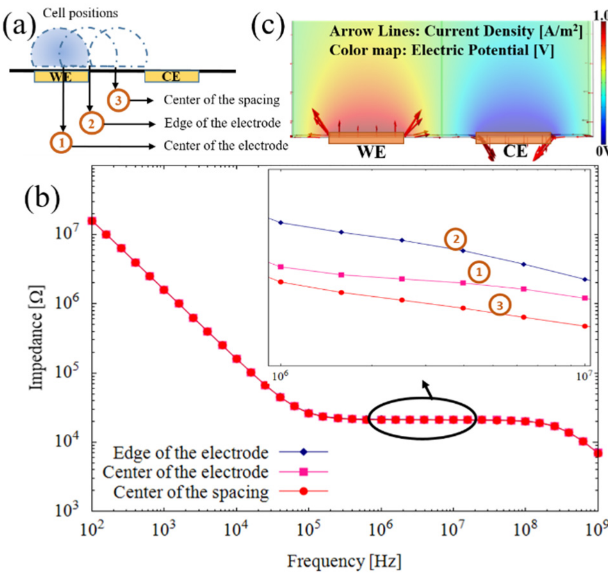

Fig. 2: (a) Schematic cell position representation (b) Bode plot representing the impact on impedance due to cell position (c) Electric potential distribution map and current density vectors.

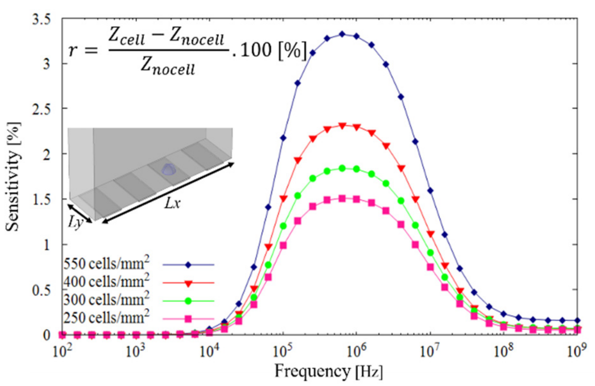

Fig. 3: Sensitivity, r, for varying cell density given by $1/(LxLy)$. Z_{cell}: impedance with cell ; Z_{nocell}: impedance without cell.

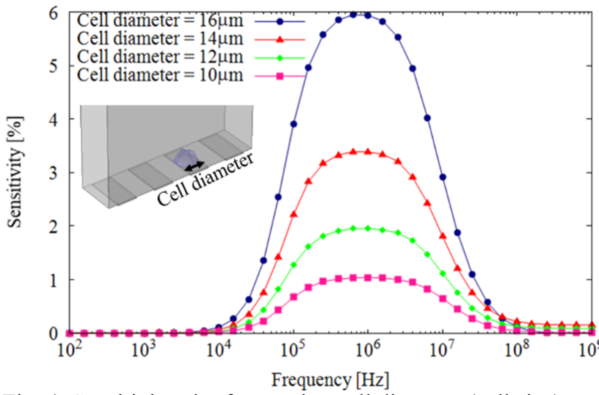

Fig. 4: Sensitivity plot for varying cell diameter (cell size).

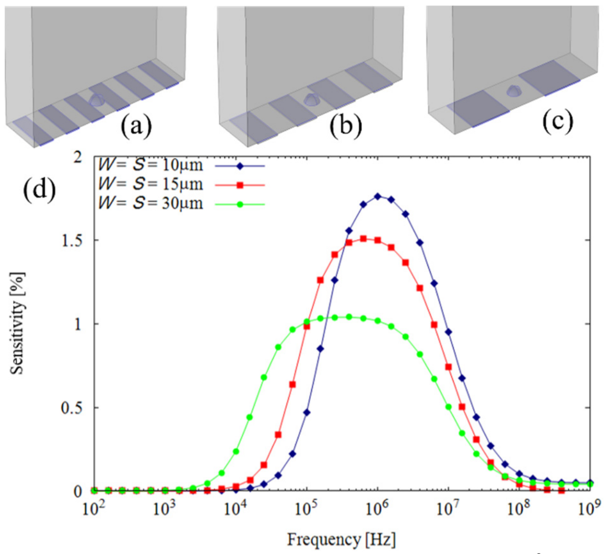

Fig. 5: Electrode geometry variation for 250 cells/mm² and cell size of 10µm (a) $W = S =$ 10µm (b) 15µm (c) 30µm (d) Sensitivity plot.

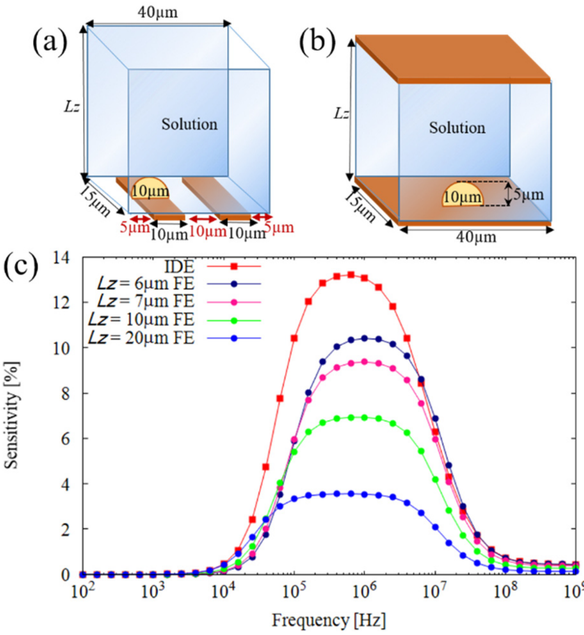

Fig.6: (a) IDE model (b) Facing electrode (FE) model (c) Sensitivity comparison between IDE snd FE by varying Lz of FE.