Cell–Electrode Models for Impedance Analysis of Epithelial and Endothelial Monolayers Cultured on Microelectrodes

C.-M. Lo[1]; W.-C Chiu[1]; W.-L. Chen[1]; Y.-T. Lai[2]; Y.-H. Hung[3]

[1]National Yang Ming Chiao Tung University, Taipei, 11221, Taiwan
[2]Research Center for Applied Sciences, Academia Sinica, Taipei 11529, Taiwan
[3]Department of Neurology, University of California, Irvine, CA 92697, USA
chunmin.lo@nycu.edu.tw

Electric cell–substrate impedance sensing (ECIS) provides a powerful, noninvasive method for monitoring the electrical characteristics of epithelial and endothelial cell monolayers cultured on microelectrodes, offering key parameters such as junctional resistance, cell–substrate separation, and membrane capacitance [1,2]. Historically, a three-path model (LGK model), which incorporates two transcellular pathways (apical and basal membranes) and a paracellular pathway through lateral intercellular spaces (LIS), has enabled detailed impedance analysis of epithelial cell layers, such as MDCK [3]. Yet, fitting this model can become challenging due to the six adjustable parameters, particularly the lateral resistance (R_l). To simplify the model fitting, we introduce a **simplified LGK model**, which omits the contribution of LIS resistance (assuming $R_l \ll$ junctional resistance, R_b) and treats the lateral membrane as a lumped impedance. This assumption yields a more tractable model with only five fitting parameters: R_b, α (related to cleft resistance α^2), apical capacitance (C_a), basal capacitance (C_b), and lateral capacitance (C_l) [4].

We demonstrate that this simplified model closely matches experimental impedance spectra measured across a frequency range of 31.25 Hz to 100 kHz for both MDCK and OVCA429 epithelial cell monolayers. Moreover, the model provides insight into how variations in each parameter, particularly C_a and C_b, affect the impedance response. When applied to cell types with substantially lower junctional resistance (e.g., HUVEC endothelial cells and HaCaT keratinocytes), the lateral current pathway becomes negligible. Under this condition, the simplified LGK model further reduces to a **modified two-path GK model**, involving only four parameters: R_b, α, C_a, and C_b. The impedance measurements for these cells closely align with predictions from the two-path model [4].

In summary, this study presents a hierarchy of cell–electrode models, moving from the full LGK model to a simplified five-parameter version and finally to a streamlined four-parameter model, tailored for different cell types depending on their junctional resistance. These models conserve accuracy while easing parameter fitting and interpretation, enhancing ECIS's utility in assessing cell–cell and cell–substrate interactions across diverse monolayer types.

References:

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