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千葉大学審査学位論文（要約）（Summary）

基幹工学 専攻 機械工学 コース
Division Department

氏 名 張 安
Name ZHANG AN

電気インピーダンス分光法による細胞の誘電特性と境界反射特性の抽出法
Extraction Method of Cell's Dielectric Properties and Boundary Reflection Properties by Electrical Impedance Spectroscopy

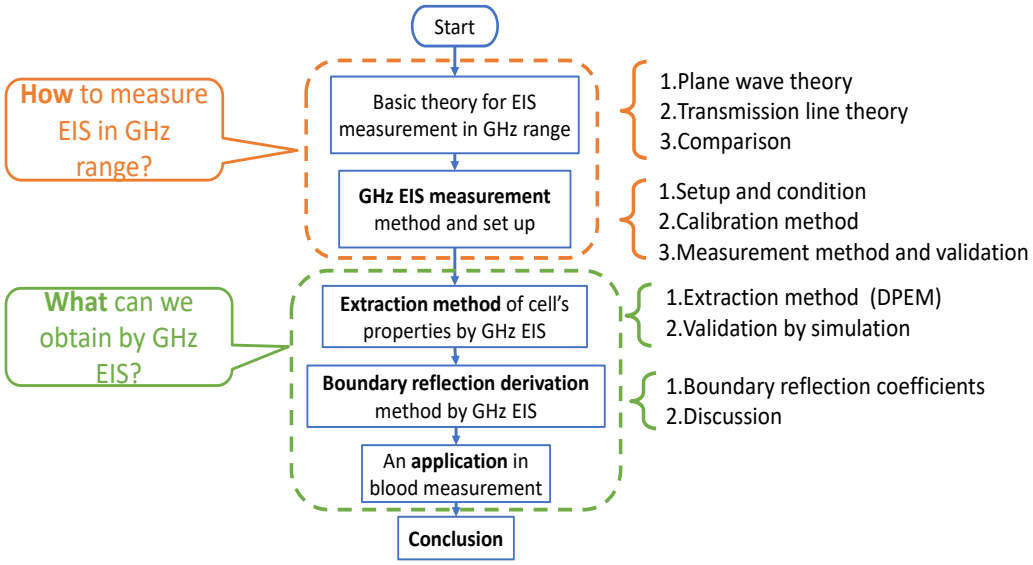

Figure 1. Research methodology.

The aim of this study is to realize the EIS measurement of dielectric properties of cells in the sub GHz range and to extract the dielectric properties of cells from cell solutions by a novel electrical impedance spectroscopy-dielectric properties extraction method (EIS-DPEM). Then, this study clarifies the "intracellular structure" among the cell wall, membrane and cytoplasm in the frequency range from 1 MHz to 3 GHz by EIS-DPEM. Finally, the impedance of native blood and blood with various fibrinogen concentrations have been measured and discussed as AN application of GHz EIS measurement. The details of present study explain in this thesis can be summarized as follows:

Chapter 1

The essential background of this study were explained in details. The theoretical issues of GHz Electrical Impedance Spectroscopy measurement of cells were explained alongside with its current states and problems. The main objectives to solve the problems also has been clarified.

Chapter 2

This chapter introduces the theories of the electromagnetic field in order to clarify the main principle of the GHz EIS measurement method from the physical viewpoint. The plane wave theory and transmission line theory were introduced as basic theories of the GHz EIS measurement. Through the derivation of plane wave theory and transmission line theory, the four most important parameters in GHz EIS were obtained and explained in this chapter, which are propagation constant γ^*, intrinsic impedance η^*_w, characteristic impedance Z^*_0 and geometric parameter G_f. These parameters and related equations described the physical relationship among the dielectric properties of cell solution, EM field and geometric parameter of the sensor. Besides, Bruggeman-Hanai equation and Asami multi-shelled model were introduced to describe the dielectric relationship among the cell solution and components of the cell solutions.

Chapter 3

This chapter demonstrated the experimental setup of GHz EIS measurement, which uses a connector as a sensor. Then, an equivalent circuit model was established to theoretically describe the coaxial sensor base on the plane wave and transmission line theory. By the model, pure water was measured by the coaxial sensor after calibration to validate the measurement results. Secondly, we proposed a new dielectric properties extraction method (DPEM) to extract the complex dielectric properties of cells in cell solutions in GHz EIS. The extraction results were shown using yeast cells as an example. Finally, the extraction results of DPEM were validated by comparing with the results from B-H equations and simulation.

Chapter 4

This chapter proposed the boundary reflection derivation method to profoundly investigate the "intracellular structure" among the cell wall, membrane and cytoplasm in both MHz and GHz frequency range. The boundaries reflection coefficients at the intracellular boundaries between the cell wall and membrane Γ^*_{wm}, and between the membrane and cytoplasm Γ^*_{mc} were proposed. The living (LC) and dead (DC) yeast cell

solutions with various volume concentrations φ were prepared as an example. Then, Γ^*_{wm} and Γ^*_{mc} were calculated by the boundaries reflections derivation method. The reflection coefficient Γ^*_{wm} and Γ^*_{mc} shows different patterns in both MHz range and GHz range for living and dead yeast cells. Γ^*_{wm} and Γ^*_{mc} were proved to be a powerful indicator and practically identical to living and dead yeast cells and volume concentration φ even in GHz range. By comparing both living and dead yeast cells, Γ^*_{wm} and Γ^*_{mc} separately showed that the electromagnetic wave in MHz range was almost reflected at the boundary between cell wall and membrane, which indicates that electromagnetic wave in MHz range was unable to penetrate the yeast cell membrane and cytoplasm, while the electromagnetic wave in GHz range was partly reflected by the yeast cell membrane and cytoplasm.

Chapter 5

In this chapter, the impedance of native blood and blood with various fibrinogen concentrations have been measured in the frequency range from 1 MHz to 3 GHz. The permittivity and conductivity of blood as they vary with the fibrinogen concentration were extracted from the measured impedance. Finally, the complex permittivity of native blood and blood with fibrinogen were compared to illustrate that the influence of fibrinogen on the blood dielectric properties. The complex blood permittivity with various fibrinogen concentrations were compared to explain that blood dielectric properties change caused by various fibrinogen concentrations.

Chapter 6

This chapter concluded this study. In this study, a novel dielectric properties extraction method combining plane wave theory and the transmission line theory was proposed to establish the relationship between the experimental impedance $Z^*_{sol,exp}$ and dielectric properties of the cell ε^*_{cell} in the frequency range up to 3 GHz. A boundary reflection derivation method was established to clarify “intracellular structure” among the cell wall, membrane and cytoplasm in the frequency range from 1 MHz to 3 GHz. A normal electromagnetic wave enter yeast cell from the dispersed medium was considered. The reflection coefficient at the boundaries between cell wall and membrane Γ^*_{wm}, between membrane and cytoplasm Γ^*_{mc} were obtained based on the GHz EIS-DPEM. Besides, the influence of various fibrinogen concentrations on the blood dielectric properties in the frequency range from 1 MHz to 3 GHz were investigated by the proposed GHz EIS measurement method.