Measurement of Complex Permittivity for Biological Cells by Waveguide Penetration Method

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***Abstract—In vitro* studies to investigate biological effect of electromagnetic field are performed for microwave to millimeter-wave frequency band. A reliable measurement method of complex permittivity for biological cells is required for the dosimetry. The feasibility of applying the waveguide penetration (WP) method to measure complex permittivity for cells in the frequency range from microwave to millimeter-wave frequency band is investigated. In this study, complex permittivity measurement was performed in the frequency ranges from 1.7 to 2.6 GHz and from 50 to 65 GHz by the WP method. Real part and imaginary part of complex permittivity of CHO-K1 cell were estimated to be 59.9-64.1 and 15.6-20.2 in the frequency ranges from 1.7 to 2.6 GHz, and 10.6-14.2 and 15.2-20.0 in the frequency ranges from 50 to 65 GHz, respectively.**

Key words: complex permittivity measurement, waveguide penetration method, biological cells, and millimeter-wave

I. INTRODUCTION

Recently application of microwaves (MW) and millimeter-waves (MMW) are increasing. The opportunity that common people are exposed to MW and MMW will increase. Thus, it is necessary to assess the effects of MW and MMW on the biological body.

Currently, we are preparing to investigate biological effect of MW to MMW frequency band on the biological body by *in vitro* study. Electromagnetic field dosimetry is required to evaluate the effect of high frequency electromagnetic field (EMF). Theoretical, numerical, and experimental approaches have been examined to estimate specific absorption rate (SAR) for *in vitro* studies [1], [2].

Microdosimetry for cellular and subcellular is one of the research subjects of priority [3]. Complex permittivities ε^* (= $\varepsilon' - j\varepsilon''$) of biological cells are required for microdosimetry. In past works, there have been few studies on complex permittivity of biological cells [4], [5]. Those studies are performed in the frequency range from 45 MHz to 26.5 GHz, and indicated effectiveness to measure complex permittivity of cells. However, those studies do not consider measuring complex permittivity at MMW frequency band. We focused this study on the waveguide penetration (WP) method developed by Nishikata [6], [7] as a candidate for measuring complex permittivity from MW to MMW frequency band.

The purpose of this study is to estimate complex permittivity for biological cells. The measurement of the complex permittivity only cell is not feasible, because it is difficult to obtain sufficient volume of cells for measurement. We use mixed samples which consist of isosmotic liquid and biological cells, for measurements. The relationship between the complex permittivity of mixed sample and the volume ratio of cells in mixed sample was used for estimation. And, complex permittivity of the 100 % volume ratio of biological cell was estimated by complex permittivity measured each volume ratio. In this paper, the measurement frequencies are from 1.7 to 2.6 GHz and form 50 to 65 GHz. These frequency ranges have not been measured in WP method yet.

II. WAVEGUIDE PENETRATION METHOD

A. Experimental setup

Figure 1 shows a schematic diagram for the WP method. This is a method to perform two-port scattering parameters measurement by a vector network analyzer. Complex permittivities are calculated from scattering parameters measured in three conditions, waveguide only, waveguide with dielectric tube without specimen, waveguide with dielectric tube filled with specimen. The detail of the theory to estimate complex permittivity is explained in [6], [7].

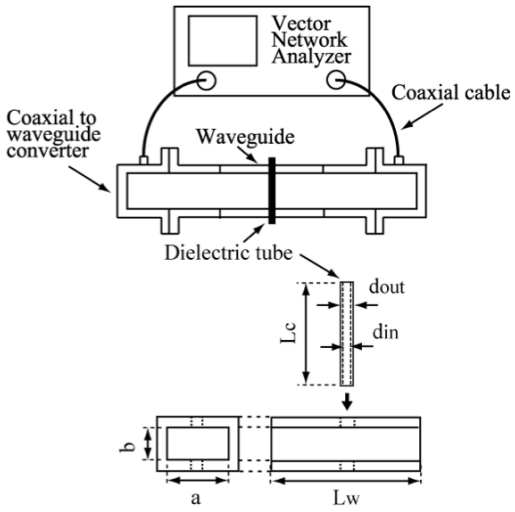


Fig. 1 Waveguide penetration method

The measurement frequency ranges were selected from 1.7 to 2.6 GHz (MW frequency range in this paper) and 50 to 65

GHz (MMW frequency range in this paper), which are restricted by the waveguide dimensions presented in Table 1. The size of dielectric tube is also presented in Table 1.

TABLE 1

DIMENSIONS OF WAVEGUIDE AND DIELECTRIC TUBE

Frequency [GHz]	a [mm]	b [mm]	Lw [mm]	dout [mm]	din [mm]	Lc [mm]
1.7-2.6	109	54.6	610	6.04	4.11	110
50-65	3.76	1.88	21.0	0.73	0.28	31.9

The volume of the specimen is 1.46 ml in the MW and 1.97 μl in the MMW, respectively. If the coaxial probe (Agilent 85070E) is used for these frequency ranges, the volume of specimen is required more than 100 ml in the MW and at least 500 μl in the MMW, respectively. Thus, this method has an advantage over the coaxial-line probe method in the volume, because required volume of specimen is much less than the coaxial probe method.

B. Validation of reliability by measuring pure water

The performance of this system was validated by measuring pure water. The measured data were compared with the values from calculated Debye's formula [8]. The temperature was 25.0 ºC. The measurements were performed five times, and the obtained data were averaged. Figure 2 indicates dependence of complex permittivity of pure water on the frequency. As a reference the measured values with a coaxial probe were also shown. This probe covers 500 MHz to 50 GHz. The black line indicates theoretical value calculated by Debye's formula at 25.0 ºC, the blue line indicates measured values by coaxial-line probe, and the red line indicates measured values by WP method. In this paper, the solid line indicates real part (ε'), and the dotted line indicates imaginary part (ε''). The measured values by WP method agreed well with theoretical values. The reliability of this system was confirmed by the measurement of pure water in these frequency ranges.

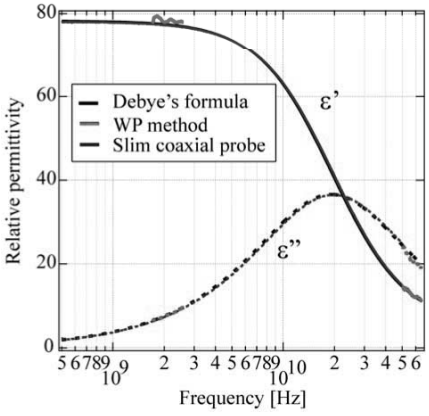


Fig. 2 Validation of WP method

III. ESTIMATION OF COMPLEX PERMITTIVITY FOR BIOLOGICAL CELL

A. Estimation method

We assumed the complex permittivities of mixed samples depend on the volume ratio of cells to the total volume. The complex permittivity of mixed sample was measured in estimation. Then, the volume ratio of cells was changed, and complex permittivity of the 100 % volume ratio of biological cells was estimated by complex permittivity measured each volume ratio. Here, the substructure of biological cells was ignored and biological cells were assumed as having homogeneous complex permittivity.

Chinese hamster ovary (CHO)-K1 cell was measured as a sample of biological cell. The cell was assumed a sphere with diameter 20 μm. Ham's F-12 medium and aqueous solution of mannitol were used as isosmotic liquid with the cell. Ham's F-12 medium was used to cultivate the cells, and the mol concentration for aqueous solution of mannitol was controlled 0.296 mol/l.

B. Measurement of only Ham's F-12

Complex permittivity of only Ham's F-12 was measured. The temperature was 26.0 ºC. Figure 3 indicates dependence of complex permittivity of only Ham's F-12 on the frequency. The black line indicates the measured values by coaxial probe, and the red line indicates the measured values by WP method. ε' was bigger than ε'' under the 20 GHz. However, ε'' was bigger than ε' over the 20 GHz. The measured values by WP method agreed well with the measured values by coaxial probe in the MW, and were on the extrapolated curve of the coaxial probe in the MMW.

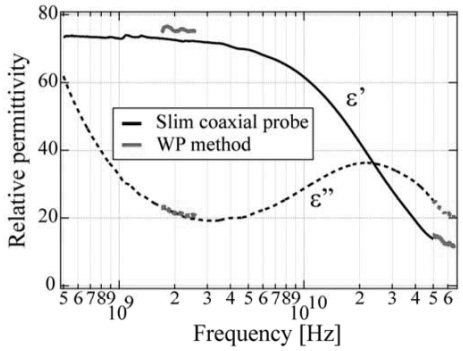
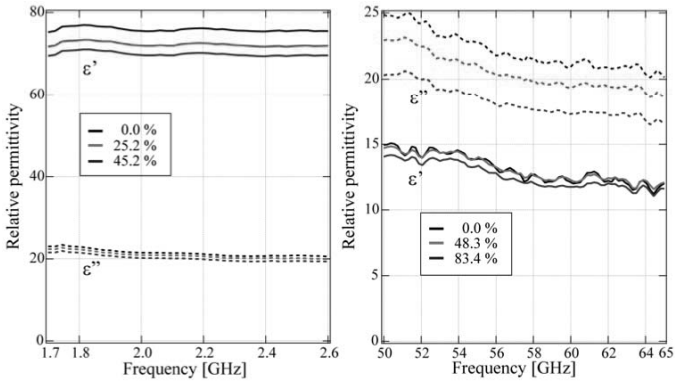


Fig. 3 Dependence of complex permittivity of only Ham's F-12 on the frequency

C. Measurement of Ham's F-12 with cells

Complex permittivities of Ham's F-12 with cells were measured. The temperature was 26.0 ºC. Figure 4 indicates dependence of complex permittivity of Ham's F-12 with cells on the frequency for the MW (Fig. 4 (a)) and the MMW (Fig. 4 (b)), respectively. The black line indicates measured values of only Ham's F-12, and the red line and the blue line indicate measured values of mixed samples. In Fig. 4 (a), the volume ratios of cells were 25.2 % and 45.2 % respectively. In Fig. 4 (b), the volume ratios of cells were 48.3 % and 83.4 % respectively. Here, ε' and ε'' decreased with the increase of the volume ratio of cells.

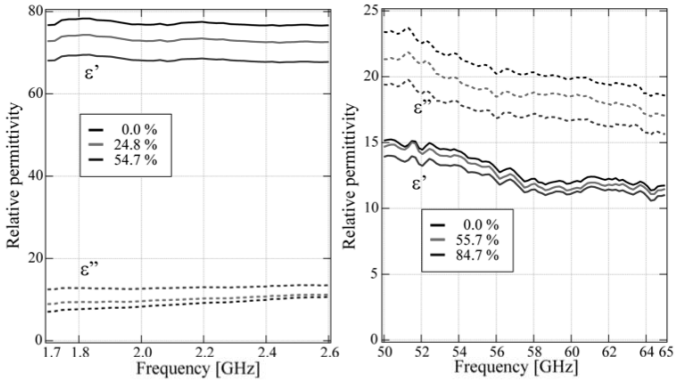


(a) (b)

Fig. 4 Dependence of complex permittivity of Ham's F-12 with cells on the frequency

D. Measurement of mannitol with cells

Complex permittivities of aqueous solution of mannitol with cells were measured. The temperature was 26.0 ºC. Figure 5 indicates dependence of complex permittivity of aqueous solution of mannitol with cells on the frequency for the MW (Fig. 5 (a)) and the MMW (Fig. 5 (b)), respectively. The black line indicates measured values of only aqueous solution of mannitol, and the red line and the blue line indicate measured values of mixed samples. In Fig. 5 (a), the volume ratios of cells were 24.8 % and 54.7 % respectively. In Fig. 5 (b), the volume ratios of cells were 55.7 % and 84.7 % respectively. In Fig. 5 (a), ε'' increased with the increase of the volume ratio of cells. The dependence of ε'' on the volume ratio was inverted compared with the Ham's F-12 case. Other characteristics were almost same as the Ham's F-12 case.

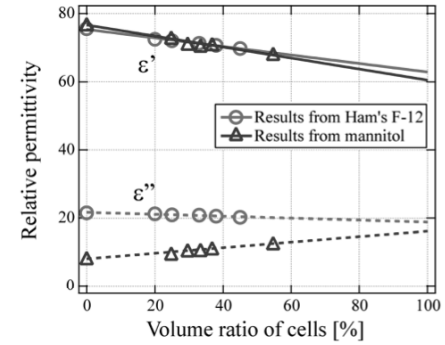


(a) (b)

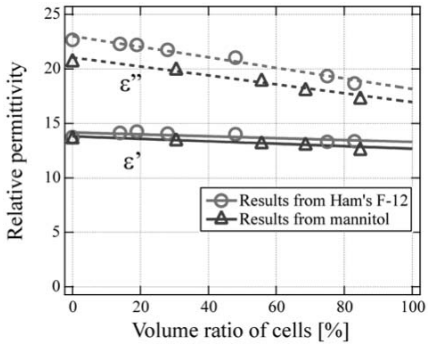
Fig. 5 Dependence of complex permittivity of aqueous solution of mannitol with cells on the frequency

E. Estimation of complex permittivity of cells

Complex permittivity of the 100 % volume ratio of CHO-K1 cell was estimated by complex permittivity measured each volume ratio. Figure 6 indicates dependence of complex permittivity of mixed sample on the volume ratio of cells at 2.45 GHz case (Fig. 6 (a)) and 60 GHz case (Fig. 6 (b)), respectively. Red circles indicate measured values of Ham's F-12, and blue triangles indicate measured values of aqueous solution of mannitol. Here, we estimate complex permittivity of cells by the linear least squared method. Lines in Fig. 6 indicate fitted values. Fitted values of Ham's F-12 case and mannitol case fairly agreed with each other at 100 %.



(a)

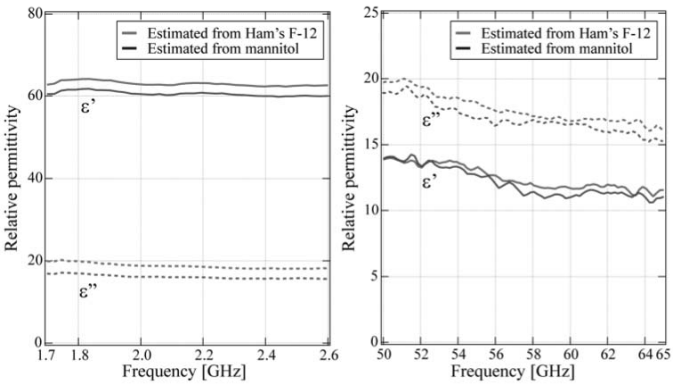


(b)

Fig. 6 Dependence of complex permittivity of mixed sample on the volume ratio of cells

E. Estimated complex permittivities of cells

Figure 7 indicates dependence of estimated complex permittivity of cells on the frequency, for the MW (Fig.7 (a)) and the MMW (Fig. 7 (b)), respectively. The red line indicates the estimated values from Ham's F-12, and blue line indicates the estimated values from aqueous solution of mannitol. ε' and ε'' of CHO-K1 cell were estimated to be 59.9-64.1 and 15.6-20.2 in the MW, and 10.6-14.2 and 15.2-20.0 in the MMW, respectively. The maximum difference between red line and blue line was 3.2 in Fig. 7 (a), and 1.1 in Fig. 7 (b). Estimated complex permittivities in two conditions were almost the same values.



(a) (b)

Fig. 7 Dependence of estimated complex permittivity of cells on the frequency

G. Discussion

Here we discuss the validity of linear approximation by Lichtenecker's logarithm mixed law (LLML) [9]. According to LLML, the effective complex permittivity for the mixture of two kinds of dielectric materials is expressed by Eq. (1):

$$\log(\varepsilon^*_{eff}) = v_1 \log(\varepsilon^*_1) + v_2 \log(\varepsilon^*_2). \quad (1)$$

Where ε^*_{eff} is the effective complex permittivity of mixed sample, ε^*_1 and ε^*_2 are complex permittivities, and v_1 and v_2 are the volume ratios of each dielectric material, respectively. Here, $v_1 + v_2 = 1$ must be satisfied. This formula means that the effective complex permittivity consists of two kinds of dielectric material is obtained by the relationship of each complex permittivity and volume ratio.

Calculation conditions were presented in Table 2. ε^*_1 were assumed complex permittivity of CHO-K1 cell, $\varepsilon^*_{2\text{-ham}}$ and $\varepsilon^*_{2\text{-man}}$ were assumed complex permittivity of Ham's F-12 and mannitol, respectively. Figure 8 indicates dependence of calculated complex permittivity of mixed sample on the volume ratio of cells, for the MW (Fig. 8 (a)) and the MMW (Fig. 8 (b)). Red line indicates calculated values of Ham's F-12, and blue line indicates calculated values of aqueous solution of mannitol. Estimations with LLML under the conditions of Table 2 became linear approximation, according to the results shown in Fig. 8. This is caused by the relatively small difference of complex permittivities between two materials. We think that the assumption of the linear least squared method is appropriate for the estimation of complex permittivities for cells.

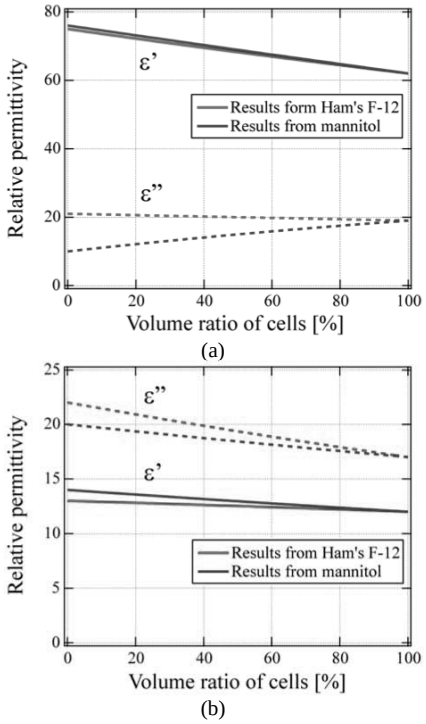


Fig. 8 Dependence of complex permittivity calculated by LLML on the volume ratio of cells

TABLE 2

CALCULATION CONDITIONS

Frequency [GHz]	ε^*_1	$\varepsilon^*_{2\text{-ham}}$	$\varepsilon^*_{2\text{-man}}$
1.7-2.6	62 - j19	75 - j21	76 - j10
50-65	12 - j17	14 - j22	13 - j20

IV. CONCLUSION

In this study, we estimated complex permittivity of CHO-K1 cells in the MW and in the MMW by WP method. It was assumed that cells have homogeneous complex permmitivity and spheare shape in this estimation. As results, ε' and ε'' of CHO-K1 cell were estimated to be 59.9-64.1 and 15.6-20.2 in the MW, and 10.6-14.2 and 15.2-20.0 in the MMW, respectively. The feasibility of applying WP method was investigated for the measurement of complex permmitivity for biological cells. We also discussed the validity in use of linear least squared method for estimation by LLML. It was found that employment of linear approximation was appropriate under the conditions shown in Table 2, i.e. difference between ε^*_1 and ε^*_2 were relatively small.

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