# Application of a Miniaturised Probe for the Acquisition of Dielectric Data in Living Systems

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*Dedicated to Werner Müller-Warmuth on the occasion of his 65th birthday*

The complex permittivity $\varepsilon^*$ has been measured non-invasively in the cornea of two types of animal eyes and in erythrocyte suspensions in the frequency domain 1 ... 18,000 MHz. These measurements shall help to distinguish between eye diseases in a very early stage and to track the possible effect of "microthermics", respectively. The analysis of the miniaturised probe used for the reflection method and the experimental set-up with its automatic scanning facility are presened.

## Introduction

The use of information from both the frequency and temperature dependence of the complex permittivity is not new: Early models have been proposed about 1930 [1, 2], experimental work began to yield reliable data about 1940 [3, 4]. Although magnetic and dielectric relaxation processes could be compared in polar liquids as early as 1965 [5], the breakthrough of interest in this method in the field of biophysics occurred with the need for dielectric data of different types of human tissues and organs to have a broad base for hyperthermia planning to aim at cytostatic effects in tumour treatment [6]. Naturally, for in vivo experiments these data must be acquired by using non-invasive methods. In contrast to methods where resonant cavities are utilised to measure the real part $\varepsilon'$ of the complex permittivity $\varepsilon^*$ from the detuning and the imaginary part $\varepsilon''$ from the resonance broadening, the reflection method can be used to give reliable results via the standing wave pattern between the transmitter and the reflecting plane, i.e. the surface of dielectric under test, in the frequency domain between 1 ... 10,000 MHz.

If either small amounts of tissue are available or if the organ under test has tiny dimensions, the probe diameter has to be extremely small to make sure that at least 98 ... 99% of the electric field energy is concentrated in the volume of interest. This demand had

to be fulfilled, as we plan measurements of the dielectric behaviour of the human eye's cornea in the frame of a cooperation with the Department of Ophthalmologics of the University of Tübingen. There is one more reason for miniaturised probes. In the field of biophysics, the interest in possible non-thermal interactions between systems on the cellular level and electromagnetic oscillations is of high actuality. The question behind is the following: Although the moderate electric field density at frequencies far below the critical frequency of 18,000 MHz (where $\varepsilon''$ of water reaches its maximum value) should result in temperature rises below $10^{-6}$ deg/s, the strong electric dipole moments inherent to the head groups of the phospholipids forming the cell membrane could possibly cause temperature gradients in the vicinity of the cells and/or over the membranes itself. We are interested in investigating these "microthermal" effects in the frame of a project "Interactions of High Frequency Electromagnetic Fields with Biological Matter", sponsored by the Bundesamt für Strahlenschutz.

Four of these probes using the reflection method – one described here – have been tested for non-invasive measurements on animal eyes and on erythrocyte suspensions in the frequency domain 1 ... 1,000 MHz; the data presented here in the domain 2,000 ... 18,000 MHz have been taken at the Munich site of the Bundesamt für Strahlenschutz. Naturally, to get highest accuracy at the low frequency limit of the real part of $\varepsilon^*$, data must be taken in the 0.1 ... 1.0 MHz region; the experimental set-up to yield these results is under construction.
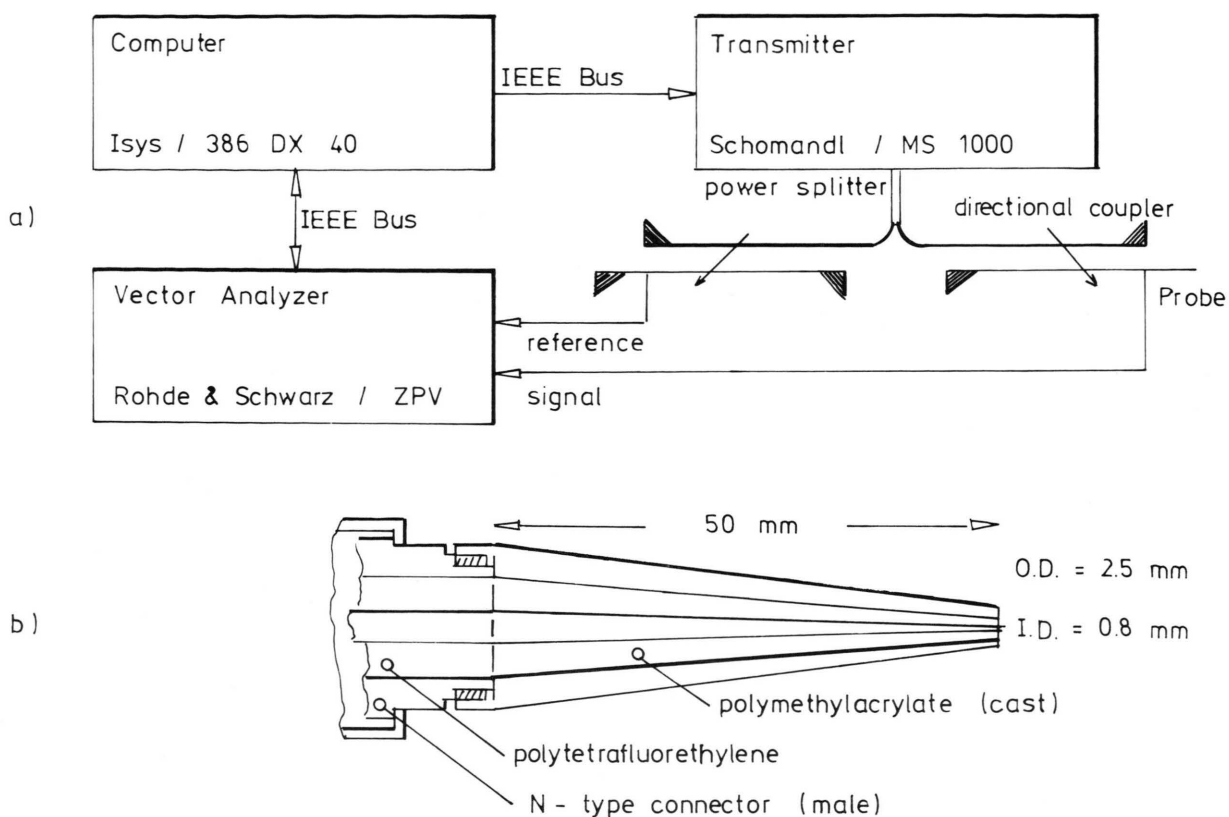
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Fig. 1. a) Block scheme for admittance measurements in the frequency range 1 … 1000 MHz. b) Tapered open ended coxial line.

## Method

Under the assumption of an infinite sample terminating an open ended coaxial line, the terminating complex impedance $Z_t^*$ is governing the standing wave pattern along with the real resistance $Z_0$ of the line. Calibration of the whole propagation behaviour using the distinctive values $Z_t^* = Z_0$ and $Z_t^* = 0$ allows for the calculation of both the resistance $R_t$ and the reactance $X_t$ of the quantity $Z_t^* = R_t + jX_t$ from the standing wave ratio and the shift of the standing wave minimum. At a given site $z = l$ between transmitter and measuring plane $z = 0$ we find in this signal channel the transformed impedance

$$Z_s^*(l) = Z_0 \frac{Z_t^* + jZ_0 \tan(2\pi\, l/\lambda)}{Z_0 + jZ_t^* \tan(2\pi\, l/\lambda)}$$

for a coaxial line assumed to be lossless. This value has to be compared to the value $Z_r^*(l')$ in a reference channel with termination $Z_0$ (see Figure 1). This is done automatically when scanning the frequency using a transmitter and a vector analyser both triggered by a common computer that is as well responsible for the correct transform given above. We choose the presentation in terms of conductance $G$ and susceptance $B$ of the complex admittance $Y^* = G + jB$ instead of $Z^* = 1/Y^*$, as the dielectric behaviour $\varepsilon^* = \varepsilon' - j\varepsilon''$ can be expressed in a much more convenient form, then.

Since the early 80's this technique is well understood both experimentally [7, 8] and theoretically [9, 10], and many interesting results have been published since [11, 12]. In the case of the reflection method instead of resonant studies, the terminating complex impedance is represented by a capacitance $C$, partly filled with the dielectric, consisting of the fringe part $C_f$ thought inside the line and the part $C_0$ outside the open-ended line to be loaded with the substance;

$$C = C_f + (\varepsilon' - j\varepsilon'')\, C_0,$$

$$Y_t^* = \omega\varepsilon'' C_0 + j\omega(\varepsilon' C_0 + C_f). \tag{1}$$
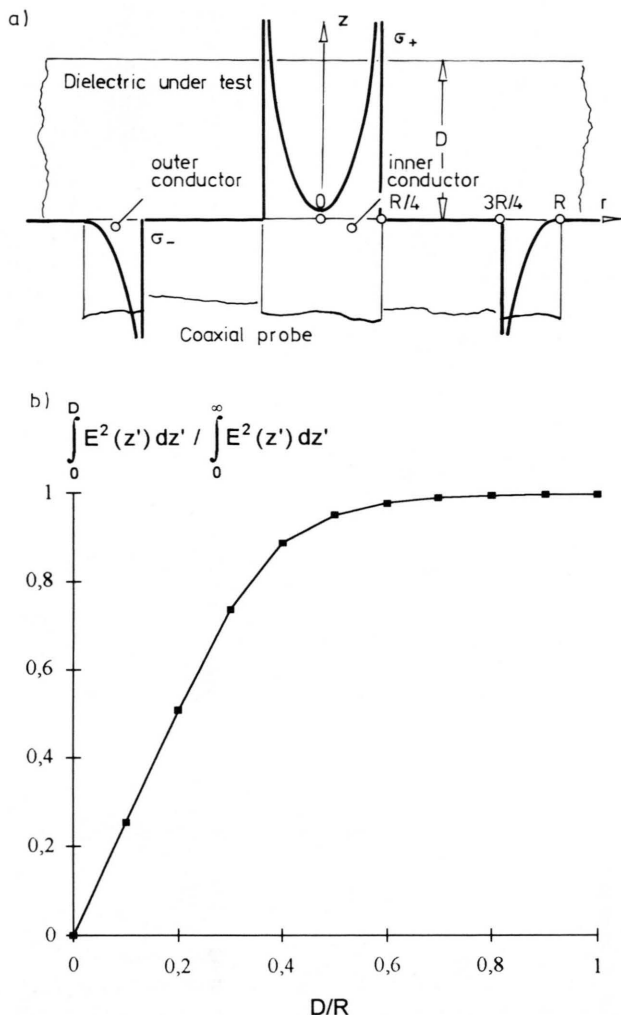
a)



b)



Fig. 2. a) Maximum charge density vs. radius of the coaxial probe. b) Normalized energy density vs. relative sample thickness.

The disadvantage of this method consists in the need to calibrate with two dielectrics with well known behaviour $\varepsilon^*(\omega)$ the two parameters $C_f$ and $C_0$. In anticipation of our results as given in Fig. 3, we found from a calibration with bidistilled water and dry air the values $C_f = 2.056$ pF and $C_0 = 0.022$ pF, respectively, for the miniaturized probe of 2.5 mm outer diameter and 0.8 mm inner diameter (having $Z_0 = 50\ \Omega$ when filled with polymethylacrylate).

To be able to judge the stringent condition of "infinite sample", we calculated the dependence of the electric field energy $W(r, z)$ based on the electric field

components $E_z(r, z)$, $E_r(r, z)$ as following from the charge distributions on the top of the inner and outer conductor endplates (see Figure 2). The integration over $r$ can easily be done numerically, as $E^2(r, z) = E_z^2(r, z) + E_r^2(r, z)$ is falling off rapidly for values $r > R$. So we are left with the influence of finite thickness $D$ of the sample in $z$-direction. The normalised quantity

$$f(D) = \frac{\displaystyle\int_0^D E^2(z)\,\mathrm{d}z}{\displaystyle\int_0^\infty E^2(z)\,\mathrm{d}z}$$

is a criterion for the "filling factor" of the parameter capacitance $C_0$: If we choose $f$ to be 0.99, which corresponds to a limiting relative accuracy of $\pm 1\%$ in the resulting values of $\varepsilon'$ nd $\varepsilon''$, the thickness of our sample has to be $D \cong 0.7$ R at least. In the case of measurements on animal eyes we have to think in the reverse direction, yielding a probe radius of $R = 1.4$ mm for a given cornea thickness of $D = 1.0$ mm. The value of $C_0$, by the way, can be calculated from the limiting value of the integral, $\int_0^\infty E^2(r, z)\,r\,\mathrm{d}r\,\mathrm{d}z$. We come close to the measured value, which proves not so much the quality of our fitting then the correctness of our assumption concerning $E_r(r, z)$ and $E_z(r, z)$ (see Figure 3).

The limits of the methods applied here follow from two facts. From (1) we can deduce the errors $\Delta\varepsilon'$ and $\Delta\varepsilon''$ from the uncertainties $\Delta G$ and $\Delta B$ of the complex admittance. With the values $\Delta G = \Delta B = 0.005$ mmho of the vector analyser, we can be sure to add a relative error smaller than 1% for values of $\varepsilon'$ taken above 6 MHz, and of $\varepsilon''$ taken above 3 MHz. The frequency dependence of $\varepsilon^*$ is given by the Debye relations

$$\varepsilon' = \varepsilon_\infty + (\varepsilon_{st} - \varepsilon_\infty)\frac{1}{1 + (f/f_0)^2},$$

$$\varepsilon'' = (\varepsilon_{st} - \varepsilon_\infty)\frac{f/f_0}{1 + (f/f_0)^2}. \qquad (2)$$

As for high frequencies $f \gg f_0$ the difference $\varepsilon' - \varepsilon_\infty$ is comparable to the absolute error $\Delta\varepsilon'$, we are sure to add less than 1% relative error in determining our three parameters $\varepsilon_\infty$, $\varepsilon_{st}$, and $f_0$ from (2), when we restrict ourselves to the region 5 MHz $\leq f \leq$ 400 MHz. This is not valid for the values taken between 1,000 ... 18,000
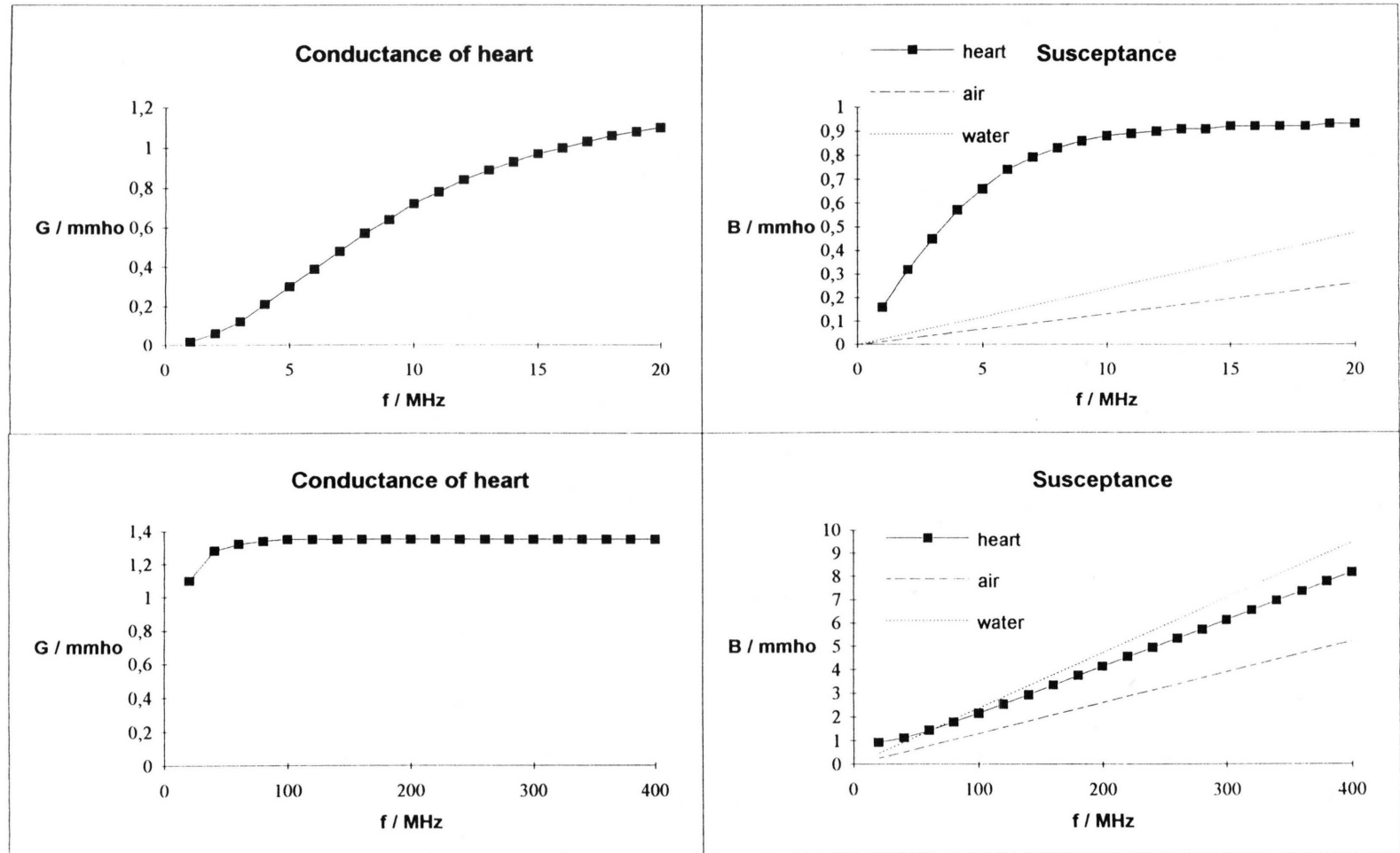
Fig. 3. Conductance and susceptance of heart in the range 1 ... 400 MHz. As fitting region we used the domain 5 ... 400 MHz (lower part). The values on top of the figure are extrapolated, showing the necessity of extending our measuring capabilities to still lower frequencies.
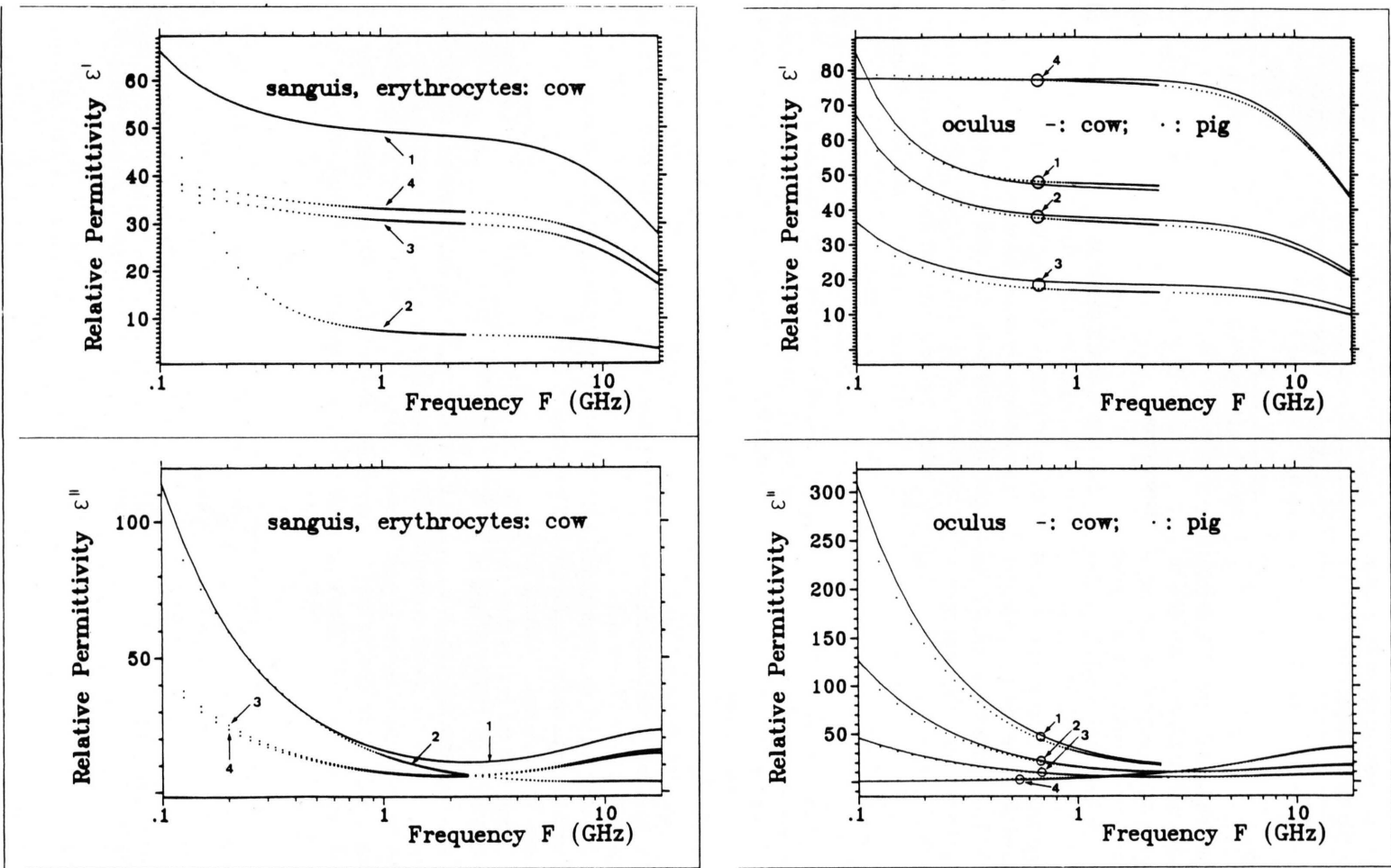
Fig. 4. *Left-hand side:* Comparison of relative permittivities between 1: blood (sanguis), 2: erythrocytes, 3: 2× thawed erythrocytes (31% water content) and 4: 4× thawed erythrocytes (27% water content). – *Right-hand side:* Comparison of relative permittivities between 1: cornea, 2: cortex lentis, 3: nucleus lentis and 4: corpus vitreum of cow and pig.

MHz, as $\varepsilon'(f)$ and $\varepsilon''(f)$ are varying again because of the neighbourhood to the water dispersion and -absorption.

## Preparation and Results

The animal eye was taken from the central slaughter site directly after the animals' death and kept at 4 °C until our measurements started. Except for the invasive measurements of the *nucleus lentis* and the *corpus vitreum*, the eyes were kept humid to avoid changes in the collagen structure by drying (see Figure 4). The blood samples from our collaborators in the Medical Department were treated the same way except for the thawed samples. In the latter case we destroyed the erythrocyte membranes to overcome the large permittivity contribution: Cooling down to −20 °C, adding 75% of water and thawing results in a rupture of the membranes in the hypotonic surrounding (see also Figure 4).

As a basis for an interpretation we want to restrict ourselves to measurements of the cornea and the erythrocytes, because the heart muscle tissue is a kind of "calibration dielectric" well known since 1986 [6]. In the case of erythrocytes we can extract the parameters $\varepsilon_\infty$, $\varepsilon_{st}$ and $f_0$ describing but one region of dispersion and absorption of the cells, as the water content in any of our four samples is well known. These data are necessary, especially for samples of neuroblastoma and fibroblast cells to form the basis of a model for the description of a possible "microthermic" heating far from the water contribution. For the cornea data the situation is quite different. Here, the Debye equations (2) have to yield two sets of parameters, namely $\varepsilon_{\infty,1}$, $\varepsilon_{st,1}, f_{0,1}$ and $\varepsilon_{\infty,2}$, $\varepsilon_{st,2}, f_{0,2}$, as the water content cannot be varied experimentally. As a matter of fact, just this water content is one of two criteria for an early diagnosis of an abnormal behaviour of this type of tissue (see the following table).

| Substance | $\varepsilon_\infty$ | $\varepsilon_{st}$ | $f_0$/MHz |
|---|---|---|---|
| Erythrocytes | 6.8 | 156.4 | 70.6 |
| Cornea | 45.5 | 145.0 | 74.1 |
| | 4.4 | 45.5 | 18.000 |

All errors are assumed to be ±2% (see "Method").

## Discussion

The miniaturised probe as a part of an automated set-up for reflection type measurements of the complex permittivity meets two demands. It is sufficiently tiny to allow precision measurements for small thickness in cornea diagnosis and for small volumes in suspensions of cells other than erythrocytes and, furthermore, it guarantees relative errors smaller than 1% in the frequency range 5 ... 400 MHz despite of the relatively low value of $C_0 = 0.022$ pF.

The strong frequency (in the easily accessible region) dependence for the cornea of both $\varepsilon'$ and $\varepsilon''$ gives a reliable criterion for diagnostic purposes concerning the value of $\varepsilon_{st}$ as reflecting the water content, and the value of $f_0$ reflecting the mobility of the permanent electric dipole moments. The relatively strong contribution of the cellular dielectric behaviour to the cell/water mixture for the erythrocytes gives hope to get results in suspensions of cells down to concentrations as used to measure data of proliferation, adhesion and ion-fluxes [13, 14].

[1] P. Debye, Polare Molekeln, Hirzel, Leipzig 1929.
[2] J. Pätzold, Z. techn. Physik **13**, 212 (1932).
[3] H. Schafer and H. Schwan, Ann. Physik **43**, 99 (1943).
[4] J. A. Straton, Electromagnetic Teory, McGraw-Hill, New York 1941.
[5] K. Kramer, W. Müller-Warmuth, and N. Roth, Z. Naturforsch. **20a**, 1391 (1965).
[6] M. Ota, Dissertation Fachbereich Physik, Freie Universität Berlin 1986.
[7] M. A. Stuchly and S. S. Stuchly, IEEE Transactions **IM 29**, 176 (1980).
[8] E. C. Burdette, F. L. Cain, and J. Seals, IEEE Transactions **MTT 28**, 414 (1980).

[9] G. B. Gajda and S. S. Stuchly, IEEE Transactions **MTT 31**, 380 (1983).
[10] T. P. Marsland and S. Evans, IEEE Proceedings **134**, 341 (1987).
[11] C. P. Jenin and H. P. Schwan, Biophys. J. **30**, 285 (1980).
[12] U. Kaatze, Progr. Colloid. Polymer Sci. **67**, 117 (1980).
[13] R. B. Gennis, Biomembranes, Springer-Verlag, New York 1989.
[14] H. Mohamed-Ali, H. Kalkenbrock, N. Ulbrich, K. Kramer, and H. J. Merker, Eur. J. Clin. Chem. Clin. Biochem. **32**, 1 (1994).