# FURTHER STUDIES ON THE LOW FREQUENCY DIELECTRIC SPECTROSCOPY OF LIPOSOMES

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It has previously been demonstrated (Barker at al, 1989) that low frequency dielectric spectroscopy is of value in the study of liposomes. In this investigation we have used this technique to study the lipid bilayer phase transition temperature ($T_c$) of liposomes based on L-α-dipalmitoylphosphatidylcholine (DPPC). Multilamellar liposomes of diameter 1.5 μm were produced, containing 0, 25, 33, 50 mole% cholesterol and having total lipid content 25 mg/ml. The aqueous phase used was deionised water. The samples were analysed by the dielectric spectrometer as before (Barker et al, 1989), over a frequency range of 1E5 Hz to 1E-3 Hz and a temperature range of 305 to 335 K. An example of the spectra produced is shown in Figure 1. The low frequency region of the spectra has been found to be dependant on the lipid bilayer of the liposomes (Barker et al, 1989). In this study, account has been taken of the external aqueous phase of the system. The liposomes and the external water have been assumed to be electrically in parallel. A value for the capacitance of the liposomes themselves has been derived, the "intrinsic capacitance", which is defined as:

Intrinsic capacitance (liposomes) = Capacitance (system) - 85% Capacitance (water)

The intrinsic capacitance at low frequencies is a function of both the cholesterol content and the temperature of the sample.

Fig.1: The dielectric response of DPPC liposomes at 305 K

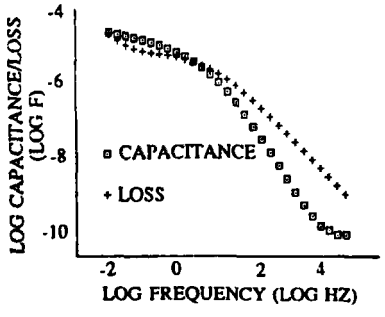
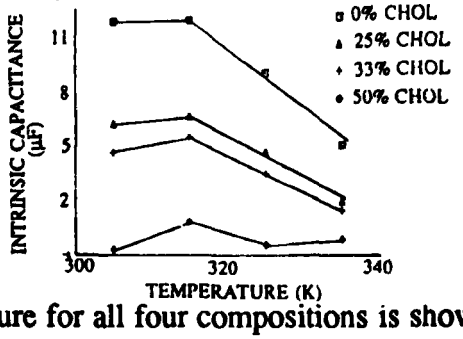



Fig.2: The intrinsic capacitance at 3.162E-2 Hz of liposomes based on DPPC at various temperatures




A plot of the intrinsic capacitance against temperature for all four compositions is shown in Figure 2. At a temperature of 315 K a discontinuity is seen in the curve. There is a linear relationship between intrinsic capacitance and temperature above this point for liposomes containing 0, 25 and 33 mole% cholesterol (r = -0.9959. -0.9959, -1.000 respectively), but there is no such correlation for the sample containing 50 mole% cholesterol. The gradients of these lines also show a linear relationship with percentage cholesterol content (r - 0.9998). The above results indicate that there is some change in the behaviour of the liposomal sample at 315 K. This change is progressively less marked as the percentage cholesterol content of the liposomes is increased, until at 50 mole% cholesterol no change is observed. It is well known that the $T_c$ of DPPC is 315 K and that the magnitude of the phase transition in liposomes is reduced as the cholesterol content is increased, until at 50 mole% cholesterol the transition is abolished. Therefore it would appear that the change in the intrinsic capacitance observed with low frequency dielectric spectroscopy is a measure of the $T_c$ of the liposomes. The linear relationship between the gradients of Figure 2 and percentage cholesterol content of the liposomes indicates that the discontinuity observed at 315 K is a function of the cholesterol content of the samples.

In conclusion, these results have shown that it is possible to measure the $T_c$ of the lipid bilayer using the technique of Low Frequency Dielectric Spectroscopy, and that the value obtained is in agreement with literature values.

Barker, S.A. et al (1989) J. Pharm. Pharmacol. 41:1P