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A THEORETICAL MODEL OF ULTRASONIC ATTENUATION IN BLOOD

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1. INTRODUCTION

There has been a considerable interest in the ultrasonic properties of blood, stimulated by a number of different objectives. Firstly it is the most freely available source of human cells for fundamental experiments directed at establishing the mechanisms of interaction of the ultrasonic waves with cells – a topic in which firm results are still relatively elusive [1,2]. Secondly it is of importance as one of the foundation stones of the vast field of ultrasonic blood flow measurement using doppler techniques [3]. Thirdly it is of importance in terms of the potential contribution of ultrasonic diagnostics to the field of haematology [4,5].

The majority of the published work has been experimental, since theoretical models that are appropriate are not always easy to identify. The present paper describes a comparison of experimental results of ultrasonic attenuation with computational results obtained from a model based on an assembly of scatterers, each consisting of a spherical shell (the membrane) surrounding a viscous fluid. It is found that while the model can give reasonable agreement with the experimental results for old and heated blood, it does not for fresh blood, indicating the importance of the shape of the cells in contributing to the scattering of ultrasound from fresh blood. The implications of this for future modelling are briefly discussed.

2. THEORETICAL MODELS

There is a wide variety of mathematical approaches in the literature to the problem of the propagation of acoustic waves in random media, including suspensions of one type of particle in a fluid matrix [6]. One of the most instructive from the point of view of elucidating mechanisms of interaction, is based on the solution of the scattering problem for a single, isolated scatterer, (a blood cell in the present discussion), and utilising the results from this to obtain values for the ultrasonic velocity, attenuation, or scattering from an assembly of such scatterers.

Solution of the single body scattering problem is considerably facilitated if a shape is chosen for the scatterer so that its surface corresponds to a constant value for one of the coordinates in one of the systems of coordinates in which the wave equation is separable. (It is explicitly assumed that the problem considered is a linear one, even when multiple scattering is involved.)

The simplest of these shapes that can be considered is a sphere, and this appears to be a good approximation for several types of mammalian cells in suspension[7].

The cell membrane clearly has acoustic properties different from both the intracellular contents and the suspending medium – indeed there is evidence [8]that it can support shear waves. Thus a model of the cell may consist of a sphere of viscous fluid, (the intracellular contents, which have dimensions very much less than the wavelengths involved and whose specific architectures may thus, in the first instance, be neglected), surrounded by a viscoelastic shell (the cell membrane), immersed in the viscous fluid of the suspending medium. Only longitudinal waves will propagate in the outer- and inner-most fluids, while both longitudinal and shear waves can propagate in the membrane. The temperature effects established by the differing thermodynamic properties of the media, can lead to the generation of thermal waves at both of the shell boundaries, and these may propagate in all three media. It is only recently [9] that this last effect has been formally included in shell scattering models in the literature.

In the format identified above, the model requires 22 input parameters. For the majority of these the literature does not provide values appropriate for biological cells. Much of the data which is in the literature has been obtained for red blood cells, and is therefore particularly relevant to the present investigations. In spite of the serious restriction that the absence of appropriate data potentially represents, the model has been found to give good agreement with experimental measurements of attenuation on Hela, Hybridoma, and BHK cell suspensions [7].The limitations of the work previously reported were firstly that measurements were made only at frequencies up to 27 MHz, and secondly that they were only made on dilute suspensions (up to 0.2% by volume, or 12×10^5 cells per ml), in which the cells can be considered to act as independent scatterers, and multiple scattering effects can be neglected. The present work extends this comparison, albeit on a different type of cell, by considering frequencies up to 140 MHz, and concentrations up to a haematocrit of 40%, in which multiple scattering effects are mandatory [10].

The prime advantage of a computational model is that it can be used to identify the relative importance of the different parameters, and to direct the efficient planning of experiments. Preliminary computational results [7] indicate that the membrane on the mammalian cells used in the previous investigations accounts for less than 4% of the attenuation at 20 MHz, and its contribution decreases as frequency increases. Above 20 MHz, the dominant mechanisms are absorption within the cells and scattering effects. At 20 MHz they are approximately equal in magnitude, and as frequency increases, the former falls while the latter rises in importance, with the scattering contributing 70% of the attenuation at 30 MHz. Detailed analysis of the sensitivity of the results to variations in the values of the different input parameters have been commenced, but have proved difficult to normalise [11]. In many ways the discuss-

ion of a specific type of cells (as in the present case) is likely to be more productive.

Before proceeding to the comparison of the computational results obtained using the model with experimental data on attenuation in blood (from the literature of one of the authors), the vital problem of the incorporation of multiple scattering into the model computations needs to be discussed. There are a number of approaches to this problem [6]. The one adopted here was a method of successive approximations, following Beltzer [12]. The suspending fluid is considered initially to contain a low concentration of scatterers, such that independent scattering can be assumed. From the single scattering approach, the ultrasonic properties of this suspension can then be calculated. These values are, in turn, considered to be the effective parameters of a new suspending medium into which, again, a low concentration of scatterers is suspended. The effective propagation parameters of this new suspension are determined, and the process repeated until the total number of scatterers that have been considered to have been suspended has reached the required value. The major differences between the approach of Beltzer and Brauner [12] and that used here are two. Firstly the former authors obtained a value for the longitudinal wave velocity in the medium using the Kramers-Kronig relation, whereas the present authors used the method of Waterman and Truell [13]. Secondly, the former authors did not include viscous and thermal terms. In the present analysis the viscous and thermal waves are included, but are assumed to die out within the inter-cell distance, thus producing no contribution to the multiple scattering. This is equivalent to saying that the suspension retains the thermal and viscous properties of the plasma.

3. COMPUTATIONAL PARAMETERS

The values of the input parameters used for the present calculations were obtained from references [4,5,7,14-19]. A full discussion of the problems of identifying appropriate values and their importance has bee given previously [7,11].The main differences from the values used in the earlier work [7] are the higher values of the attenuations, due to their frequency dependence, and the use of data for the absorption of the intracellular contents derived directly from lysed red blood cells by Collings [5].

The choice of an appropriate value for the radius is difficult to make by a priori arguments. Taking the red blood cells as discs of approximate diameter 8μm and thickness 1-2μm, it appeared reasonable to start with a radius of 4μm, with a view to reducing it as needed.

4. RESULTS

The importance of including multiple scattering is emphasised in figure 1, where the single and multiple scattering results are shown for 2.75μm

radius shells at 100 MHz, as a function of concentration. The continued increase of the former with concentration is not consistent with the experimental results [4,5] which show limiting behaviour more consistent with the multiple scattering results.

The questinn of the value of the radius to use is addressed in figure 2, where the results of the multiple scattering shell model with radii of 4μm and 2.75μm are compared with the experimental results [4,5] on fresh blood, old blood and heated blood. It is clear that the 4μm curve fits none of the experimental results well, while the 2.75μm curve gives quite good agreement to the old and heated blood data. The value of 2.75μm was chosen as the one which gave the best fit as judged by eye. There is some divergence at higher frequencies, but the agreement is excellent between 10 MHz and 80 MHz. This agreement with the old and heated blood suggests that the main reason causing the fresh blood results to differ from the calculations is the specific shape of the healthy red blood cells.

The importance of the membrane, i.e. of using a shell model rather than a fluid sphere is seen in figure 3. The model calculations for a 2.75μm radius shell and spherical liquid drop are compared with the experimental data for the old and heated blood. The differences between the two models are small, ranging from about 10% at 10 MHz to 1% at 140 MHz. However the shell model does provide a good fit up to at least 80 MHz, whereas the liquid drop model agrees only over a limited frequency range of approximately 70-100 MHz.

5. CONCLUSIONS

In spite of the gross assumptions needed to establish a computational model of the type described here, the agreement of the model results with the experimental data is quite impressive, when the cellular geometry can be reasonably approximated by a sphere. The lack of agreement for fresh blood raises the question of other geometrical models. Olszewski [20] carried out calculations on oblate spheroids, but the main problem that arises as soon as the pleasant symmetry of the sphere is discarded is the need to include the orientation distribution of the cells in the model.

In considering the results on old and heated blood, it is clear that although the differences between the shell model and the liquid model are small, the former provides significantly better agreement than the latter. It therefore appears that the presence of the membrane should be formally included in calculations of this type.

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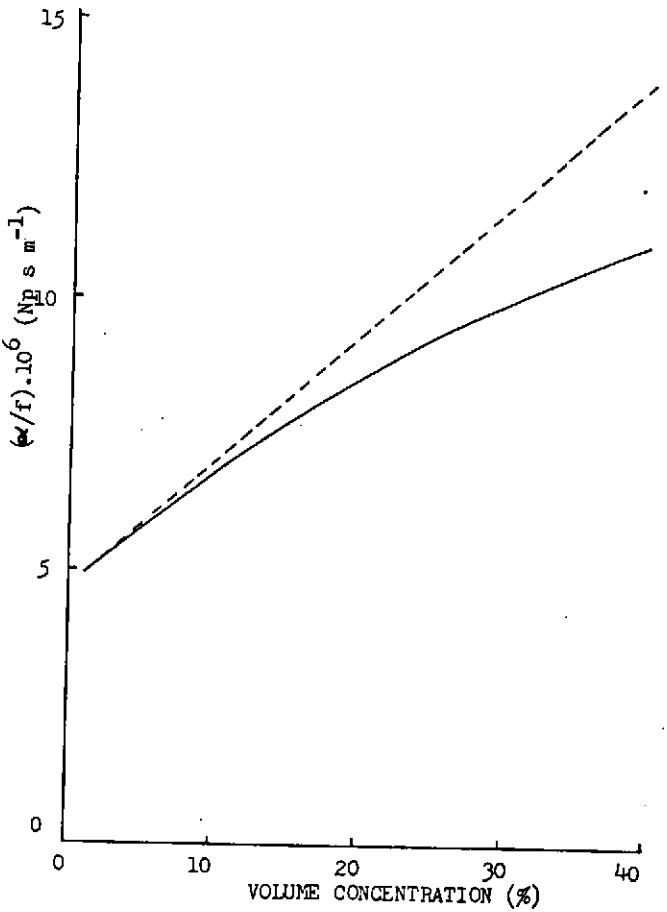

FIGURE 1. Comparison of single scattering (-----) and multiple scattering (———) approaches for 2.75μm radius shells at 100 MHz.

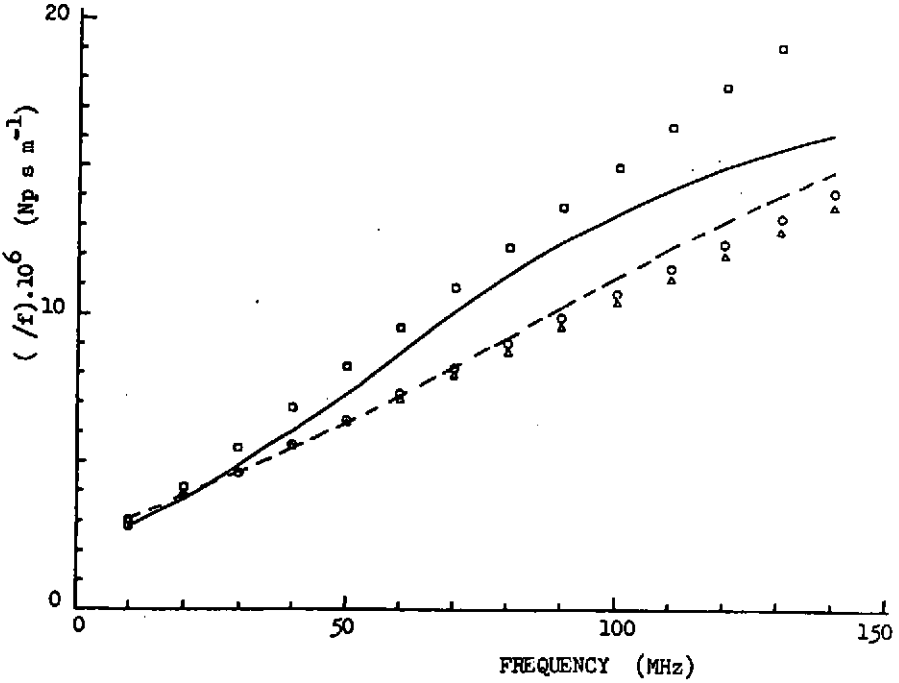

FIGURE 2. Multiple scattering shell model calculations for 4μm (——) and 2.75μm (----) radius cells. Experimental data represents: □ fresh blood, △ old blood, and ○ heated blood.

ULTRASONIC ATTENUATION IN BLOOD

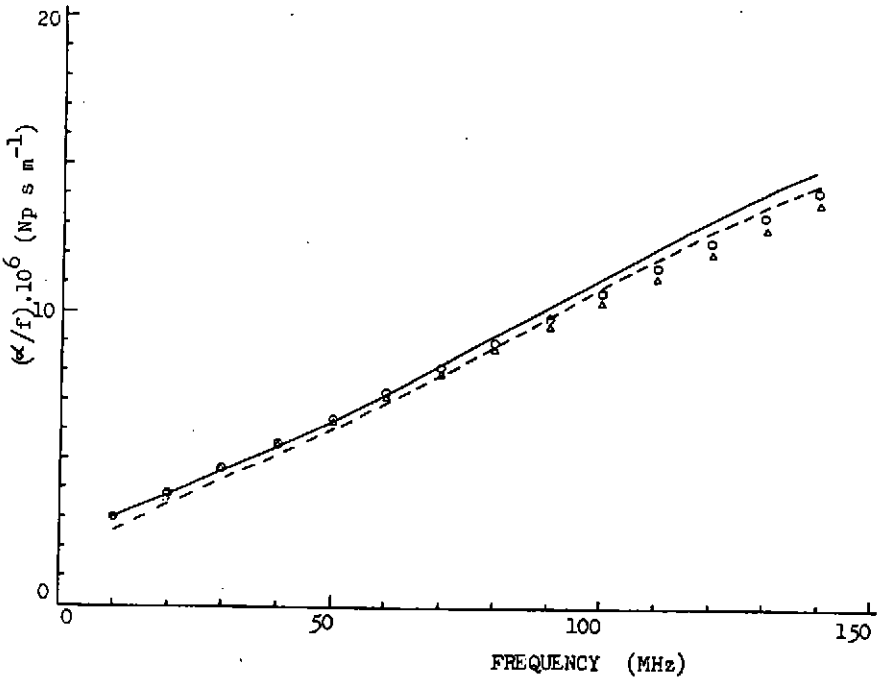

FIGURE 3. Comparison of multiple scattering shell model (——) and liquid drop model (----) for 2.75μm radius cells with experimental data: △ old blood, and ○ heated blood.