Ultrasonic determination of the nonlinearity parameter B/A for biological media

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The nonlinearity parameter B/A has been determined for solutions of bovine serum albumin, of dextrans, of sucrose, of hemoglobin extracted from blood, and for fresh whole blood. The value of B/A for solutions of bovine serum albumin has been observed to increase nearly linearly with concentration. Further, B/A appears to exhibit no dependence upon the molecular weight of dextrose and dextrans over the molecular weight range from 10^2 to 10^6.

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INTRODUCTION

It is well accepted that liquidlike media, and water in particular, propagate acoustic phenomena by nonlinear processes. Several such materials have been studied and the nonlinear parameter B/A ranges from approximately 5–12.[1] However, because of the analytic complexities of dealing with nonlinear propagation phenomena, it has long been considered useful and acceptable to treat acoustic propagation phenomena as following linear relationships.[2] In recent years the propagation of ultrasound in biological media has become an important topic, in particular with regard to its clinical diagnostic employment. Now that diagnostic instrumentation is reaching an appreciable level of sophistication for which more comprehensive details of the propagation phenomena can be utilized, it is considered important to determine the extent to which biological media exhibit acoustic nonlinear phenomena and to consider methods of observation having the potential for providing measures of such nonlinearity *in vivo*.

Nonlinear ultrasonic propagation in biological media has been considered experimentally and theoretically.[3,4] More recently nonlinear phenomena at diagnostic frequencies and intensities in water have been studied,[5] the effect upon thresholds for lesion production in excised liver has been observed,[6] as have effects upon the absorption coefficient of tissue.[7] This note reports initial results of an investigation of the nonlinearity parameter in biological materials.

I. METHODS

The method employed involved determining the amplitude of the fundamental at the source and that of the second harmonic as a function of propagation distance from the sound source. Measurements were made in a 3.8-cm-diam cylindrical chamber filled only with the specimen liquid, with the temperature maintained at 30°C. The 3.44 MHz, 1.27-cm-diam source (PZT-8) was driven by RF bursts of 5 μs duration, i.e., long enough to approximate cw conditions yet short enough to prevent standing waves. The amplitude of the second harmonic was determined by analyzing spectrally the output of a 10 MHz broadband receiver of diameter 1.5 times that of the source. All measurements were made at distances from the source less than one-third the extent of the near field, allowing approximation by plane-wave analysis.

As derived from the Fubini solution[8]

$$\left.\frac{p_2(x)}{xp_1^2(0)}\right|_{xp_1(0)\to 0} = \left(\frac{B}{A}+2\right)\frac{\pi f}{2\rho_0 c_0^3}, \tag{1}$$

where $p_1(0)$ and $p_2(x)$ are, respectively, the magnitude of the acoustic pressure of the fundamental at the source and of the second harmonic, c_0 is the velocity of infinitesimal waves, ρ_0 is the density, x is distance from the sound source, and f is the frequency. For small values of $p_1(0)$, it was found that the ratio $[p_2(x)/xp_1^2(0)]$ decreased exponentially with distance in absorbing media, in agreement with calculations,[9] allowing extrapolation to $x=0$ for determination of B/A using Eq. (1) (see Fig. 1).

Both the source and receiver (calibrated using a 6.88 MHz, 1.27-cm-diam source) were calibrated in

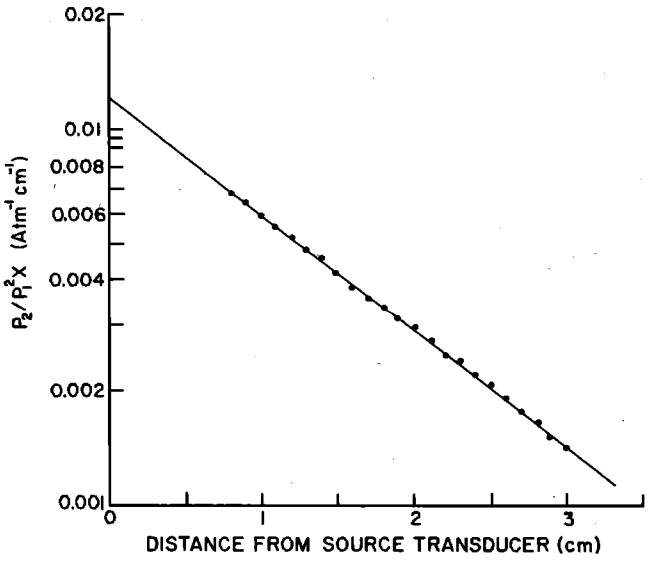

FIG. 1. Sample plot of measured $[p_2(x)/xp_1^2(0)]$ *versus* distance from source transducer.

sodium chloride solutions, covering the range of acoustic impedances exhibited by the samples, by a radiation force technique which determined total acoustic power.[4] The magnitude of the source pressure $p_1(0)$ was calculated from the plane-wave relationship for intensity which was taken as the acoustic power divided by the source area. The accuracy of the methodology was determined to be ±10% by comparison with reported values of B/A for degassed water, ethylene glycol, and glycerin.[10]

The solutions of dextrose, dextran, sucrose, and bovine serum albumin were prepared by dissolving the corresponding powdered solids in degassed water. The porcine whole blood was treated with 3% sodium citrate as an anticoagulant and was used within 2 h of slaughter. Repeated measurements with the same sample at 30 min intervals yielded the same value of B/A. The hemoglobin solutions were obtained by first separating the red cells from the porcine blood by centrifugation, then lysing the cells with toluene, and finally removing the cellular debris by high speed centrifugation.

II. RESULTS

Figure 2 shows the nonlinearity parameter B/A as a function of concentration for aqueous solutions of bovine serum albumin, considered as a tissue model.[11,12] Also shown is the B/A value measured in a porcine hemoglobin solution and in porcine whole blood plotted at the appropriate coordinates for the dry weight contents. It is seen that the nonlinearity parameter of

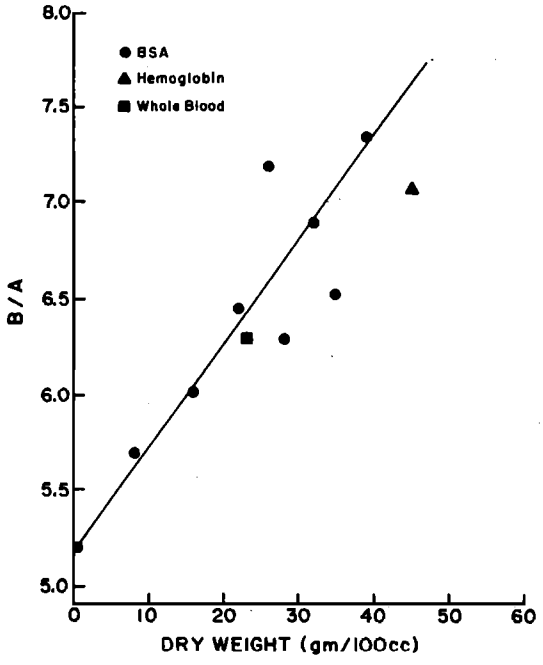

FIG. 2. Value of B/A for bovine serum albumin, hemoglobin (extracted from porcine blood), and porcine whole blood *versus* dry weight (concentration).

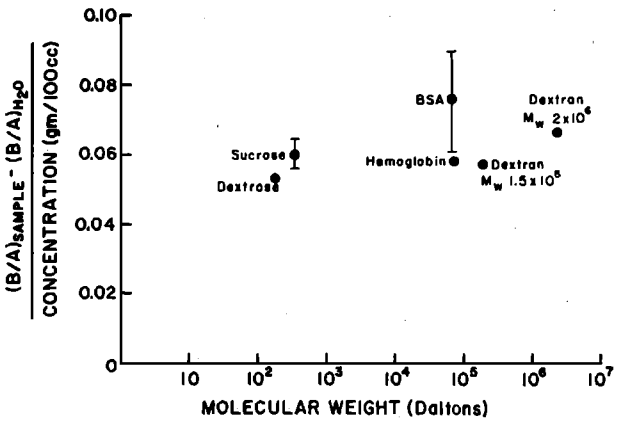

FIG. 3. Excess B/A per unit concentration for several solutions with different solute molecular weights *versus* molecular weight.

bovine serum albumin is approximately a linear function of dry weight content (concentration), implying that the nonlinearity of the medium increases as the spacing distance between the solute molecules decreases and that intermolecular interactions may not contribute significantly, at least over this concentration range.

Figure 3 shows the excess B/A (due to the presence of the solute) per unit concentration, for several solute molecules, as a function of molecular weight, over a rather appreciable molecular weight range. Here it is seen that B/A exhibits virtually no dependence upon solute molecular weight, for the organic materials considered, suggesting no dependence upon intramolecular interaction, for both globular and linear molecular species.

Additionally, for the aqueous solutions studied herein, B/A was observed to increase with increasing speed of sound, contrary to that found for some pure liquids.[1] Here, it is interesting to observe that B/A increases with increasing velocity for water over the temperature range approximately 0°–60° C. It should be noted that the simultaneous increase in B/A and in velocity lead to opposing effects on harmonic generation and that the amplitude of second harmonic generated remained relatively constant for the different solutions examined.

III. CONCLUDING REMARKS

It thus appears that the nonlinearity parameter may be very important in ultrasonic propagation in tissues and that its role in diagnostic procedures should be considered for more complete characterization of normal and diseased states.

ACKNOWLEDGMENTS

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