Acoustically enhanced bubble growth at low frequencies and its implications for human diver and marine mammal safety

Lawrence A. Crum and Yi Mao[a)]
Applied Physics Laboratory, 1013 NE 40th Street, University of Washington, Seattle, Washington 98105

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Computations are made of the conditions necessary to obtain bubble growth by rectified diffusion under a variety of conditions associated with low-frequency sonar propagation in the ocean. The complex issue of microbubble nuclei stabilization is treated by assuming either a sufficient level of supersaturation to stabilize the initial bubble size, or by examining a microbubble nucleus with zero surface tension. The bubble growth rates and thresholds are obtained for a range of sound-pressure levels (*re*: 1 μPa) from 150–220 dB, for initial bubble radii from 1–10 μm, and for levels of the dissolved gas concentration from 100% to 223% of saturation. It was determined that for the range of conditions examined, it was necessary to utilize three different formulations of the equations for bubble growth. The results of these calculations (and assumptions concerning nuclei stabilization) indicate that for SPL's in excess of 210 dB, significant bubble growth can be expected to occur, and divers and marine mammals exposed to these conditions could be at risk. For SPL's below about 190 dB, however, except under relatively extreme conditions of supersaturation, significant bubble growth is unexpected. © *1996 Acoustical Society of America.*

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INTRODUCTION

Considerable recent interest has been associated with the effects of underwater sound fields on marine mammals and humans. One of the mechanisms through which sound can have a deleterious biological effect is to initiate the growth of stabilized microbubbles that are known to exist in mammalian tissue. The presence of gas bubbles larger than a few tens of microns can lead to the blockage of capillaries and microvascular channels, which in turn can lead to pathological conditions (Elliot and Hallenbeck, 1975; Griffiths *et al.*, 1971; Spencer *et al.*, 1969). This article examines the theoretical conditions under which this growth is expected to occur, on the basis of some broad assumptions concerning microbubble stabilization, and for the specific conditions of divers (or marine mammals) who may have experienced temporary levels of dissolved gas supersaturation. Although there are no new equations developed or measurements made, the application of the existing equations of rectified diffusion to the conditions of current interest to the acoustics community is original; furthermore, the results are of interest because they are nonintuitive—one would expect a larger effect, and important—some contraindications for the efficacy of diving in the vicinity of high intensity sound sources is demonstrated. [A more detailed report with a much more extensive series of calculations is available elsewhere (Crum and Mao, 1993).]

In order to define the relevant issues that pertain to this problem, we first introduce some background concerning the growth of gas bubbles in liquids by rectified diffusion, the concepts of bubble nucleation and stabilization, and the acoustic and environmental conditions that may give rise to bubble growth.

A. Rectified diffusion

Whenever an acoustic field of moderate amplitude is propagated through a liquid containing dissolved gases, it is common to observe the production of small gas bubbles in the path of the acoustic beam. These bubbles are often attributed to the phenomenon of acoustic cavitation, but this attribution is misleading. A preexisting gas bubble that is present in the liquid is forced to oscillate about its equilibrium radius by the acoustic pressure fluctuations. When the bubble is large, gas diffuses into the bubble; when it is small, gas diffuses out. Because the diffusion is proportional to the area, over a complete cycle, more gas diffuses in than out; thus, there is a ''rectification'' of mass into the bubble. The ''area effect'' is enhanced by the fact that a small shell of liquid surrounding the bubble is compressed during expansion, thus concentrating the dissolved gas near the bubble wall and enhancing the diffusion rate; just the opposite happens during compression. The combination of the ''area effect'' and the ''shell effect'' is that under certain conditions, a significant quantity of gas is pumped into the bubble each acoustic cycle and the bubble's equilibrium radius increases with time; this phenomenon is called ''rectified diffusion'' (Harvey *et al.*, 1944; Blake, 1949; Strasberg, 1959; Strasberg, 1961; Hsieh and Plesset, 1961; Eller and Flynn, 1965; Eller, 1969; Crum, 1980a, 1984). These effects are opposed by the normal tendency of a bubble existing in a liquid that is saturated with gas to dissolve. Because of surface tension, the pressure inside the bubble is higher than that in the liquid immediately adjacent to the bubble. This so-called Laplace pressure, given by the expression, $P_L = 2\sigma/R$, where σ is the surface tension and R is the radius of the bubble can be quite large for very small bubbles. The end result of these compet-

[a)]Present address: National Center for Physical Acoustics, Coliseum Drive, University of Mississippi, Oxford, MS 38677.

ing diffusion effects is that there is a threshold acoustic pressure amplitude, above which a bubble of a given size will grow, and below which it will tend to dissolve.

Since this process occurs so readily in water, and since humans are often exposed to ultrasound in a variety of modalities, it has been of continual concern that acoustically enhanced bubble growth might occur within tissues (Rubissow and Mackay, 1974; ter Haar and Daniels, 1981; Crum and Hansen, 1982). The presence of bubbles in mammalian tissues can be pathological, especially if they can grow to sizes sufficient to block vascular pathways. The mechanism of rectified diffusion will cause bubbles to grow even more rapidly toward the bubble's natural resonance size, slightly above which they will essentially cease growth (Crum, 1984); of course, for situations involving growth by static diffusion in a supersaturated medium there is no growth limit. Since lower frequencies correspond to resonant bubbles of larger size, this effect may be greatly magnified at 250 Hz, say, where the resonance radius is on the order of a cm. In 1981, a critical experiment was performed at medical ultrasound frequencies by ter Haar and Daniels (1981) who examined guinea pigs for the presence of gas bubble formation when exposed to moderate levels of therapeutic ultrasound (frequency range of interest: 0.75–3.0 MHz). They scanned guinea pig legs with a diagnostic ultrasound imaging device simultaneously with the application of therapeutic ultrasound and saw echogenic returns characteristic of individual gas bubbles. It is fairly well accepted in the scientific community that this experiment, and subsequent ones (ter Haar *et al.*, 1982; Daniels and ter Haar, 1986; Daniels *et al.*, 1987; Crum *et al.*, 1987) present strong evidence that gas bubble growth can occur *in vivo* from ultrasound exposure. This conclusion does have its detractors, however; see, for example, Watmough *et al.*, 1991.

B. Bubble nucleation

The measured dynamic tensile strength of liquids has long been known to be significantly less than theoretically predicted. This reduced strength has historically been attributed to the presence of inhomogeneities in the liquid that serve as preferential sites for liquid rupture (Harvey *et al.*, 1944; Strasberg, 1959; Apfel, 1970; Crum, 1982). These inhomogeneities are often given the generic term of ''nuclei,'' and are thought to be the origin of cavitation activity. When nuclei behave in this way, they are said to act as ''nucleation sites.''

These nucleation sites are ubiquitous, and are thought to be the origin of a variety of common everyday phenomena such as boiling, freezing, crystal formation, precipitation, etc. In each particular case, the nucleus takes on a different form. For cavitation inception, or for gas bubble growth in liquids (rectified diffusion), an inhomogeneity (in the otherwise homogeneous liquid) in the form of a microscopic gas bubble is thought to be the most likely candidate for a nucleation site. Fortunately, all liquids possess some level of surface tension and thus a free gas bubble present in a liquid is unstable; that is, it will tend to dissolve due to the equivalent external pressure generated by surface tension that will force the gas out of the bubble into solution in the liquid. Epstein and Plesset (1950) have examined the expected lifetime of air bubbles in water, and using their equations we can calculate the expected lifetime of a pure air bubble in a liquid saturated with gas. For example, they determined that a bubble 1 mm in radius will take nearly 10 min to dissolve, while a 10-μm bubble will dissolve in less than 7 s. Thus some form of ''nuclei stabilization'' is required if microscopic gas nuclei are to be present in mammalian tissue.

There are a variety of stabilization models (Crum, 1982), among which are the organic skin model (Fox and Herzfeld, 1954), the ionic skin model (Akulichev, 1966), the film of surface-active substances model (Sirotyuk, 1970), the variable permeability model (Yount and Strauss, 1976; Yount *et al.*, 1977; Yount, 1978, 1982), and the crevice model, which is preferred by most researchers in the field. In the crevice model, a small microscopic crack or crevice can stabilize gas contained within the crevice, if there exists hysteresis between the advancing and receding contact angles (Harvey *et al.*, 1944; Strasberg, 1959; Apfel, 1970; Crum, 1979; Crum, 1980b). Each of these forms of nuclei stabilization are individually quite complicated, and a detailed description is beyond the scope of this report. However, it is important to note that in our study of potential gas bubble growth by sonars, the initial conditions for growth are extremely important in the determination of the growth threshold. By making some broad assumptions concerning these nuclei, we shall circumvent their nucleation and stabilization complexity, thus enabling us to obtain some crude estimates of the requirements for bubble growth.

C. ''The bends''

Some of the earliest reports of ''decompression sickness,'' ''the bends,'' or ''caisson disease'' were associated with the construction of the Brooklyn Bridge and the Tyne Road Tunnel (in England) (Young, 1989), in which construction workers were housed in caissons at elevated pressures. It was discovered that when the workers were transported from the pressurized containers to the surface, they complained of pain in the joints and outer extremities that was not present when they remained submerged. There were even some fatalities before it was discovered that small gas bubbles were forming in their bodies as a result of the rapid decompression. Gas that was in equilibrium at the elevated pressure was not removed rapidly enough by the lungs and appeared in the form of bubbles, noticeably in the joints, where tribonucleation of gas pockets could occur. As airplanes were designed to go higher and higher, and before cabins were pressurized, pilots were the most frequent recipients of the illness (Gray *et al.*, 1947). Finally, when it began to become a severe hazard for Navy divers, decompression schedules were instituted so that the bubbles were gradually dissolved by the body before they became symptomatic, or, the gas was removed from the body before nucleation of microscopic gas bubbles even occurred. Now there are regulations, followed even by amateur divers, that require the utilization of decompression techniques to prevent the incidence of the illness. If divers are required to work long intervals at large depths, the decompression times are so long that some even remain underwater for days (in special compressed air chambers) before they return to the surface.

In general, the occurrence of the decompression sickness is thought to require nucleation sites in order to initiate bubble growth. The fact that it readily occurs in mammals, even in fetal tissue (Powell and Smith, 1985), suggests quite strongly that these nucleation sites are at the origin of the gas bubble growth acoustically activated in experiments such as those by ter Haar and Daniels, and also, perhaps more importantly, that these nucleation sites exist in most mammals. Of course, because there are no existing systems that can reliably detect the existence of microbubbles in tissue, there are still some uncertainties concerning the role of nucleation sites and gas bubbles in decompression sickness. For example, there is radiographic evidence of gas in decompressing aviators without demonstration of clinical decompression sickness (Gray *et al.*, 1947), some individuals are much more susceptible to the illness than others (Gray *et al.*, 1947), and relatively poor correlation exists between the incidence of vascular bubbles and individual decompression sickness risk (Bayne *et al.*, 1985). Nonetheless, current decompression tables, based upon statistical risk models, generally assume that bubbles are directly or indirectly involved in decompression sickness (Weathersby *et al.*, 1992; Tikuisis *et al.*, 1991).

D. Low-frequency sonars

A variety of active sonar devices are used for underwater imaging. Of recent interest are low-frequency systems that have relatively large source strengths. Of related interest are transducers used in global warming studies that propagate sound for large distances. Most of these systems operate in the frequency range between 50 Hz and 5 kHz, with source intensities that can exceed 220 dB (*re*: 1 μPa) (Hosterman and Schmidt-Schierhorn, 1993; Beresford *et al.*, 1993). Although most of these units operate in a pulsed mode of operation, the pulse lengths can approach minutes in duration.

Since human divers and marine mammals are increasingly exposed to the acoustic fields produced by low frequency sonars, and since there is evidence that bubble growth by rectified diffusion can be made to occur in mammals at high frequencies, we have examined the thresholds for bubble growth by rectified diffusion at low frequencies for conditions similar to those generated by existing sonars. Of course, at the highest levels considered in this study—220 dB—this sound would also be very painful to the ears of both humans and marine mammals and, unless constrained in some macabre way, would immediately vacate the area.

I. APPROACH

A. Physical model

If nucleation sites are to be involved, and bubble growth is to occur from these nucleation sites, it is necessary first to find some approach to the examination of the conditions necessary for these nuclei to grow. Because these nuclei are quite different in form, such an approach is quite difficult and beyond the scope of this study. Accordingly, it was necessary to find some simple method to permit the nuclei to exist and be involved in the critical initial growth, without introducing high levels of complexity. As indicated earlier, a variety of nuclei-stabilization models exist. A common feature of all these models is that a pocket of gas of some initial size exists and can be activated by external influences such as ultrasound or supersaturation (resulting from rapid decompression, say). An important issue is how to treat the initial conditions that gave rise to bubble stabilization. Because of the complexity of current nuclei-stabilization models, and because few of these models have ever been subjected to careful experimental scrutiny, it was found necessary to make some simplifying assumptions concerning the nature of these nuclei in order to perform the necessary calculations. In essence then, we seek to determine the broad limits for which bubble growth may be important, rather than develop a rigorous treatment of this complex area.

One of our approaches is to assume that the nucleus is a free gas bubble that is stabilized by an effective level of supersaturation. Some justifications for this approach are as follows: Consider a pocket of gas stabilized by an impermeable organic skin or by a sharp crevice in a hydrophobic material. If the gas bubble is caused to grow slightly, then the skin grows along with it, or the liquid–gas interface advances along the crevice, continuing to stabilize it. If the organic skin or crevice were not there, the bubble would quickly dissolve, and the nucleation site would dissolve and disappear. Since nuclei do not appear and disappear periodically, but remain distributed throughout the tissue, some form of free-bubble stabilization is deemed necessary. Consider also divers that are located at some depth below the surface of the ocean, say 20 m, who are breathing compressed gas, and have remained at that depth long enough so that their body fluids have become saturated with gas at that pressure. If they experience a threat of some sort, they may consider it wise to immediately return to the surface. In so doing, they will have supersaturated their bodily fluids by two atmospheres of pressure and their blood supersaturation level will be 300% (at 0 m it is 100%). Of course, unless they were to immediately undergo recompression, they would very likely experience symptoms of decompression sickness, and with this level of decompression, probably die. Thus in this work, in order to treat the important requirement of nuclei stabilization and to address the issue of divers and marine mammals quickly changing their depths, various levels of supersaturation of the host liquid are considered. Some of these levels are admittedly quite extreme, but the authors wish to demonstrate the basic physics, rather than set guidelines for behavior. Furthermore, marine mammals (other than humans) don't breath compressed gas, but ''hold their breath,'' and thus would not develop the same levels of supersaturation as would humans.

It is thought that gas pockets stabilized within the body are on the order of a few microns in size (diameter). If they were much larger than this, they would tend to block capillaries and other vascular channels; furthermore, the lungs will tend to filter particles with sizes larger than about 10 μm. Thus we have considered levels of supersaturation sufficient to stabilize free bubbles of various sizes. Some representative levels and bubbles sizes at an ambient pressure of 1.0 atmosphere are as follows: 103%—50 μm; 113%—10 μm; 127%—5 μm; and 223%—1 μm. Note also that in water, one atmosphere is approximately equivalent to 10 m of depth; thus some representative supersaturation levels and diver depths are as follows: 300%—20 m; 200%—10 m; 150%—5 m; 127%—2.7 m; 113%—1.3 m; and 103%—0.3 m. It is readily seen that divers will often experience significant levels of supersaturation, and that supersaturation levels of 110% to 130% are not uncommon (Weathersby, 1994). It is important to recognize that seldom do divers achieve ''saturation'' conditions; this is, with dissolved gas levels in their body fluids equal to that of the gas that they are breathing (which would be ''supersaturated'' with respect to surface conditions). Only for very deep diving, (to depths over a few hundred feet for periods of several hours) do divers reach ''saturation levels'' (i.e., ''saturated'' at depth). Of course, bubbles larger than about 10 μm will be filtered by the blood and the oxygen tension is somewhat reduced on the venal side of the lung, thereby compensating in part for supersaturation conditions. Thus we will consider only modest levels of ''supersaturation.''

One approach to the treatment of the problem of nuclei stabilization is to establish a base level of supersaturation that would stabilize gas bubbles of various sizes. One flaw with this approach is that the use of supersaturation for nuclei stabilization provides only a point of unstable equilibrium. If a bubble of 10 μm is stabilized by a supersaturation level of 113%, for example, then its growth to 11 μm results in its now being unstable to growth by static diffusion. In our studies we shall examine both threshold conditions and growth rates in order to obtain some indication of the acoustic and environmental conditions required to induce and sustain significant bubble growth.

We also wish to consider a second approach to nuclei stabilization. The reason a bubble tends to dissolve is that the surface tension effectively increases the gas pressure inside the bubble; thus it is then higher than the ambient (dissolved gas) pressure outside the bubble, and gas diffuses out of the bubble into the liquid. If the surface tension is set equal to zero, then automatic stabilization occurs. Thus a second approach to the nuclei-stabilization problem is to simply set the surface tension equal to zero. For this case, there is no tendency for the bubble to dissolve and a bubble of a given size will tend to remain at that size unless it is caused to grow by levels of supersaturation or acoustically induced rectified diffusion. There are some indications that the assumption of nuclei with low surface tension (below 5 dyn/cm) has both biological plausibility and fits quantitative models for decompression sickness (Weathersby *et al.*, 1982). Of course, this approach would probably not be rigorously encountered in reality, and thus serves as a lower bound on the conditions necessary for bubble growth. It is useful in that this approach does not lead to unstable conditions, as does supersaturation stabilization, and also because the surface tension does not play an important role in the growth rate.

B. Theoretical model

In order to obtain the applicable expressions necessary to calculate the rectified diffusion threshold and the bubble growth rate, it is necessary to obtain first the equations that describe the bubble dynamics.

We shall use as the equation of motion for a gas bubble in this calculation the familiar Rayleigh–Plesset equation, as given by

$$R\ddot{R}+\frac{3}{2}\dot{R}^2+\frac{1}{\rho}\left\{P_\infty+\frac{2\sigma}{R}-\left(P_\infty+\frac{2\sigma}{R_0}\right)\left(\frac{R_0}{R}\right)^{3\eta}+\frac{4\mu}{R}\dot{R}\right.$$
$$\left.-P_A\cos\omega t+\rho R_0\frac{\omega_0^2}{\omega}(b_t+b_r)\dot{R}\right\}=0,$$

where R is the radius of the bubble, R_0 is the equilibrium radius, σ is the surface tension, P_∞ is the pressure outside of the bubble, μ is the coefficient of viscosity, P_A is the amplitude of the acoustic pressure, ω is the driving frequency, ρ is the density of the liquid, and the resonance frequency ω_0 is given by

$$\omega_0^2=\left[3\eta\left(P_\infty+\frac{2\sigma}{R_0}\right)-\frac{2\sigma}{R_0}\right]\Big/\rho R_0^2.$$

Also, the thermal damping constant b_t is given by

$$b_t=3(\gamma-1)\left(\frac{XS_+-2C_-}{X^2C_-+3(\gamma-1)XS_-}\right),$$

where

$$S_\pm=\sinh X\pm\sin X,$$

$$C_-=\cosh X-\cos X,$$

$$X=R_0(2\omega/D_1)^{1/2}.$$

and D_1 is the thermal diffusion constant of the gas.

The radiation damping constant b_r is given by

$$b_r=\rho R_0^3\omega^3\Big/3\eta\left(P_\infty+\frac{2\sigma}{R_0}\right)c\left[1-2\sigma\Big/3\eta R_0\right.$$
$$\left.\times\left(P_\infty+\frac{2\sigma}{R_0}\right)\right],$$

where c is the speed of sound in the liquid and

$$\eta=\gamma(1+b_t^2)\left[1+\frac{3(\gamma-1)}{X}\left(\frac{S_-}{C_-}\right)\right]^{-1},$$

where γ is the ratio of specific heats and η is normally called the polytropic exponent; it represents a treatment of the thermal effects in the gas. Note that these equations assume that the gas bubble is ''free;'' i.e., it is neither stabilized by some mechanism nor constrained in growth. After solving the Rayleigh–Plesset equation for the bubble radius as a function of time, we can use the following equation to calculate the rate of change of the equilibrium bubble radius with time:

$$\frac{dR_0}{dt}=\frac{Dd}{R_0}\left[\left\langle\frac{R}{R_0}\right\rangle+R_0\left(\left\langle\left(\frac{R}{R_0}\right)^4\right\rangle\Big/\pi Dt\right)^{1/2}\right]$$
$$\times\left(1+\frac{4\sigma}{3R_0P_\infty}\right)^{-1}\left(\frac{C_i}{C_0}\right.$$
$$\left.-\left\langle\left(\frac{R}{R_0}\right)^4\frac{P_g}{P_\infty}\right\rangle\Big/\left\langle\left(\frac{R}{R_0}\right)^4\right\rangle\right),$$

where $\langle\ \rangle$ means time average over one period of acoustic pressure, D is the diffusion constant of gas in the liquid, $d=kTC_0/P_\infty$, k is the universal gas constant, T is the equilibrium temperature, and C_0 is the ''saturation'' concentration of the gas in the liquid in moles. This equation is due principally to Eller and Flynn (1965), and has been used extensively. The straightforward application of this equation is to integrate numerically the Rayleigh–Plesset equation to obtain the radius-time curve, and then to introduce these numbers directly into the Eller–Flynn expression to obtain the bubble growth rate. Of course, when the growth rate is zero, the corresponding acoustic pressure amplitude is said to be the ''threshold'' for rectified diffusion. In some of the calculations presented in the results to follow, the Rayleigh–Plesset equation was numerically integrated to obtain the time-dependent radius of the bubble, and then the diffusion equation above was numerically integrated to obtain the growth (or decay) of the bubble. These results will be called the ''Eller'' results.

It is possible to introduce considerable simplification into this approach and avoid some of the time-consuming numerical integration that is involved. For example, the Rayleigh–Plesset equation can be written as

$$R\ddot{R}+\frac{3}{2}\dot{R}^2+\frac{1}{\rho}\left\{P_0\left[1-\left(\frac{R_0}{R}\right)^{3\eta}\right]-P_A\cos\omega t\right.$$
$$\left.+\rho R_0\frac{\omega_0^2}{\omega}b\dot{R}\right\}=0,$$

where

$$P_0=P_\infty+\frac{2\sigma}{R_0},\quad b=b_t+b_r+b_\nu,$$

and

$$b_\nu=4\omega\mu\Big/\left(3\eta P_0\left(1-\frac{2\sigma}{3\eta R_0P_0}\right)\right).$$

Here, b_ν is the expression for the viscous damping. The solution for this simplified Rayleigh–Plesset equation has the form:

$$\frac{R}{R_0}=1+\alpha\left(\frac{P_A}{P_\infty}\right)\cos(\omega t+\delta)+K\alpha^2\left(\frac{P_A}{P_\infty}\right)^2+\cdots,$$

where

$$\alpha^{-1}=\left(\frac{\rho R_0^2}{P_\infty}\right)[(\omega^2-\omega_0^2)^2+(\omega_0^2b)^2]^{1/2},$$

$$K=\frac{(3\eta-1-\beta^2)+(2\sigma/R_0P_\infty)(3\eta+1-2/3\eta)}{4[1+(2\sigma/R_0P_\infty)(1-1/3\eta)]},$$

$$\delta=\cos^{-1}\left(\frac{-\omega_0^2b}{[(\omega^2-\omega_0^2)+(\omega_0^2b)^2]^{1/2}}\right),$$

and

$$\beta=\frac{\rho\omega^2R_0^2}{3\eta P_0(1-2\sigma/3\eta R_0P_0)}.$$

Using these expressions, we obtain the time averages $\langle R/R_0\rangle,\langle(R/R_0)^4\rangle,\langle(R/R_0)^4P_g/P_\infty\rangle$, which are needed to calculate the rate of the equilibrium bubble radius change with time.

$$\left\langle\frac{R}{R_0}\right\rangle=1+K\alpha^2\left(\frac{P_A}{P_\infty}\right)^2,$$

$$\left\langle\left(\frac{R}{R_0}\right)^4\right\rangle=1+(3+4K)\alpha^2\left(\frac{P_A}{P_\infty}\right)^2,$$

$$\left\langle\left(\frac{R}{R_0}\right)^4\frac{P_g}{P_\infty}\right\rangle=\left[1+\left(\frac{3(\eta-1)}{4}-K\right)(3\eta-4)\alpha^2\left(\frac{P_A}{P_\infty}\right)^2\right]$$
$$\times\left(1+\frac{2\sigma}{R_0P_\infty}\right).$$

If these expressions are inserted directly into the Eller–Flynn expression for the growth rate, then an explicit analytical expression is available to obtain the rate of growth of the bubble; subsequently, this equation can be numerically integrated (quite simply) to obtain the change in the equilibrium radius with time. This approach was advanced by Crum (1980a, 1984) and in our present context, the analytical results that are obtained in his way are called the ''Crum'' results.

For relatively low acoustic pressure amplitudes, say less than 0.05 MPa, and for values of the dissolved gas concentration near saturation, the Crum results agree quite well with the measured experimental data (Crum, 1980a). These data were obtained for true free-bubble conditions, and thus do not reflect the effect of stabilization conditions or tissue constraints. In this approach, which utilizes the Eller-equation, it is assumed that in order to calculate the gas flow into and out of the bubble, a small shell of liquid containing dissolved gas surrounds the bubble when it oscillates. The mass flow is assumed to occur into and out of this shell, and thus one need not worry about the gas concentration gradient that extends to infinity. Of course, this assumption works best when the gradient is not large, and breaks down when it is.

A second assumption, inherent in the Crum approach, is that the bubble dynamics can be treated by a second order Taylor series expansion. That is, a solution of the Rayleigh–Plesset equation is obtained by a Taylor series expansion and terms higher than the second order are truncated. Similarly, this assumption breaks down when the acoustic pressure amplitude is sufficiently large.

It was first thought possible that the range of conditions of interest in this study could be examined by the Crum approach for small SPL's and the Eller approach for larger SPL's. However, it was discovered that there are conditions under which the exclusive application of the Crum or the

Eller equations would give misleading (and essentially incorrect) results. Thus a more general treatment of the extreme conditions was sought.

Fortunately, we were able to obtain a preprint of a recent paper by Fyrillas and Szeri (1994) that exhaustively treats the case of rectified diffusion without the limiting assumptions inherent in the Crum and Eller formulations. Their expression for the bubble growth rate is given below and shall be called the ''Fyrillas'' solution:

$$\frac{dR_0}{dt}=\frac{Dd}{R_0}\left(1+\frac{4\sigma}{3R_0P_\infty}\right)^{-1} \times\left(\frac{C_i}{C_0}-\frac{(1+2\sigma/R_0P_\infty)\langle(R/R_0)^{4-3\eta}\rangle}{\langle(R/R_0)^4\rangle}\right) \Bigg/ \int_0^\infty \frac{dx}{\langle[3x+(R/R_0)^3]^{4/3}\rangle}.$$

It should be noted that in this expression, an integral of the radial coordinate x (which is related to the ratio R/R_0 through expressions given in the original reference) is buried within the differential equation. Although this expression has a broader range of applicability, it is difficult to implement because of its computer-intensive nature. In the results presented below, one of these three approaches was used to obtain the calculated values. In general, for sound pressure levels below 190 dB, it was possible to use the ''Crum'' approach; for levels between 190–210 dB, it was necessary to use the Eller numerical integration approach; for levels above about 210 dB, it was necessary to use the Fyrillas solution.

II. RESULTS AND DISCUSSION

We shall examine a variety of conditions for which we will calculate the growth rate of bubbles exposed to low-frequency acoustic fields. We shall consider bubbles with initial sizes on the order of microns, frequencies in the region of hundreds of Hertz, dissolved gas concentrations near and significantly above saturation (100%–200%) and sound-pressure levels in the range of 150–220 dB. We shall present our acoustic parameters in decibel units because of the prevailing terminology *vis a vis* sonar output levels. The reader is reminded that 220 dB (*re*: 1 μPa) is equivalent to 0.1 MPa (1.0 bar) in absolute units. Furthermore, because the sizes of the bubbles that are of concern lie in the micron size range, unless the frequency is on the order of hundreds of kilohertz, there is essentially no frequency dependence—the bubbles are driven much below resonance. Terms involving frequency dependent terms such as the resonance frequency of the bubble, for example, have little effect on the final result. Of course, since this work needs to be done with a computer anyway, analytical simplification is not cost effective. Thus we shall restrict our computations to a few frequencies in the 300–500 Hz range and presume that similar behavior extends over the range of 50 Hz to 5 kHz. For these computations, we shall use $\sigma=72.0$ dynes/cm, $P_\infty=1.01\times10^5$ N/m^2, $D=2.4\times10^{-5}$ cm^2/s, and $d=2.0\times10^{-2}$.

Shown in Fig. 1 is a comparison of the results from various formulations for the growth rate of a bubble with an initial radius of 10 μm, a frequency of 500 Hz, and for a value of the dissolved gas concentration of about 113%. This particular value of the gas concentration is that value which is necessary to stabilize a bubble of 10 μm in water. Thus our initial conditions are that this ''free'' bubble is present in the liquid, but ''stabilized'' against dissolution by this particular level of supersaturation. As indicated earlier, bubbles are known to be present in mammalian tissues and stabilized by unknown mechanisms. Our ''supersaturation'' approach to nuclei stabilization is crude but useful.

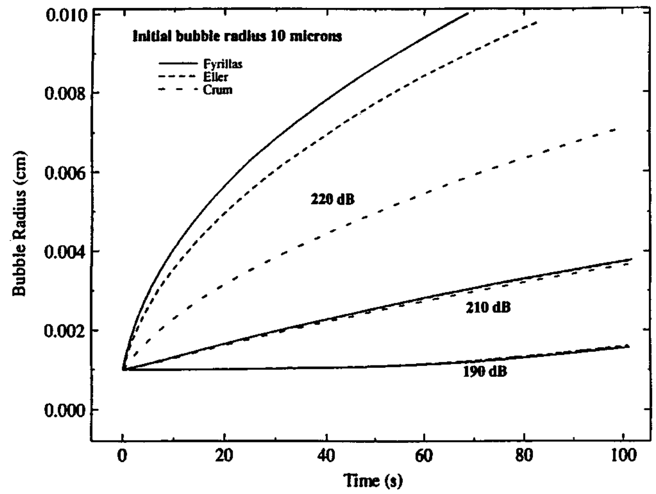

FIG. 1. Comparison of various formulations for the growth rate of gas bubbles by rectified diffusion. For this case the initial bubble radius is 10 μm, the acoustic frequency if 500 Hz, and the liquid is supersaturated to 113.5%, the dissolved gas concentration necessary to stabilize a bubble of 10 μm. The various curves show the results of three different formulations used in this study to calculate the bubble growth rates. Except for the highest SPL, the different formulations give similar results.

The principal information to be presented in Fig. 1 is the comparison between the three separate formulations for the bubble growth rate. For SPL's below about 210 dB, it is seen (for these particular conditions) that the three formulations (Fyrillas, Eller, and Crum) all give about the same values for the growth rate. However, once this level is exceeded, the Crum formulation is considerably in error, the Eller formulation is much better but still somewhat low. Of course, the Fyrillas formulation is assumed to be exact, at least in this context. (It is beyond the scope of this present paper to evaluate the accuracy of the Fyrillas formulation—suffice it to say that it is a more rigorous treatment of the diffusion problem.)

Shown in Fig. 2 are a series of curves showing the growth rate of a bubble with an initial radius of 10 μm, a driving frequency of 500 Hz, and a dissolved gas concentration of 113.5%. The various curves are for various sound-pressure levels (at the location of the bubble). Note that significant growth is expected for SPL's in excess of 180 dB, and that for the levels on the order of 220 dB, growth is quite rapid. For levels below about 180 dB, some growth occurs but it is so small that it doesn't show on this scale. Since this bubble is stabilized by the supersaturation, it also does not dissolve. Furthermore, since the bubble is stabilized at a radius of 10 μm, any growth in the bubble makes it unstable to growth by ordinary diffusion (as opposed to rectified diffu-

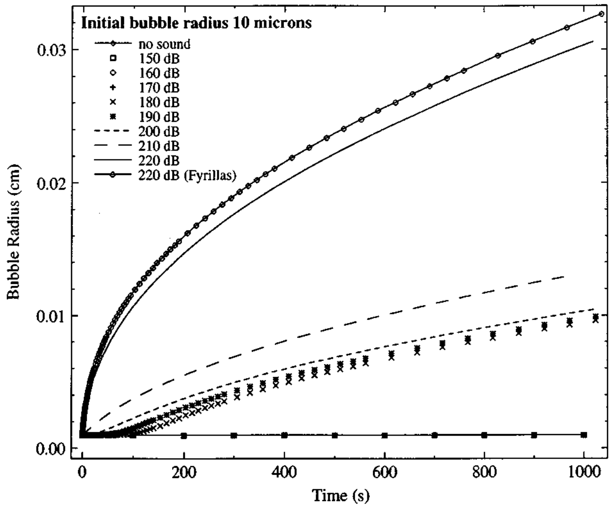

FIG. 2. Calculations of bubble growth by rectified diffusion for a variety of SPL's and a modest level of supersaturation. For this case, the initial bubble radius was 10 μm, the driving frequency was 500 Hz, and the dissolved gas concentration was 113.5%. For SPL's below about 180 dB, very little growth occurs, and the data points for these calculations are collapsed into a single point. The bubble does not dissolve for these conditions because this value of supersaturation stabilizes a bubble of 10-μm radius.

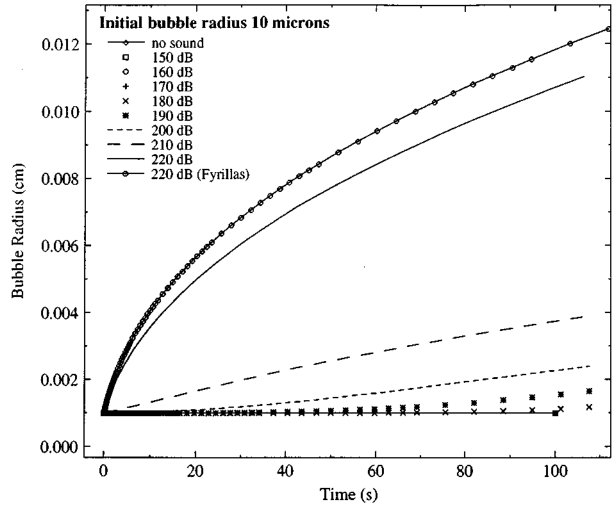

FIG. 3. Calculations of bubble growth by rectified diffusion for a variety of SPL's and a modest level of supersaturation. For this case, the initial bubble radius was 10 μm, the driving frequency was 500 Hz, and the dissolved gas concentration was 113.5%. For this figure, the time scale is expanded to show the growth during the early stages (cf. Fig. 2). The bubble does not dissolve for these conditions because this value of supersaturation stabilizes a bubble of 10-μm radius.

sion). Thus for SPL's in the range 180–210 dB, much of the observed growth is independent of the acoustic field. The effect of the field (at this SPL's) is to shift the bubble into a region of instability to growth by virtue of the level of supersaturation.

These data show the importance of the value of the level of supersaturation. If a bubble nucleus is present in tissue, and a slight level of supersaturation occurs—113.5% is equivalent to only 1.3 m of depth—bubbles can ''spontaneously'' grow as a consequence of this supersaturation (Evans and Walder, 1969; Rubissow and Mackay, 1974; Yount and Strauss, 1976). In a sense, this curve demonstrates in a quantitative manner the concept of decompression sickness or the ''bends;'' that is, if a preexisting gas bubble (stabilized by some particular mechanism) is suddenly exposed to even a slight level of supersaturation, it will grow continuously until it is constrained by tissue boundaries or some other constraint. Once the stabilized bubble becomes destabilized, it will grow without bound—or until local conditions (e.g., tissue boundaries, blood vessel walls) constrain the growth.

Figure 3 shows the same computations as presented in Fig. 2, except that now the time scale has been changed to display the early times in the growth process. It is noted that for SPL less than about 210 dB, times on the order of several minutes are required for significant bubble growth—doubling in size, say. Recall that these data are for a very slight level of supersaturation (equivalent to 1.3 m of depth), and are meant to represent the behavior near saturation (the extra 13.5% is required for bubble stabilization).

Shown in Fig. 4 are calculations of bubble growth for a case in which there is a significant level of supersaturation (equivalent to 10 m of water depth). It is seen in this figure that very rapid growth occurs, principally due to the high level of supersaturation. Note that the acoustic field has little effect on the growth below 210 dB, and is primarily due to static (i.e., nonacoustic) diffusion.

This figure demonstrates the dangers associated with rapid decompression; here, doubling in size occurs within a few seconds and significant growth occurs over a time interval of a few minutes. For a situation such as this, as long as the medium surrounding the bubble maintains this level of supersaturation, bubble growth will occur until it is constrained by the body tissues. Of course, therein is where the danger is. Such a bubble, in this particular medium, will have the capacity of exerting a local pressure of a full atmosphere.

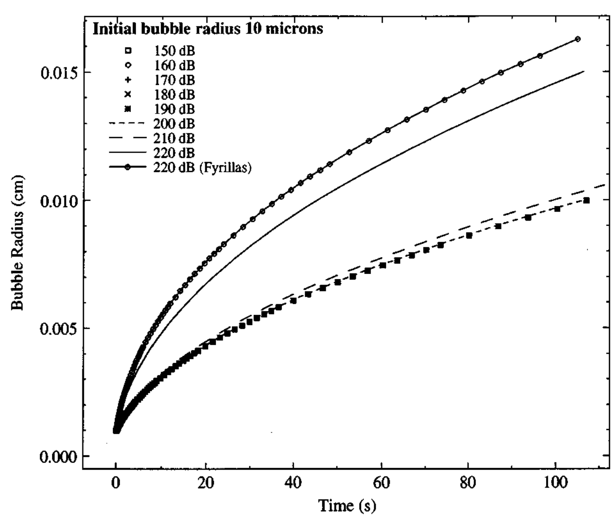

FIG. 4. Calculations of bubble growth by rectified diffusion for a variety of SPL's and a high level of supersaturation. For this case, the initial bubble radius was 10 μm, the driving frequency was 500 Hz, and the dissolved gas concentration was 200%. Note that there is little dependence on the SPL for levels below about 210 dB, and that bubble growth occurs principally by static (nonacoustic) diffusion.

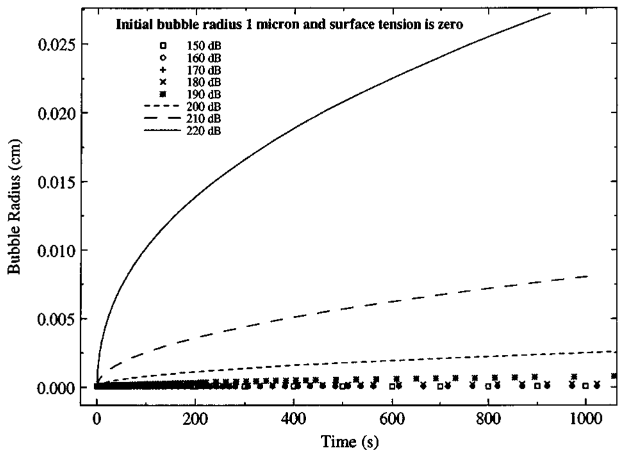

FIG. 5. Calculations of bubble growth by rectified diffusion for a variety of SPL's and a liquid surface tension equal to zero. For this case, the initial bubble radius was 1 μm, the driving frequency was 500 Hz, and the dissolved gas concentration was 100%. Note the very rapid growth for high SPL's.

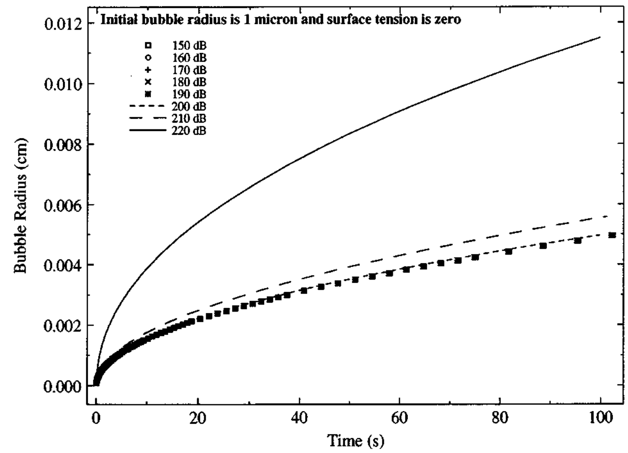

FIG. 6. Calculations of bubble growth by rectified diffusion for a variety of SPL's and a liquid surface tension equal to zero. For this case, the initial bubble radius was 1 μm, the driving frequency was 500 Hz, and the dissolved gas concentration was 125%. Note the rapid growth even in the absence of an acoustic field.

At the cellular level, this expansion can result in tissue separation, vascular blockage, and eventual tissue pathology (Elliot and Hallenbeck, 1975; Vann and Clark, 1975). Although not indicated here in this analytical model, the role of acoustics might be to ''activate'' the bubble. Suppose that a microbubble nucleus were stabilized by an organic skin that was mostly impermeable. This nucleus might be ''benign'' until the skin was disrupted, permitting diffusion to occur. (The authors know of no evidence of this particular type of activation, but it seems wholly reasonable.)

Our next approach to bubble stabilization tries to address the nucleus that is covered with some semi-impermeable organic skin. There is a wealth of information that suggests such objects exist (Yount and Strauss, 1976; Yount, 1982; Johnson and Cooke, 1981), and even evidence that this model is applicable to bubble growth *in vivo* (Weathersby *et al.*, 1982; Tikuisis *et al.*, 1983). It is reasonable to assume that in the organically rich medium of human body fluids, bubbles would be covered with a myriad of surface active materials that would result in a great reduction in surface tension. In order to consider these nuclei, we have performed the calculations shown in Figs. 5 and 6.

In Fig. 5, we present calculations of the growth of a bubble with an initial size of 1 μm that has no surface tension. (Of course, such a bubble will not dissolve, and is *always* stabilized, regardless of the dissolved gas concentration.) In this figure we consider the liquid to be saturated with gas (no supersaturation), and examine the growth as a function of various SPL's. Note that very rapid growth occurs for large SPL's, and that some growth occurs even for a ''modest'' level of 180 dB.

If the surface tension is zero, then there is no Laplace pressure to force the bubble to dissolve, and even a modest level of supersaturation will cause the bubble to grow without bound. For this case, the static (nonacoustic) diffusion overwhelms the rectified diffusion and there is little dependence on the SPL, except for large values of the level.

Finally, we demonstrate the sensitivity to our initial conditions. Shown in Fig. 7 are the results of calculations of the bubble growth rate for the conditions of insufficient stabilization; i.e., in this case the dissolved gas concentration is at 126.0% and the surface tension is equivalent to that of pure water. We also have selected a bubble of relatively small size, 5 μm, for the initial radius. In order for the bubble to be stabilized, a supersaturation level of 126.9% is required. Thus for this case, the initial conditions are such that the bubble would dissolve if not acoustically driven. It is seen that for these conditions, the bubble dissolves within a few seconds for SPL's less than 210 dB. It should also be noted, however, that for a SPL of 220 dB, the bubble can increase in size from 5 to about 40 μm in about 10 s. Thus for this

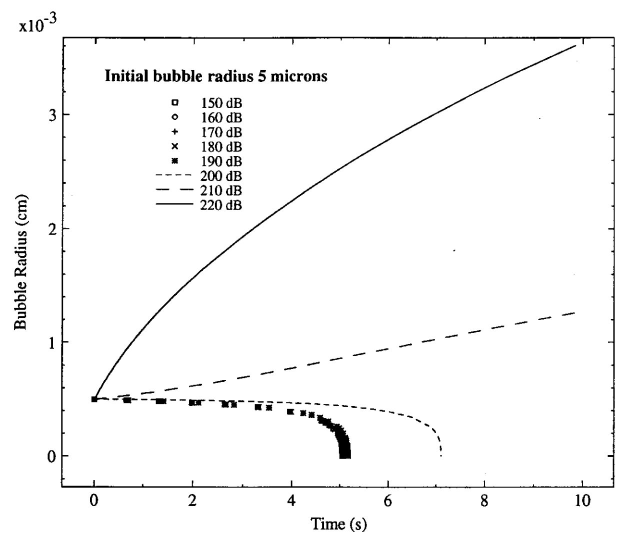

FIG. 7. Calculations of bubble growth by rectified diffusion for a variety of SPL's for a dissolved gas concentration equal to 126.0%. For this case, the initial bubble radius is 5 μm, the driving frequency is 500 Hz, and the supersaturation level required for initial bubble stabilization is 126.9%. Note that because there is insufficient supersaturation to ensure stabilization, the bubble dissolves for most of the SPL's considered. However, for the higher values of the SPL, the bubble growth is rapid and significant.

particular case, the bubble can either rapidly grow or rapidly dissolve, depending upon the SPL. Such times and SPL's are well within the conditions available to certain sonar systems. These computations suggest that a diver or a marine mammal located in the *near vicinity* of a sonar dome is under considerable risk for gas bubble growth and its associated consequences.

III. SUMMARY AND CONCLUSIONS

With the computations reported in this article, we have described some of the conditions for which gas bubble growth from preexisting nuclei can occur. The equations used in the computations account for ordinary static diffusive growth and also that by rectified diffusion. It was determined that this growth is very dependent on the nature of the microbubble nuclei. Since it is known that gas bubbles exist in most mammalian tissues, and that they are most likely stabilized against dissolution, two simple stabilization mechanisms were assumed that permitted us to apply directly the equations of rectified diffusion that are available in the literature.

In general, it was discovered that relatively large SPL's are required to induce rapid or significant (and thus dangerous) gas bubble growth, unless the degree of dissolved gas supersaturation was quite large. *Under normal conditions, enhanced diffusion produced by sonars and other high intensity acoustic projectors pose little risk to divers and marine mammals unless they are in the immediate vicinity of the source*. However, the ''contraindications'' for their use are as follows:

(1) If the local SPL at the site of the diver or marine mammal is in excess of 210 dB (*re:*1 μPa), gas bubble growth is predicted to occur within a period of a few seconds. Furthermore, bubble growth to sizes large enough to block capillaries and other small blood vessels is expected with its associated bioeffects.

(2) If a diver, breathing compressed gas, experiences rapid depth ascents such that the local body fluid is supersaturated with gas, considerably lower SPL's may result in conditions favorable for bubble growth.

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