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Mathematical Model for the oscillations of an elastic shell encapsulating a contrast agent

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ABSTRACT

In the present theoretical formulation we study the oscillations of a solid bubble (shell), surrounding a perfect gas, under an ultrasound drive pressure. The model comprehends a Rayleigh-Plesset kind equation for the liquid radius that surrounds the shell together with an equation for the oscillating pressure in the liquid and the exact solution for an elastic solid that represents the shell. We state as main parameters β which represent the quasi steady state deformation of the solid, π_X is the ratio of the ambient pressure and the elasticity modulus, and β_A which represents the ratio of the driving pressure and the dynamic pressure. As main results we give the oscillations of the liquid in time and the pressure also. For the solid we obtained a weak oscillatory and irregular behavior which predicts the final collapse of the solid.

INTRODUCTION

The development in the use of contrast agents as diagnostic enhancers and as drug carriers [1], requires not only their localization inside the body via the scattering frequencies but also to figure out how and when their collapse can happen. The traditional models include the one integral approach [2, 3], in which obtaining the scatter frequency is the main objective. These works describe the mechanics of the contrast agent via the scatter signal in response to a high frequency pressure field imposed far away, obtaining a natural frequency of oscillation of the shell from a Rayleigh- Plesset equation. In the traditional case the RP equation stands for the motion of the liquid that surrounds a stationary bubble but for the shell it is assumed a finite thickness of a shell which is between two interfaces, being inside a politropic gas and outside a liquid. Beyond this the description of the shell can take all possibilities, as an elastic solid as in [4], a viscoelastic porous solid as stated in [2] or a more complex Kelvin-Voight model in [3], or even a viscous Newtonian liquid as we can see in Allen et. al. [5], the fluid might be as simple as soybean oil. We consider that before complicating the properties of the substances a more rigorous model in parameters and in equations should be stated. In other words the previous models do not fully describe the dynamics of the system, the displacement and pressure of the liquid and the deformation of the cavity all this variables if not taken properly the physics of the phenomenon can change dramatically. As can be seen in [4], we took the pressure as a constant, and as shown in this paper give considerably big mistakes.

In this work we obtained a three equations model, an exact solution for the solid as function of the displacement in the liquid and the pressure in the liquid. We use a steady model for the elastic solid as stated in [6], this allows us to get an exact solution, the oscillatory behavior of this equation leads us to think in a nonsteady solution must be made before thinking on more complicated substances. Because the great nonlinearity of phenomenon the small changes in the values of the parameters and the conditions extreme caution should be taken in further models, in this case we showed that the oscillations happen in a very small domain of the parameters, which in this case reduce only to two, neglecting the effect of the others.

In [5] we can see how the model closes and shows all the oscillations and other relevant physical quantities such as the wall velocity for a Newtonian liquid shell in a single integral model. In [6] we have a collection models for the pressure around a coated bubble with a polymer, this equations modify the Keller-Miksis equation, and they obtained an analysis in frequency. In our case we can predict the collapse of the shell, the value of the pressure and the displacement of the liquid for the entire time domain. We can expect that the shell behaves as an oscillating solid for a period of time.

For the numerical procedure we use a Runge-Kutta 4th order method applied to the R-P equation in order to obtain the outside radius, the interface pressure and the corresponding deformation field for the solid.

The encapsulated or coated bubbles are capable of penetrating the smallest capillaries of the human tissue and can release drugs and medications into specific areas. The challenge is to follow these drug carriers by the use of ultrasound and break them in the specific area of medical treatment. The models can help to determine the amount of pressure and the frequency necessary to achieve this.

THEORY

The problem consists in a spherical symmetrical solid shell of finite thickness, which surrounds a perfect gas. The shell is bounded by a Newtonian incompressible liquid. We assume two interfaces, one between the solid and the gas (inside radius R_1) and the other between the liquid and the solid (outside radius R_2) as shown in Fig. 1. Both interfaces are subjected to distributed normal pressures P_g and P_l respectively. These pressures must be determined as a part of the problem using appropriate boundary conditions in both interfaces, as we show lines below. For the following equations we assume constant properties in all phases, uniform pressure inside the shell, and a purely elastic solid shell. We neglect the body forces, the surface tensions between the solid and the gas and the liquid and the solid and the mass diffusion through the solid.

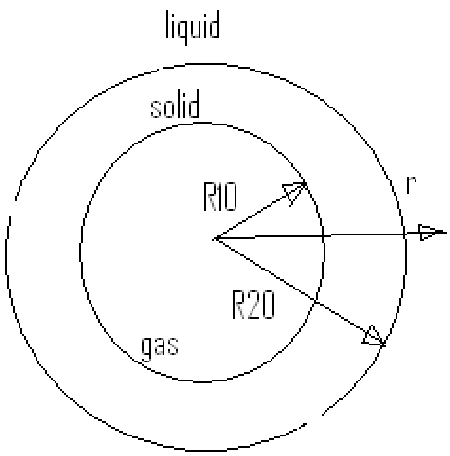

Figure 1: Solid bubble surrounded by liquid.

In the above figure, R_{20}, R_{10} are the initial outside and inside radiuses of the shell at equilibrium. For time $t>0$, we impose far away from the bubble an oscillatory pressure field denoted by $p_\infty = p_0 + p_A \sin \omega t$. For the inside of the shell, we consider for simplicity that the gas is compressed following an adiabatic process; therefore the inside pressure obeys the classical relationship $p_g = p_{g0}\left(\frac{R_{10}}{R_1}\right)^{3\gamma}$. In the present work, we use $\gamma = 1.4$.

The equation for an elastic shell can be found elsewhere, [7]

$$\frac{\partial^2 u}{\partial r^2} + \frac{2}{r}\frac{\partial u}{\partial r} - \frac{2}{r^2}u = \frac{\rho}{2G}\frac{\partial^2 u}{\partial t^2} \tag{1}$$

In order to derive the above equation, we assume spherical symmetry and therefore the components of the displacement vectors are, $u = u(r)$, $v = w = 0$. In addition, all the shear stress components vanish so that, $\tau_{r\theta} = \tau_{\theta\phi} = \tau_{\phi r} = 0$. We assume Hooke´s law to establish the strain-displacement relationship and the details can be found elsewhere (Reisman, op. cit.).

For the liquid the continuity and the momentum equations together form the Rayleygh-Plesset equation [8].

$$\rho_l\left[\frac{d^2 R_2}{dt^2} + \frac{3}{2}\left(\frac{dR_2}{dt}\right)^2\right] = p_l(R_2) - p_\infty \tag{2}$$

For both equations we have the compatibility equations, and the initial conditions for the R-P eq.

For the inside radius R_1 we have:

$$r = R_1:$$
$$p_{g,0}\left(\frac{R_{10}}{R_1}\right)^{3\gamma} = -2G\left.\frac{\partial u}{\partial r}\right|_{r=R_1} \tag{3}$$

For the outside radius R_2 we have:

$$r = R_2:$$
$$p_l = -2G\left.\frac{\partial u}{\partial r}\right|_{r=R_2} - \frac{4\mu_l}{R_2}\frac{dR_2}{dt} \tag{4}$$

The initial conditions are:

$$t = 0; R_2 = R_{20}; \frac{dR_2}{dt} = 0 \tag{5}$$

We introduce the dimensionless variables

$$\eta = \frac{r - R_1}{R_2 - R_1}; \tau = \omega t; \theta = \frac{u}{R_{20} - R_{10}}$$
$$\Delta_1 = \frac{R_1 - R_{10}}{R_{20} - R_{10}}; \Delta_2 = \frac{R_2 - R_{20}}{R_{20}} \tag{6}$$

Substituting on eqs. (1)-(5) we have:

$$\frac{\partial^2\theta}{\partial\eta^2} + \frac{2\Delta_2}{(1+\Delta_2)}\frac{\partial\theta}{\partial\eta} - \frac{2\Delta^2{}_2\theta}{(1+\Delta_2)^2} = \beta\frac{\partial^2\theta}{\partial\tau^2} \tag{7}$$

$$(1+\Delta_2)\frac{d^2\Delta_2}{d\tau^2} + \frac{3}{2}\left(\frac{d\Delta_2}{d\tau}\right)^2 = \Pi\pi_e - \beta_A \sin\tau \tag{8}$$

$$\eta = 0$$
$$1 = -\frac{2\alpha_i}{\Delta_2}\left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=0} \tag{9}$$

$$\eta = 1$$

$$1+\Pi = -\frac{2\alpha_0}{\Delta_2}\left.\frac{\partial\theta}{\partial\eta}\right|_{\eta=1} - \frac{4}{R_{e\omega}(1+\Delta_2)_2}\frac{d\Delta_2}{d\tau} \quad (10)$$

$$\tau = 0; \Delta_2 = 0; \frac{d\Delta_2}{d\tau} = 0 \quad (11)$$

The quasi stationary deformation of the solid in eq. (7) stands when parameter α<<1. Introducing a new variable $1+\eta\Delta_2 = \xi$, eq. (7) can be solved analytically, taking into account (9), (10) and (11).

$$\theta = \left[\frac{1}{\alpha_i\left(\left(1+\Delta_2\right)^3-1\right)} - \frac{1+\Pi+\frac{4}{R_{e\omega}\left(1+\Delta_2\right)}\frac{d\Delta_2}{d\tau}}{\alpha_0\left(1-\frac{1}{\left(1+\Delta_2\right)^3}\right)}\right]* \left[\frac{\left(1+\Delta_2\eta\right)}{2} + \frac{1}{4\left(1+\Delta_2\eta\right)^2}\right] + \frac{1}{4\alpha_i\left(1+\Delta_2\eta\right)^2} \quad (12)$$

As we can see from eq. (12) the deformation θ depends on a solution for the fluid radius Δ_2 and on the pressure at the interface Π. For the radius we must solve R-P eq. (8), but, as can be seen depends on Π. In [4] we used a constant value for the pressure mainly for closing the problem than for getting a result. As will be shown further, this assumption created a mistake that only a particular equation for Π would correct.

Additionally to equations (1)-(5), we need to place a condition for the interface, continuity of displacement between the deformation and the radius movement,

$$R_2 = R_{20} + u(r,t) \quad (13)$$

In the dimensionless form, at the interface for $r=R_2$ and for all t we have.

$$\Delta_2 = \left(\frac{R_{20}-R_{10}}{R_{20}}\right)\theta(\eta=1,\tau) = \sigma\theta(\eta=1,\tau) \quad (14)$$

Evaluating eq. (12) for η=1 and with the assumption that $\alpha_0 = \alpha_i$ because the initial equilibrium pressure on both sides of the shell are the same $p_0 = p_{g0}$ we can rewrite (12)

$$\sigma\theta = \pi_x\left[\frac{1}{\left(\left(1+\Delta_2\right)^3-1\right)} - \frac{1+\Pi+\frac{4}{R_{e\omega}\left(1+\Delta_2\right)}\frac{d\Delta_2}{d\tau}}{\left(1-\frac{1}{\left(1+\Delta_2\right)^3}\right)}\right]* \left[\frac{\left(1+\Delta_2\right)}{2} + \frac{1}{4\left(1+\Delta_2\right)^2}\right] + \frac{\pi_x}{4\left(1+\Delta_2\right)^2} \quad (15)$$

With (14) and (15) we get an equation for the pressure

$$\Pi = \frac{\left(\left(1+\Delta_2\right)^3-1\right)}{\left(\left(1+\Delta_2\right)^3+\frac{1}{2}\right)\left(1+\Delta_2\right)}\left[\frac{1}{2\left(1+\Delta_2\right)^2} - \frac{2\Delta_2}{\pi_x}\right] + \frac{1}{\left(1+\Delta_2\right)^3} - 1 - \frac{4}{\mathrm{Re}_\omega\left(1+\Delta_2\right)}\frac{d\Delta_2}{d\tau} \quad (16)$$

With (16) eq. (8) has the form

$$\left(1+\Delta_2\right)\frac{d^2\Delta_2}{d\tau^2} + \frac{3}{2}\left(\frac{d\Delta_2}{d\tau}\right)^2 + \frac{4}{\mathrm{Re}_\omega\left(1+\Delta_2\right)}\frac{d\Delta_2}{d\tau} = \frac{\left(\left(1+\Delta_2\right)^3-1\right)}{\left(\left(1+\Delta_2\right)^3+\frac{1}{2}\right)\left(1+\Delta_2\right)}\left[\frac{1}{2\left(1+\Delta_2\right)^2} - \frac{2\Delta_2}{\pi_x}\right]\pi_e + \left[\frac{1}{\left(1+\Delta_2\right)^3} - 1\right]\pi_e - \beta_A\sin\tau \quad (17)$$

Equation (17) can be solved numerically with a Runge-Kutta fourth order method subject to (11). With Δ_2 (16) and then (12) can also be solved.

RESULTS

The numerical results were performed taking into account the numerical and experimental values from [2], [3], [9] and [10]. All values were taken as their mean and approximated to obtain discrete values for the parameters involved. Such as $G = 12.5MPa$, $R_{20} = 1\mu m$, $R_{10} = R_{20} - 0.05R_{20}$, $\omega = 2\pi f$, $f = 3MHz$, $\mu = 0.004Pas$, $\rho = 998kg/m^3$, $p_0 = 100kPa$ and $p_A = 2MPa$.

With the numerical results we can determine which the most influential parameters were π_x and β_A, both determine how the oscillation will be, even the existence of it. The parameters α_0, α_i are related to π_x, by the parameter σ and their direct influence is only perceived in the solid. For Re_ω and π_e for their limited range of value, their influence in the whole process is unnoticed although for another spectrum of values they might be influential.

Eq. (12) diverges in $\Delta_2=0$ for $\tau=0$, the first and second right hand term in (12), go to infinity. For this singular point we jump the first step starting to calculate from the second step in time using a grid of 10 points equally spaced to calculate θ. For Δ_2 and Π we use a time step of 0.0005 for the Runge-Kutta Method, and solve simultaneously for both equations (16) and (17).

In Fig. 2 we have the evolution of radius in time for $\pi_x=0.01$ and $\beta_A=0.001$, we can se a transient oscillatory mode up to $\tau>100$, from which the oscillation stabilizes into a steady one.

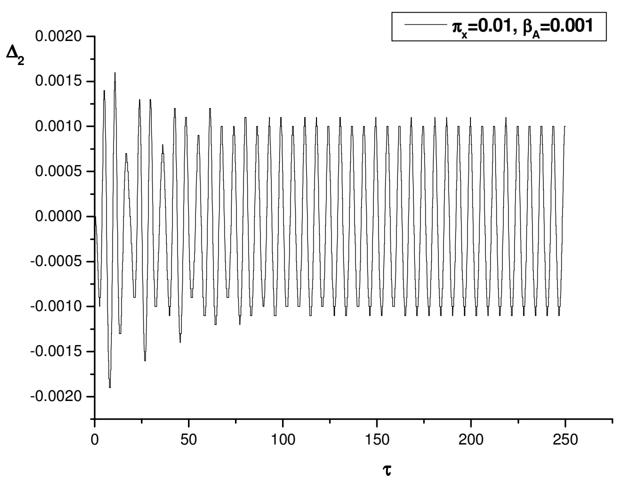

Figure 2: Radius versus time for $\pi_x=0.01$ and $\beta_A=0.001$

In Fig. 3 we see the evolution of pressure in time also for $\pi_x=0.01$ and $\beta_A=0.001$, and like the radius for times beyond $\tau>100$ the oscillation stabilizes.

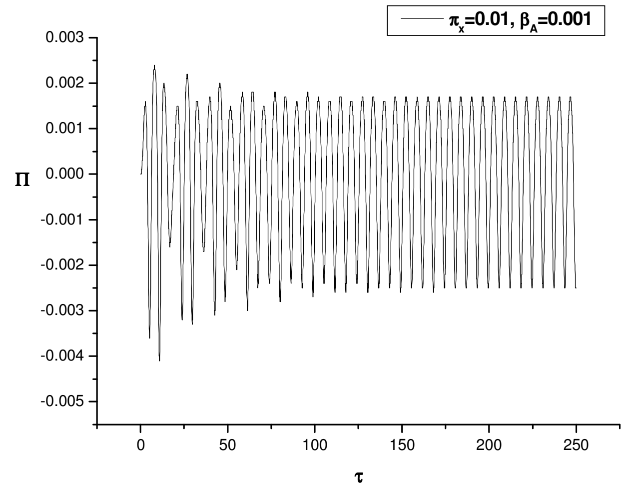

Figure 3: Pressure versus time for $\pi_x=0.01$ and $\beta_A=0.001$

Fig 4. shows the deformation of the solid at the last nth node near the liquid. We can see this spikes oscillations that resemble an accumulative elastic behavior, as time runs the spikes are longer, the oscillation damps for a period of about 50, only to return to a greater rate of deformation. This suggests that eventually as time runs further the collapse of the solid is a fact. With the numerical results of eq. (12) we can see that all the nodes have the same rate of displacement, implying that the shell moves like a whole solid structure symmetrically. As with the other two graphs we find the steady mode beyond $\tau>100$.

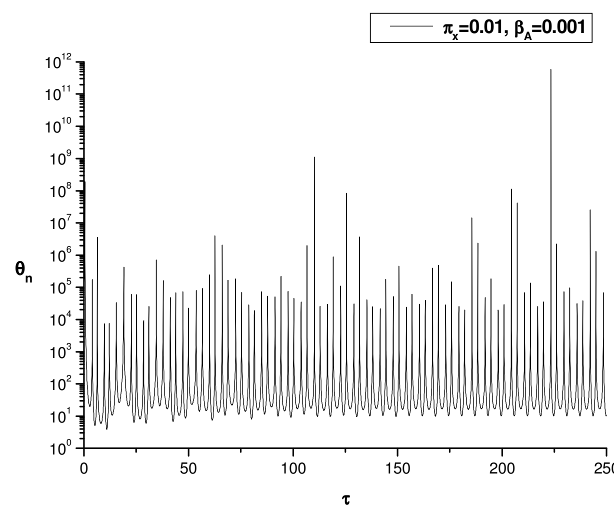

Figure 4: Rate of deformation θ_n in time for $\pi_x=0.01$ and $\beta_A=0.001$

Fig. 5 is a close up of Fig. 4 to show the oscillation in the spikes has a periodicity in a small period of time that keeps happening in the steady mode four small spikes between two big ones, being the last one bigger that the previous one.

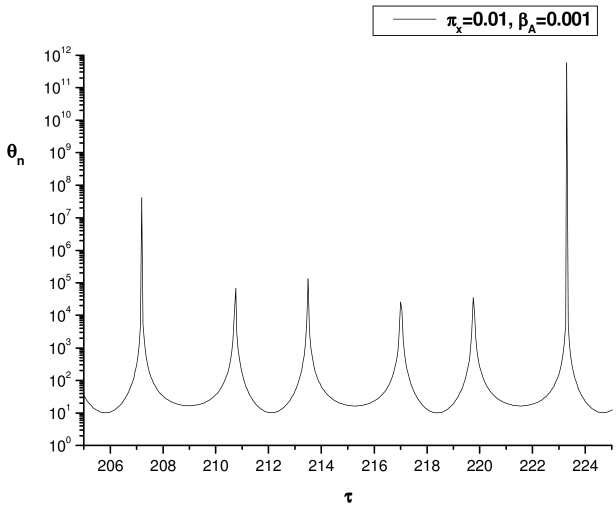

Figure 5: Close up of Fig 4. for 200<τ<224.

Fig. 6 is the close up of the lower part of the spikes, to show that even the chaotic appearance of the above spikes, beneath them we find a periodically amount of regular oscillation in the steady mode beyond τ>100 .

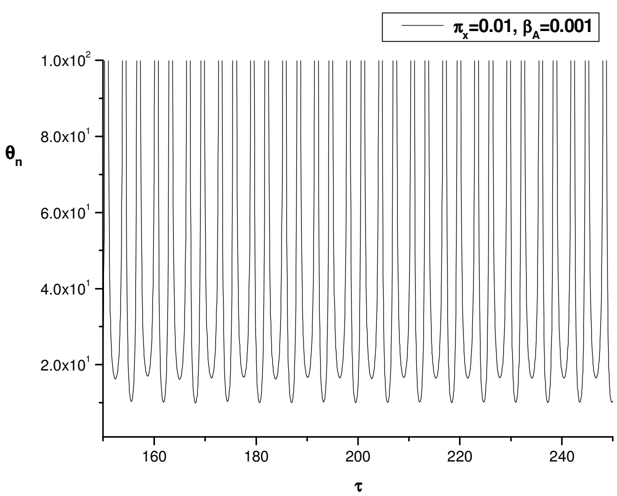

Figure 6: Close up of Fig. 4 the lower portion of the graph

Figs. 7 and 8 show the evolution of radius in time with the influence of the control parameters. We let two more values of β_A, 0.01 and 0.1, together with values for π_x, 0.1, 0.01 and 0.001. These graphs show, for increasing values of β_A the collapse is more violent, the same for π_x. This behavior shows a limiting case that cannot be reached if you need the shell to stabilize and not to collapse.

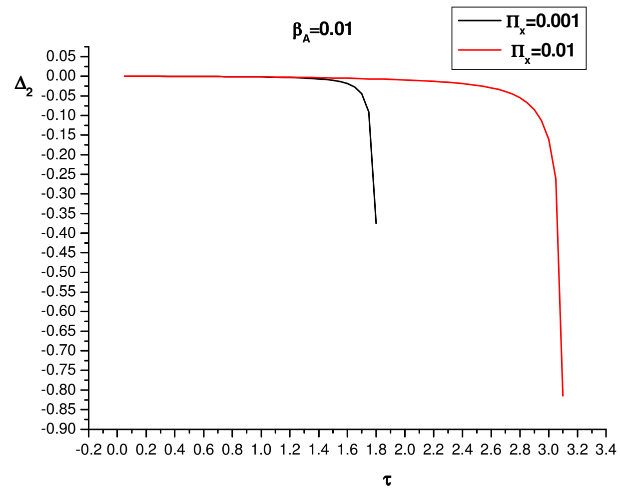

Figure 7: Evolution of radius in time for β_A= 0.01 and different π_x

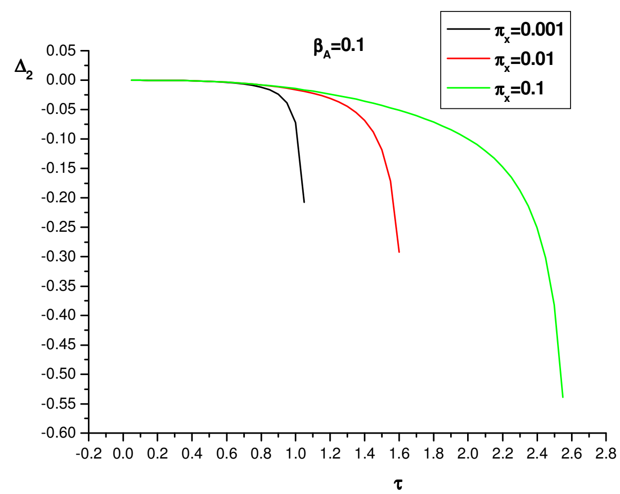

Figure 8: Evolution of radius in time for β_A= 0.1 and different π_x

DISCUSSION

The main parameters π_x and β_A, determine how the physics of the problem, how the oscillation and the collapse might be. For the most realistic interval π_x=0.01 and β_A=0.001, we have transient oscillations for the radius and the pressure which stabilizes for times τ>100. The same can be observed for the solid except that we have an ever growing amount deformation, even reaching the steady time τ>100.

Although the oscillatory spikes of the deformation seem irregular and chaotic, we have a periodic event as shown in Fig. 5, and a regular oscillation as shown on Fig. 6.

The ever growing rate of deformation shown by the spikes in Fig. 3 can only be explained by a cumulative elastic rate of deformation in time. The elasticity as stated in the solid's equation is the responsible for this behavior, even though the equation is stated as quasi stationary. This is in particular interest; in the first place although we have a steady oscillation in the liquid represented in Fig. 2, and second we have a growing rate of deformation which eventually produces collapse in the shell.

For the pressure we have an equation that let us see the oscillatory behavior of it, this equation also closes the problem and as the graphs show delivers us another physical point of view for the whole problem.

In Figs. 7 and 8, show that we cannot stretch the values of π_x and β_A for any situation. The absence of oscillations with a sudden collapse indicates us how the problem reaches a critical situation, thus confining the parameters to a very particular domain.

CONCLUSION

An equation for the pressure was one of the main scopes of the paper. This equation gives us a new perspective concerning the way the shell oscillates and how might collapse.

In the three variables we have a transient time that will reach a steady state.

The elastic model that we propose is the simpler model and as shown, is restricted by a small domain of the parameters; this will need a more sophisticated model, first in keeping the transient mode for the solid, and second on getting better values for the mechanical properties of the contrast agents in the nanoscale. This will lead us to propose a more exact model, such as a viscelastic fluid or a viscoelastic solid.

NOMENCLATURE

G	Shear Modulus [MPa]
p_0	Ambient initial press.[kPa]
$p_\infty = p_0 + p_A \sin \omega t$	Pressure in infinity [kPa]
p_A	Driving Pressure [kPa]
p_g	Gas Pressure [kPa]
p_{g0}	Gas initial Pressure [kPa]
R_1	Inside Radius [m]
$R2$	Outside Radius [m]
R_{10}	Inside Initial Radius [m]
R_{20}	Outside Initial Radius [m]
r	Radial Coordinate [m]
t	Time [s]
u	Deformation [m]
$R_{e\omega} = \dfrac{p_0}{\mu\omega}$	Reynolds number for p_0
$R_{e2} = \dfrac{\rho_l R^2{}_{20}\omega^2}{\mu}$	Reynolds Number for R_{20}

Greek Symbols

Dimensionless Parameters

$$\alpha_0 = \frac{G\sigma}{p_0}$$

$$\alpha_i = \frac{G\sigma}{p_{g0}}$$

$$\alpha = \frac{\rho\left(R_{20} - R_{10}\right)^2 \omega^2}{G}$$

$$\beta = \frac{G\sigma}{\rho_l R_{20}^2 \omega^2}$$

$$\beta_A = \frac{p_A}{\rho_l R^2{}_{20}\omega^2}$$

η

τ

$$\pi_e = \frac{p_0}{\rho_l R^2{}_{20}\omega^2}$$

$$\pi_x = \frac{p_0}{G}$$

$$\sigma = \frac{R_{20} - R_{10}}{R_{20}}$$

$$\Delta_1 = \frac{R_1 - R_{10}}{R_{20} - R_{10}}$$

$$\Delta_2 = \frac{R_2 - R_{20}}{R_{20}}$$

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