Indian Institute of Technology Gandhinagar

Computational Analysis of Encapsulation Elasticity Effects on Growth and Dissolution Dynamics of Encapsulated Microbubbles

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MA203 Project Report

Group Members

Ishan Agarwal (22110100)

Kaushik (22110113)

Keshav Sobania (22110118)

Ankit Singh (22110025)

Lovekesh Mahale (22110131)

Under the guidance of

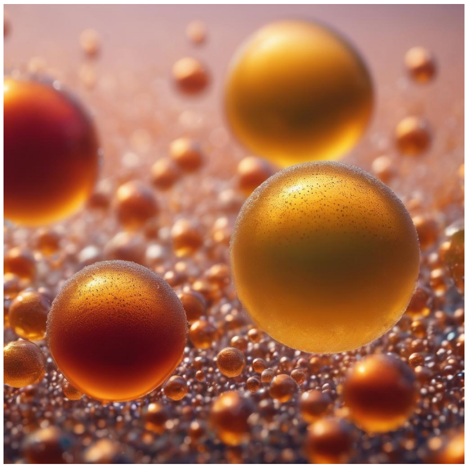
Prof. Dilip Srinivas Sundaram

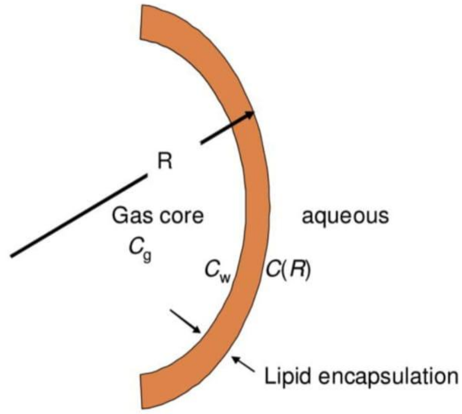
Problem Statement

Encapsulated microbubbles play a pivotal role in both medical imaging and drug/gene delivery. In the realm of ultrasound imaging, these tiny bubbles, wrapped in a protective layer of proteins, lipids, and other surface-active materials, serve as contrast agents. The encapsulation stabilizes the microbubble, preventing it from dissolving prematurely in the bloodstream. This stability is crucial for obtaining high-quality ultrasound images with improved contrast. As a result, clinicians can obtain clearer and more detailed images of tissues and structures, aiding in accurate diagnoses.

However, achieving the right balance in microbubble behavior is a delicate dance between growth and dissolution. Controlled growth is essential as it enhances the scattering characteristics of microbubbles, making them highly effective in enhancing image contrast during ultrasound procedures. Yet, unchecked growth can lead to instability and eventual disruption. Conversely, dissolution, the process of microbubbles shrinking and releasing the encapsulated gas into the surrounding liquid, is a crucial factor in determining their lifespan. The rate of dissolution is influenced by factors like surface tension, gas concentration, and the composition of the encapsulating material.

Beyond imaging, encapsulated microbubbles find an equally vital role in drug and gene delivery. These microbubbles can be loaded with therapeutic agents and directed to specific target sites within the body. When needed, controlled disruption of the microbubble releases the payload, facilitating precise drug delivery. This approach holds great promise for improving the effectiveness and efficiency of therapies while minimizing side effects.





In our project, we are developing a mathematical model to better understand how encapsulation elasticity affects the growth and dissolution dynamics of microbubbles, particularly in the presence of air dissolved in the surrounding liquid. This research has the potential to revolutionize medical imaging and drug delivery, advancing the capabilities of these microbubbles and enhancing healthcare outcomes. The specific objectives are presented below:

1.) Gather insights from existing literature and Conduct an extensive review of relevant research papers and studies pertaining to the given problem statement.
2.) Analyze the fundamental equations, assumptions, and properties associated with encapsulated microbubbles.
3.) Understand the key factors influencing microbubble behavior, including surface tension, encapsulation elasticity, and gas type
4.) Develop a comprehensive mathematical model describing the behavior of encapsulated microbubbles.
5.) Formulate the governing equations that define the dynamics of microbubbles and their interactions with the surrounding medium.
6.) Implement a numerical simulation method using MATLAB to solve the derived ordinary differential equations (ODEs).
7.) Utilize techniques such as the Runge-Kutta method to numerically solve the ODEs and analyze the impact of changing parameters, especially encapsulation elasticity, on microbubble stability.
8.) Investigate the influence of varying the saturation level of the surrounding medium, including degassed, saturated, and oversaturated conditions.

1. Physical Model

The behavior of encapsulated microbubbles is analyzed based on the following physical model and principles:

1. **Encapsulation Material Properties**: The encapsulating material is assumed to possess specific elasticity and permeability properties, represented by parameters E_s (dilatational surface elasticity) and h_g (permeability of gas through the encapsulation), respectively.
2. **Gas Behavior Inside the Microbubble:** The behavior of the gas inside the microbubble is described by its solubility and diffusivity in the surrounding medium, represented by the Ostwald coefficient L_g . This coefficient relates gas concentration inside the encapsulation to the inner gas concentration.
3. **Surface Tension Effects:** Surface tension (c_0) significantly affects the stability and dissolution of the microbubble. Variations in surface tension influence the dynamics of bubble growth and dissolution.
4. **Equilibrium Conditions:** Equilibrium conditions for the microbubble are defined based on the interplay between surface tension, encapsulation elasticity, and gas properties. The equilibrium bubble size is influenced by these factors, determining stability against dissolution.

2. Assumptions

The analysis of encapsulated microbubbles is conducted under the following assumptions:

1. **Steady-State Conditions:** The system is assumed to be under steady-state conditions, neglecting unsteady effects due to the timescales involved in bubble growth and dissolution.
2. **Spherical Symmetry:** The microbubble is assumed to maintain spherical symmetry during its growth and dissolution processes.
3. **Neglecting Convection:** Convection effects within the microbubble and the surrounding medium are neglected due to their minor influence compared to diffusion processes.
4. **Linear Permeability Model:** The permeability of gas through the encapsulation is assumed to follow a linear model, allowing for simplified mathematical treatment.
5. **Surface Elasticity Impact**: Encapsulation elasticity is considered as a stabilizing factor, influencing the resonance frequency and overall stability of the microbubble.
6. **Isotropic Behavior:** The encapsulating material is assumed to exhibit isotropic behavior concerning its elasticity and permeability properties.

3. Governing Equations

1. **Basic Diffusion Equation:**

   The process of gas transport from an encapsulated bubble is described using the basic diffusion equation in the surrounding medium:

   $$\frac{1}{r^2}\frac{\delta}{\delta r}\left(r^2\frac{\delta C}{\delta r}\right) = 0$$

   Where C is the gas concentration in the surrounding medium and r is the radial distance from the bubble center.

   Boundary conditions:- The boundary conditions for the diffusion equation are set at the outer surface of the encapsulation and far away from the bubble:

   $$-k_g\left|\frac{\delta C}{\delta r}\right|_R = h_g\left[C_w - C(R)\right], C(r\rightarrow\infty) = C_\infty$$

   Where R is the bubble radius, h_g is the permeability of gas through the membrane, k_g is the diffusivity in the surrounding liquid, C_w is the gas concentration at the inside wall of the encapsulation, and C_1 is the gas concentration far from the bubble.

   Solving this, we get

   $$C(r) = \frac{R^2\left(C_w - C_\infty\right)}{r\left(\frac{k_g}{h_g}+R\right)} + C_\infty$$

2. **Mass conservation inside the bubble leads to:**

   $$\frac{d\left(R^3C_g\right)}{dt} = 3R^2k_g\frac{\left(C_\infty - L_gC_g\right)}{\left(\frac{k_g}{h_g}+R\right)}$$

   Here, C_g is the gas concentration inside the bubble, L_g is the Ostwald coefficient relating C_w and C_g

3. **Pressure Inside the Bubble:**

   The pressure inside the bubble is determined by the Laplace pressure due to surface tension γ and gas concentration C_g inside the bubble:

   $$p_g = C_gR_GT = p_{atm} + \frac{2\Upsilon(R)}{R}$$

where P_{atm} is the atmospheric pressure, R_G is the universal gas constant, and T is the temperature. The surface tension γ(R) is modeled using a Gibbs elasticity type constitutive model:

$$E^s = \frac{d\Upsilon}{dA/A_0},$$

$$\Upsilon(R) = \left\{\Upsilon_0 + E^s\left[\left(\frac{R}{R_0}\right)^2 - 1\right], \qquad for\ \Upsilon_0 + E^s + E^s\left[\left(\frac{R}{R_0}\right)^2 - 1\right] > 0, \right\}$$

$$\Upsilon(R) = \left\{0, \qquad for\ \Upsilon_0 + E^s + E^s\left[\left(\frac{R}{R_0}\right)^2 - 1\right] \leq 0, \right\}$$

Analyzing this, we see,

$$\Upsilon(R) > 0, \qquad for\ E^s/\Upsilon_0 \leq 1$$

$$\Upsilon(R) > 0,\ R > R_s, \qquad for\ E^s/\Upsilon_0 > 1,\ where\ R_s = R_0\left(1 - \Upsilon_0/E^s\right)^{1/2}$$

$$\Upsilon(R) > 0,\ R > R_s, \qquad for\ E^s/\Upsilon_0 > 1,\ where\ R_s = R_0\left(1 - \Upsilon_0/E^s\right)^{1/2}$$

Using these equations, we find the bubble dissolution equation:

$$\frac{dR}{dt} = \frac{-3L_g k_g}{\left(\frac{k_g}{L_g}+R\right)}\left[\frac{p_{atm}(1-f) + \frac{2\Upsilon}{R}}{3p_{atm} + \frac{4\Upsilon}{R} + 2\frac{d\Upsilon}{dR}}\right]$$

Note that dγ/dR is discontinuous at R = $R_0(1 - \gamma_0/E^s)^{1/2}$

4. **Dissolution Equation (**rate of change of bubble radius *R* with respect to time *t*):

   The rate of change of bubble radius *R* with respect to time *t* is given by the following equation, considering the effects of surface tension, elasticity, and undersaturation:

$$\frac{dR}{dt} = \frac{-3L_g k_g}{\left(\frac{k_g}{L_g}+R\right)}\left[\frac{p_{atm}(1-f) + \frac{2\Upsilon_0}{R} + \frac{2E^5}{R}\left\{\left(\frac{R}{R_0}\right)^2 - 1\right\}}{3p_{atm} + \frac{4\Upsilon_0}{R} + \frac{4E^5}{R}\left\{2\left(\frac{R}{R_0}\right)^2 - 1\right\}}\right],\ for\ \Upsilon(R)\ =\ \Upsilon_0 + E^S\left[\left(\frac{R}{R_0}\right)^2 - 1\right] > 0$$

$$\frac{dR}{dt} = \frac{-L_g k_g}{\left(\frac{k_g}{L_g}+R\right)}(1 - f), \quad for\ \Upsilon(R) = 0$$

On Non - dimensionalizing this equation, we get the final required dissolution equations for the microbubble:-

$$\frac{d\widehat{R}}{d\tau} = \frac{-3L_g}{(\alpha_g+R)}\left[\frac{\widehat{R}(1-f)+\widehat{\Upsilon}+\widehat{E}\left\{\widehat{R^2}-1\right\}}{3\widehat{R}(1-f)+2\widehat{\Upsilon}+2\widehat{E}\left\{2\widehat{R^2}-1\right\}}\right],\ for\ \widehat{\Upsilon} + \widehat{E}\left\{\widehat{R^2} - 1\right\} > 0,$$

$$\frac{d\widehat{R}}{d\tau} = \frac{-3L_g}{(\alpha_g+R)}\left[\frac{R(1-f)}{3R}\right], \qquad for\ \widehat{\Upsilon} + \widehat{E}\left\{\widehat{R^2} - 1\right\} \leq 0,$$

Here $\widehat{R}$ = R/R_0, $\alpha_g = k_g/(h_g R_0)$, $\widehat{E} = 2E^S/\ (P_{atm} * R_0)$ and

- Dissolution time equation with respect to initial bubble radius R_0 is

$$t_{diss} = \frac{R_0^2}{k_g L_g}\left[\frac{P_{atm}R_0}{\gamma}\left(\frac{1}{6} + \frac{k_g}{4h_g R_0}\right) + \frac{2k_g}{3h_g R_0} + \frac{1}{3}\right]$$

4. Parameters

- C is the gas concentration in the surrounding medium
- r is the radial distance from the bubble center
- R is the bubble radius
- h_g is the permeability of gas through the membrane
- k_g is the diffusivity in the surrounding liquid
- C_w is the gas concentration at the inside wall of the encapsulation
- C_1 is the gas concentration far from the bubble.
- C_g is the gas concentration inside the bubble
- L_g is the Ostwald coefficient relating C_w and C_g
- P_{atm} is the atmospheric pressure
- R_G is the universal gas constant
- T is the temperature and γ is surface tension inside the bubble.
- C_g is gas concentration inside the bubble
- $\widehat{R}$ = R/R_0 R_0 is initial bubble radius
- $\alpha_g = k_g/(h_g R_0)$
- $\widehat{E} = 2E^S/(P_{atm} * R_0)$
- $\tau = tk_G/R_0$

Other parameters:

TABLE 1

Parameter	Value
Initial bubble radius (R_0)	$1.25 \times 10^{-6} m$
Atmospheric pressure (p_{atm})	101325 Pa
Coefficient of diffusivity of air in water (k_a)	$2.05 \times 10^{-9}\ m^2\ s^{-1}$
Coefficient of diffusivity of C_3F_8 in water (k_F)	$7.45 \times 10^{-10}\ m^2\ s^{-1}$
Surface tension (γ_0)	0.025 N/m
Ostwald coefficient of C_3F_8 (L_F)	5.2×10^{-4}
Ostwald coefficient of air (L_A)	1.71×10^{-5}
Permeability of air through the encapsulation (h_A)	$2.857 \times 10^{-5}\ m\ \ s^{-1}$
Permeability of C_3F_8 through the encapsulation (h_F)	$1.2 \times 10^{-6}\ m\ \ s^{-1}$

5. Solution Methodology

In this section, we explain the methodology employed to investigate the stability of encapsulated microbubbles in various mediums and with different interfacial elasticity values. The analysis is based on the provided equations and is exemplified through the MATLAB code.

Analytical Analysis

Upon solving the dissolution equation analytically, the equilibrium radius ($R_{Equilibrium}$) of the encapsulated air bubble can be expressed as follows:

1. $for\ f > 1\ and\ E^S \geq \gamma_0$

$$R_{equilibrium} = R_0\left[\varepsilon + \sqrt{\varepsilon^2 + \left(1 - \frac{\gamma_0}{E^S}\right)}\right],$$

2. $for\ f \geq 1 + \frac{4}{P_{atm}R_0}\sqrt{(\gamma_0 - E^S)}\ and\ E^S < \gamma_0$

$$R^{(1)}_{equilibrium} = R_0\left[\varepsilon + \sqrt{\varepsilon^2 + \left(1 - \frac{\gamma_0}{E^S}\right)}\right]$$

$$R^{(2)}_{equilibrium} = R_0\left[\varepsilon - \sqrt{\varepsilon^2 + \left(1 - \frac{\gamma_0}{E^S}\right)}\right],\ where\ \varepsilon = \frac{R_0 P_{atm}(f-1)}{4E^2}$$

Here, for $E_s < c_0$, there are two possible equilibrium solutions, but numerically, only $R(1)_{equilibrium}$ is stable, while $R(2)_{equilibrium}$ is unstable.

3. $for\ f = 1\ and\ E^S \geq \gamma_0$

$$R_{equilibrium} = R_s = R_0(1 - \gamma_0/E^S)^{1/2}$$

In the provided analysis, the dissolution time equation is solved numerically to obtain the equilibrium values ($R_{Equilibrium}$). A comparison is made between the numerical results and the analytical expressions to validate the accuracy of the model.

Interpretation of Results:

1. ***f<1*** ***:*** Bubble dissolution occurs eventually. In a saturated (f=1) medium, a non-zero equilibrium radius is attained only if the interfacial tension ($C_{0)}$ is counterbalanced by encapsulation elasticity ($E^S > c_0$).
2. ***f=1*** ***:*** For $E^S>0$, the bubble reaches a stable non zero radius, with the dissolution time being smaller than a limit, $t_{\text{limit\_diss}}$. Increasing E^S decreases the time to reach stabilization, saturating at $R_{\text{stable}} = R_0$ beyond $E^S>20c_0$. For $E^S \leq 1$, the bubble dissolves rapidly as the surface tension remains non-zero despite the compressive stress buildup.
3. ***f>1*** ***:*** Strong oversaturation ($f>1$) overcomes interfacial tension, resulting in a non zero equilibrium radius. For ($E^S \leq c_0$), dissolution occurs driven by surface tension and undersaturation. For ($E^S>c_0$)the stability and dissolution behavior of encapsulated air bubbles under different conditions, shedding light on the complex interplay between surface tension, elasticity, and oversaturation.

Numerical Analysis

Modeling Bubble Dynamics

We start by considering an air bubble with an initial diameter of 2.5 μm, characterized by the properties outlined in Table 1. The bubble radius evolution over time is studied for different mediums: saturated (f = 1), unsaturated (f = 0), and oversaturated (f = 1.5). The influence of interfacial elasticity (E^S/γ_0) on bubble stability is examined.

Numerical Simulation Setup

Given Parameters:

Initial bubble radius (R_0)	$1.25 \times 10^{-6} m$
Atmospheric pressure (p_{atm})	101325 Pa
Coefficient of diffusivity of air in water (k_a)	$2.05 \times 10^{-9}\ m^2\ s^{-1}$
Surface tension (γ_0)	0.025 N/m
Ostwald coefficient of air (L_A)	1.71×10^{-5}
Permeability of air through the encapsulation (h_A)	$2.857 \times 10^{-5}\ m\ \ s^{-1}$

f values:

- Saturated air medium(f=1),
- Degassed medium (f=0)
- oversaturated medium(f=1.5)

Set the values of E^S/γ_0 for analysis of growth and dissolution of microbubble in various mediums.

Algorithm used

Runge Kutta for dissolution stability of the encapsulated microbubble

The algorithm can be explained step by step as follows:

Initialization:

- Define the given parameters such as initial bubble radius (R_0), atmospheric pressure (P_{atm}), diffusivity of air in water (k_A), permeability of air through encapsulation (h_A), surface tension (c_0), Ostwald coefficient of air for LA (L_A), and oversaturation factor (f).
- Specify the values of interfacial elasticity (E_S) to consider, and define time parameters (initial time (t_{start}), end time (t_{end}), and number of time steps (num_steps)).

Numerical Integration:

- For each value of E_s (or E_s/c_0) specified in the **'es_values'** array, calculate the corresponding values of a_g and e.
- Initialize the dimensionless time parameter τ using the formula τ = $t \times k_A / R_0^2$.
- Set the initial condition $r(t = 0) = 1$, representing the normalized bubble radius.
- Implement the Runge-Kutta method to update the bubble radius (r) at each time step (t_i) using the provided differential equations.
- The Runge-Kutta method involves calculating intermediate values (*k1, k2, k3,k4*) based on the derivatives at different points, and then using a weighted average of these values to update the radius r for the next time step.
- The integration loop runs from i = 2 to num_steps updating the radius at each step.

Plotting:

- After obtaining the numerical solutions for different E_s values, plot the results to visualize the dissolution dynamics.
- The **'semilogx'** function is used for semilogarithmic x-axis plots, and the '**plot'** function is used for regular plots.
- Customize the plot labels, title, legends, and grid to enhance readability and understanding of the results.

Multiple Plots:

- The code contains multiple sets of simulations, each with its own specific scenario (e.g., saturated air medium, oversaturated medium, degassed medium).
- Each set of simulations iterates over different E_s values to observe the effects of interfacial elasticity on bubble dissolution.
- The resulting plots provide a visual representation of how bubble radius changes over time under various conditions.

Interpretation:

- The plotted results help in interpreting the stability and dissolution behavior of encapsulated air bubbles under different circumstances, aiding in the analysis and understanding of the physical phenomena.

Numerical Integration and Visualization

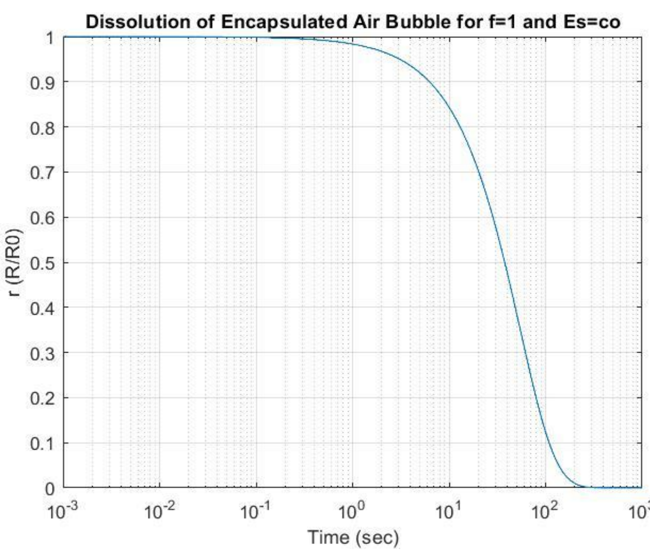
The provided MATLAB code utilizes the Runge-Kutta method to numerically integrate the given equations. The dissolution dynamics of encapsulated gas bubbles are simulated for various E^S/γ_0 values and mediums, resulting in time-dependent bubble radius (R/R_0) plots.

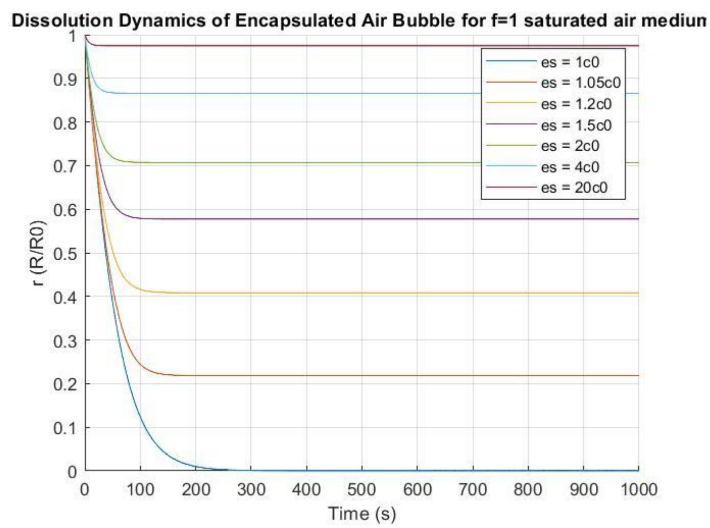
6. Results and Discussion

By following these steps, the code systematically explores the dissolution dynamics of encapsulated air bubbles and provides valuable insights into their behavior under different conditions.

The encapsulation is made of a mixture of three different lipids: DPPA ((R)-hexadecanoic acid, 1-[(phosphonooxy)methyl]-1,2-ethanediyl ester, monosodium salt), DPPC ((R)-4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxo hexadecyl)-oxy]-3,4,9-trioxa-4-phosphapentacosan-1-aminium, 4-oxide, inner A. Katiyar et al. / Journal of Colloid and Interface Science 336 (2009) 519–525 521 salt), and MPEG5000 DPPE ((R)-a-[6-hydroxy-6-oxido-9-[(1-oxo hexadecyl) oxy]-5,7,11-trioxa-2-aza-6-phosphahexacos-1-yl]-xmethoxypoly(ox-1,2- ethanediyl), monosodium salt).

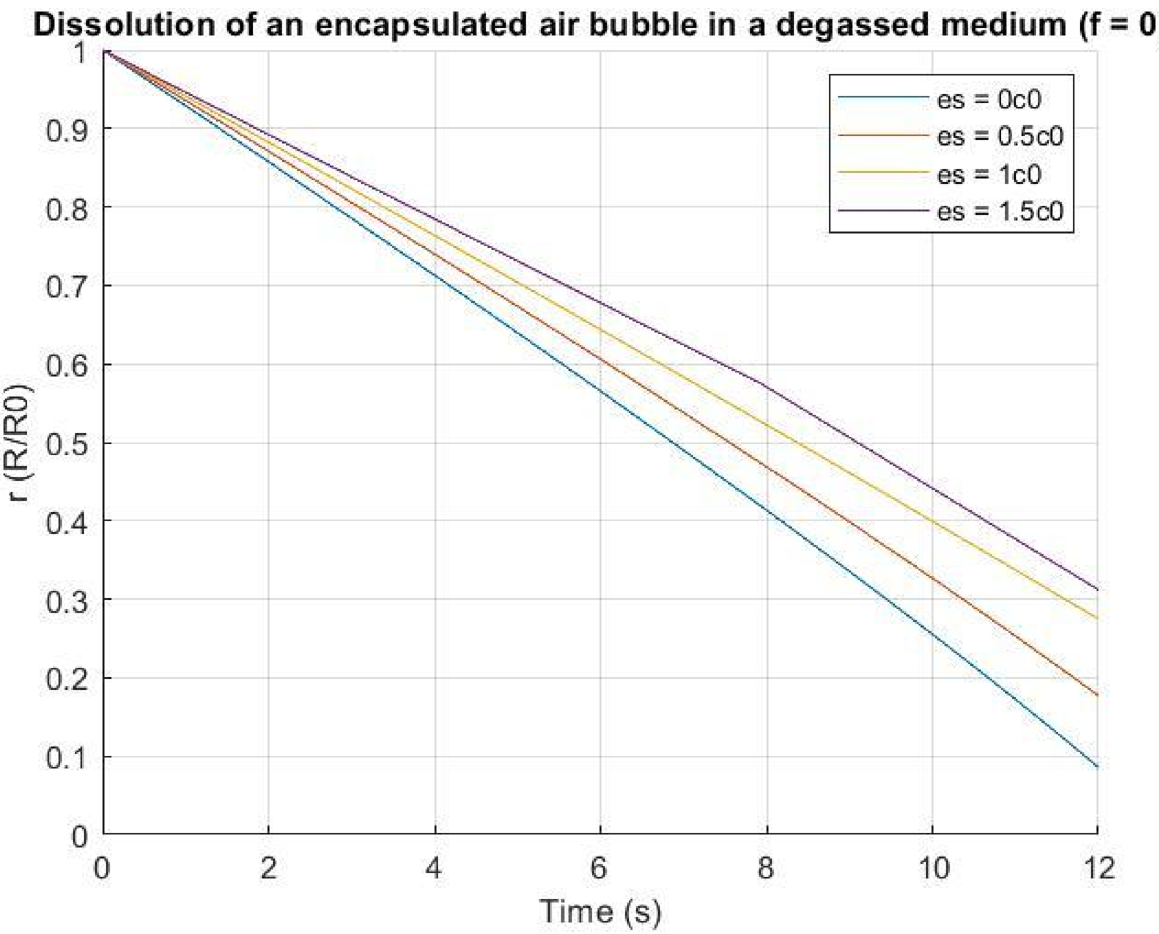
The property values utilized in this simulation are obtained from chemical literature and are presented in table 1.



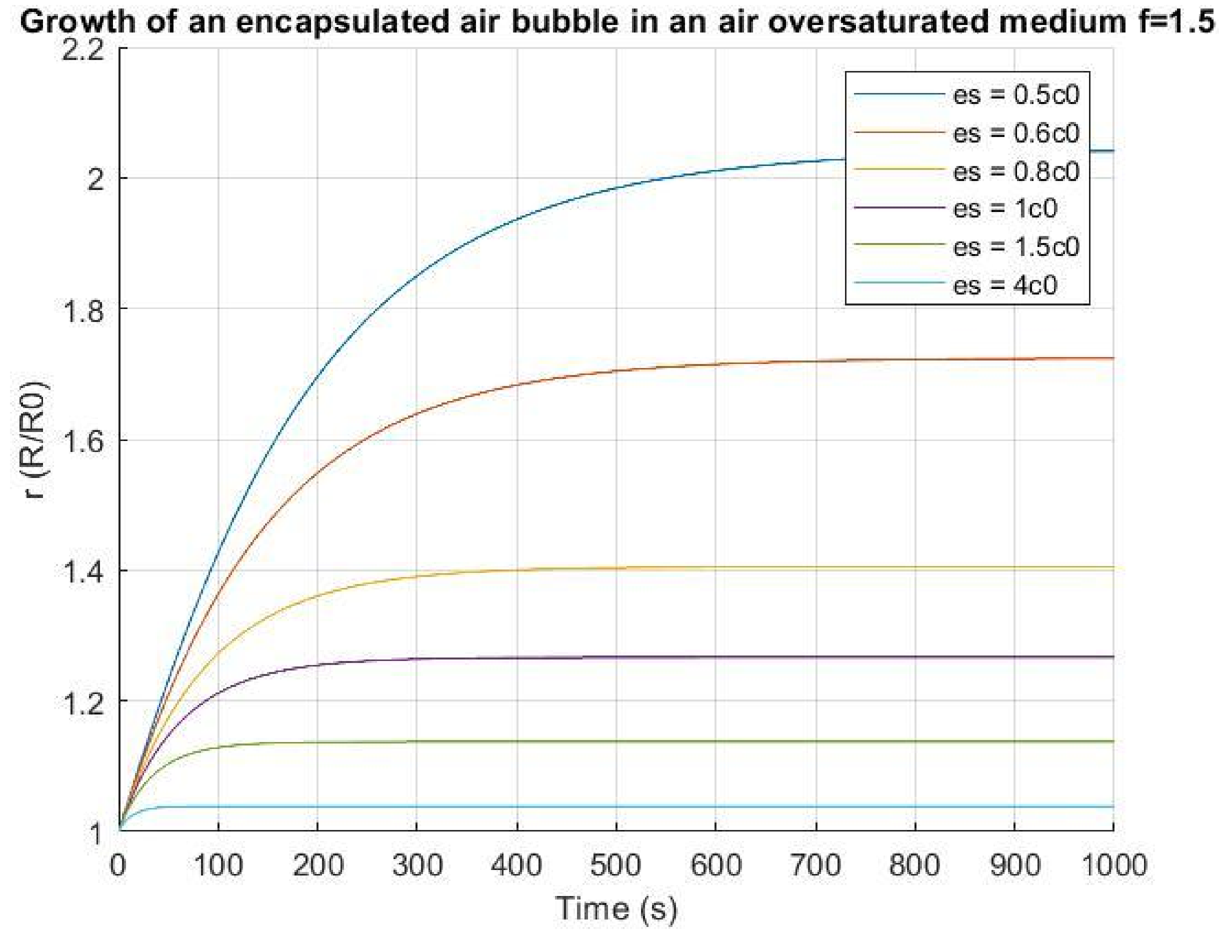


- **Fig. 1:** Effect of interfacial elasticity on bubble stability in an air-saturated medium (f = 1).
    - Analytical equilibrium radius ($R_{Equilibrium}$) is asymptotically matched by the numerical solution.
    - A critical condition $E_s / c_0 > 1$ for stable non-zero radius is observed.
    - $E_s < c_0 = 1$ sets the dissolution t_{limit_diss}, below which bubbles dissolve rapidly.
    - Numerical solution asymptotically matches the analytical equilibrium radius.
- Saturated Medium ($f = 1$):
    - Stable non-zero radius occurs for $E_s/c_0 > 1$, below which rapid dissolution is observed.
    - Increasing E_s/c_0 decreases the time to stabilization but saturates beyond E_s/c_0 =

20.



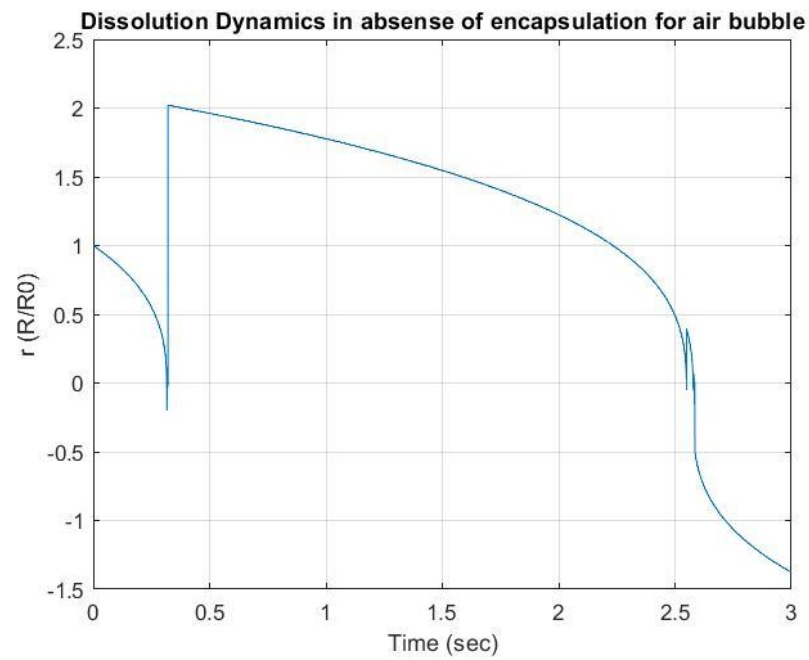
- **Fig. 2:** Dissolution dynamics in a degassed medium (f = 0).
  - Undersaturation leads to dissolution, with surface tension *(c(R))* aiding the process.
  - Dissolution times are smaller than in the saturated medium due to undersaturation.
- Degassed Medium (*f* = *0*):
  - Dissolution is driven by surface tension and undersaturation.
  - Dissolution times are shorter compared to the saturated medium.



- **Fig. 3:** Bubble stability in an oversaturated medium (f = 1.5).
  - Nonzero equilibrium radius ($R_{Equilibrium}$) is attained for $E^S > c_0$ as per Eq. (11).
  - Critical condition for stable equilibrium is satisfied for $E^S \leq c_0$.
- Oversaturated Medium (*f = 1.5*):
  - Equilibrium radius is attained for $E_s/c_0 > 1$, with stability observed for all E_s/c_0 values.
  - Equilibrium radius increases for decreasing E_s/c_0 values, and the other equilibrium solution ($R^{(2)}_{equilibrium}$) is unstable.

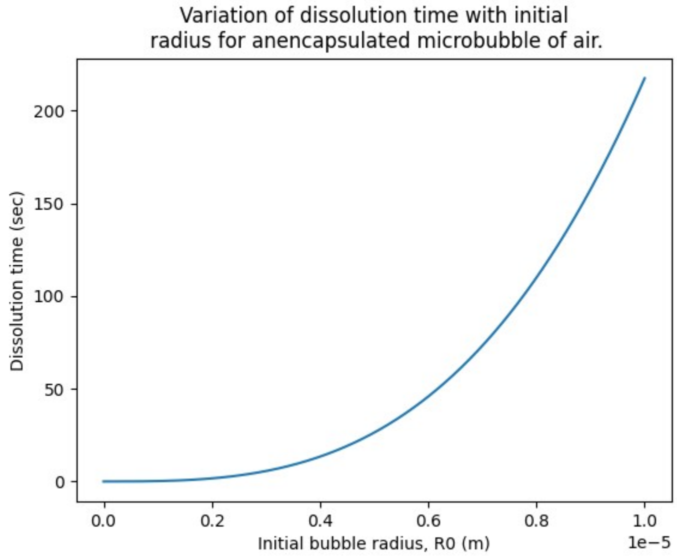
The presented results provide valuable insights into microbubble stability under different conditions, emphasizing the critical influence of interfacial elasticity and medium saturation levels. The code and simulations robustly demonstrate the observed behaviors, facilitating a comprehensive understanding of encapsulated microbubble dynamics.

In the absence of encapsulation, where $h_g \rightarrow \infty$ (or in terms of non-dimensional numbers $\alpha_g, k_g/(h_g R_0) \rightarrow 0$ and $E^S \rightarrow 0$ or $(\widehat{E},\ 2E^S/(P_{atm} * R_0) \rightarrow 0)$ we conducted a study using MATLAB, modifying parameters for f=1 and an initial bubble radius of 2.5 µm.



This analysis illustrates the extreme instability of an unencapsulated bubble in the saturated medium.

Variation of Dissolution time equation with respect to initial bubble radius R_0 is



- This behavior is consistent with the underlying physics of bubble dissolution. More giant bubbles generally take longer to dissolve because they have a larger volume of gas that needs to diffuse out into the surrounding liquid.
- As the bubble size increases, the surface area-to-volume ratio decreases, which reduces the rate of gas exchange with the surrounding medium. Therefore, larger bubbles tend to persist for longer periods before completely dissolving.
- The exponential increase in dissolution time with increasing initial bubble radius is a characteristic feature of many physical processes involving diffusion, as it reflects the diminishing rate of diffusion as the concentration gradient across the bubble interface decreases with increasing bubble size.

7. Citation

1. Amit Katiyar, Kausik Sarkar, and Pankaj Jain. 2009. “Effects of Encapsulation Elasticity on the Stability of an Encapsulated Microbubble.” 336 (2): 519–25.
2. Sarkar, Kausik, Amit Katiyar, and Pankaj Jain. 2009. “Growth and Dissolution of an Encapsulated Contrast Microbubble: Effects of Encapsulation Permeability.” *Ultrasound in Medicine & Biology* 35 (8): 1385–96.
3. Hao, Yue, Yuhang Zhang, and Andrea Prosperetti. 2017. “Mechanics of Gas-Vapor Bubbles.” *Physical Review Fluids* 2 (3).
4. Azami, Roozbeh H., Mitra Aliabouzar, Jenna Osborn, Krishna N. Kumar, Flemming Forsberg, John R. Eisenbrey, Sanku Mallik, and Kausik Sarkar. 2022. “Material Properties, Dissolution and Time Evolution of PEGylated Lipid-Shelled Microbubbles: Effects of the Polyethylene Glycol Hydrophilic Chain Configurations.” *Ultrasound in Medicine & Biology* 48 (9): 1720–32.
5. Sarkar, Kausik, William Y Shi, Dhiman Chatterjee, and Flemming Forsberg. 2005. “Characterization of Ultrasound Contrast Microbubbles Using *in Vitro* Experiments and Viscous and Viscoelastic Interface Models for Encapsulation.” *Journal of the Acoustical* .
6. Kothandaraman, Anjana, Anthony Harker, Yiannis Ventikos, and Mohan Edirisinghe. 2018. “Novel Preparation of Monodisperse Microbubbles by Integrating Oscillating Electric Fields with Microfluidics.” *Micromachines* 9 (10): 497.
7. Dollet, Benjamin, Philippe Marmottant, and Valeria Garbin. 2019. “Bubble Dynamics in Soft and Biological Matter.” *Annual Review of Fluid Mechanics* 51 (1): 331–55.
8. Qin, Dui, Qingqin Zou, Shuang Lei, Wei Wang, and Zhangyong Li. 2021. “Cavitation Dynamics and Inertial Cavitation Threshold of Lipid Coated Microbubbles in Viscoelastic Media with Bubble–Bubble Interactions.” *Micromachines* 12 (9)

8. Acknowledgement

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