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Surfactant properties differentially influence intravascular gas embolism mechanics

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Abstract

Gas bubble motion in a blood vessel causes temporal and spatial gradients of shear stress at the cell surface lining the vessel wall as the bubble approaches the cell, moves over it and passes it by. Rapid reversals occur in the sign of the shear stress imparted to the cell surface during this motion. These may result in injury to the cell. The presence of a soluble surfactant in the bulk medium reduces the level of the shear stress gradients imparted to the cell surface as compared to an equivalent surfactant-free system and is an important therapeutic aid. This is particularly true for a very small vessel. In this study, we analyze various physical and chemical properties of any given soluble surfactant to ascertain the relative significance of the property of the surfactant on the reduction in the level of the shear stress gradients imparted to the cell surface in such a vessel. While adsorption, desorption, and maximum possible monolayer interface surfactant concentration significantly impact the shear stress levels, physical properties such as the bulk or surface diffusivity do not appear to have large effects. At a given diameter, surfactants with $k_a/k_d d > \mathcal{O}(10^{-5})$ and $\Gamma_\infty/C_0 d > 9.5 \times 10^{-4}$ are noted to be preferable from the point of view of an increased gap size between the bubble and vessel wall, and a corresponding reduction in the shear stress level imparted to an endothelial cell. The shear stress characteristics of nearly occluding bubbles, in contrast with smaller sized bubbles under identical conditions, are most affected by the introduction of a surfactant in regard to shear stress levels. These observations could form a basis for choosing surfactants in treating gas embolism related illnesses.

Keywords

finite-sized bubble motion; blood vessel; soluble surfactant

1 Introduction

An understanding of the motion of a gas bubble through a blood vessel is of fundamental importance in gas embolism studies related to illnesses such as decompression sickness. Gas bubbles may enter the blood stream during cardiopulmonary bypass for cardiac operations or in vascular procedures. This may also happen due to decompression from hyperbaric exposures, such as in diving or extravehicular activity during space exploration. The intravascular gas emboli may deposit into organs, like the heart or the brain, and as a result cause permanent injury.

A gas bubble moving in a blood vessel may cause damage to the endothelial cells lining the interior wall of the vessel. The mechanisms for the injury appear to be related to the shear stress level imparted and the stress reversals that occur at the cell surface during the bubble motion

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[31]. Independently, experiments in our laboratory have shown that such an injury to the cell may be mitigated by the addition of a soluble surfactant to the continuous phase [54]. The surfactant in the blood stream appears to significantly change the dynamics of the bubble-cell interaction [3]. Furthermore, a non-toxic, soluble, inert surfactant introduced into the bulk phase opportunistically adsorbs onto the gas-liquid interface and modifies the interfacial tension [22]. This results in a change of the bubble shape and its residence time adjacent to the cell surface as compared to an equivalent surfactant-free system [55]. The adsorbed surfactant molecules may also shield biological moieties in the blood stream from encountering the adsorptive surface [22]. Recently, we have also experimentally shown that surfactants provide a cytoprotective influence on gas microbubble induced endothelial cell death [21], validating our numerical findings.

In this paper, we have investigated finite sized bubble motion in a blood flow laden with a soluble surfactant. A number of numerical techniques for the treatment of the motion of a fluid particle or bubble through a surfactant laden fluid, either soluble [35,20,15] or insoluble [57, 25,61,11,12] have been described in the literature. These are complemented by experimental studies [44,2] and some analyses [36,41,29,45]. The numerical methods for the study of free-surface flows include, front-tracking or immersed-boundary [49,59,56], level set [37,52], phase-field [18], volume-of-fluid [47,19], coupled level-set and volume-of-fluid [53], immersed interface [23], ghost-fluid methods [58], and moving mesh interface tracking [43].

In earlier studies, we have experimentally and numerically investigated the motion of a bubble through a surfactant-laden Newtonian fluid and through a blood-like liquid medium (Casson fluid) without the presence of a surfactant [5,10,34,31,62,32,33]. Recently, we have attempted to understand the effect of a surfactant on the motion of a gas bubble in a blood vessel [55]. It was shown therein, that the presence of a soluble surfactant in the bulk medium considerably reduces the level of shear stress gradients imparted to the cell surface as compared to an equivalent surfactant-free system. However, the suitability of any particular choice of the surfactant was not explored.

The choice of any particular surfactant is dictated by its properties such as its diffusivity, adsorption and desorption. In this paper, we attempt to study the effect of change of some of these surfactant properties on bubble motion and the impact on a cell lining the vessel wall. Each of the properties may have a distinct effect. In order to comprehensively understand the effects, we delineate the roles of the properties by varying the individual parameters associated with them. Admittedly, under realistic conditions, surfactants can not be designed with variable individual properties such as diffusivity or adsorption. However, our approach of decoupling the variation of the surfactant parameters to study the effects allows us to clearly describe the role of each of these. Such a description may assist in the selection of the suitable surfactant.

Four sets of parameters have been examined. These consist of *a*) the ratio of the adsorption and desorption coefficient of the surfactant (k_a/k_d), *b*) the maximum interface concentration of the surfactant (Γ_∞) and its associated bulk concentration (C_0), *c*) the surface diffusivity of the surfactant (D_s) and *d*) its bulk diffusivity (D_l). Bulk fluid flow properties, such as the density, viscosity and the inlet velocity, are not varied. The hematocrit (volume fraction of RBCs) is set at 0.45. The degree of bubble occlusion is characterized by the ratio of equivalent-volume bubble radius to vessel radius (aspect ratio), λ , in the range $0.9 \leq \lambda \leq 1.05$. Table 1 shows the parameters used in the estimation of the Reynolds number of various vessels. In [55], we have shown that surfactant based intervention of gas embolism is most effective in vessel sizes representing arterioles, which have a characteristic Reynolds number (Re) in the range of $0.2 - 2$ (see [31] and the references therein for a description of the estimation of this Re). On that basis, here we restrict ourselves to the flow conditions present in a vessel with $Re \sim 0.2$ representing small arterioles. The in vivo clinical manifestations of gas-embolism induced

brain injury accompanying cardiac surgery are compatible with multifocal microcirculatory events occurring in arterioles [42,16]. Focussing our attention on the fluid dynamics, transport mechanics and surfactant effects relevant in this regime is therefore appropriate. Furthermore, the variation of every parameter and λ with respect to each other for all the ranges considered here will lead to an unwieldy set of data. Instead, we have chosen to vary the relevant parameters in three, logically grouped, sets. In the first set, we vary the surfactant parameters associated with the adsorption to desorption ratio and the bulk and maximum interface concentration while keeping the bulk and surface diffusivities fixed. In the second set, we vary the bulk and interface diffusivities while holding the other parameters constant. In the third set, we vary each of the surfactant parameters individually for different aspect ratios of the bubble.

The “impact” of any given surfactant may be estimated by evaluating the value of the minimum gap between the bubble and the vessel wall, and by the magnitude of the shear stress variation experienced by the surface of the cell lining the interior of the vessel in the presence of that surfactant. By examining the trends associated with the variation of each of the four parameters listed individually, we see that these trends remain mostly similar for all choices of the other fixed parameters. This justifies our approach of grouping the parameters individually into non-dimensional numbers and varying them one at a time.

2 Problem Formulation

The axisymmetric motion of a nearly occluding gas bubble of density ρ_g and viscosity μ_g in a cylindrical vessel of radius R (diameter d) has been considered here as shown in figure 1. For the vertical configuration of the vessel, gravity acts in the direction from top to bottom.

Both the gas and the liquid phases are modeled as incompressible fluids governed by the continuity and the Navier-Stokes equations [62]:

$$\nabla \cdot \mathbf{u} = 0. \quad (1)$$

$$\rho \left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \nabla \cdot \mu (\nabla \mathbf{u} + \nabla^T \mathbf{u}) + \int_{S(t)} \left[\sigma(\Gamma(s)) \mathcal{C} \mathbf{n}_f + \frac{\partial \sigma(\Gamma(s))}{\partial s} \mathbf{t}_f \right] \widehat{\delta}(\mathbf{x} - \mathbf{x}_f) dS + \rho \mathbf{g}. \quad (2)$$

Here, $\mathbf{u} \equiv (v_r, v_z)$, is the fluid velocity with v_r, v_z as the velocity components along the radial and axial directions, p is the pressure, ρ and μ are the density and the viscosity of the medium, $\mathbf{g}$ is the gravitational acceleration, s is an arc length measure on the interface, $\mathcal{C}$ is the curvature of the interface, σ is the surface tension coefficient which is a function of the surfactant concentration Γ , $S(t)$ denotes the instantaneous location of the interface, $\mathbf{n}_f$ denotes the unit normal vector on the interface (pointing into the bulk fluid), $\mathbf{t}_f$ is the unit tangential vector at the interface, $\mathbf{x}_f$ denotes the position vector on the interface, and $\widehat{\delta}(\mathbf{x} - \mathbf{x}_f)$ stands for the 2D axisymmetric Dirac delta function that is non-zero only when $\mathbf{x} = \mathbf{x}_f$. The density and viscosity of the medium are

$$[\rho, \mu](r, z, t) = [\rho_l, \mu_l] \mathcal{H}(r, z, t) + [\rho_g, \mu_g] (1 - \mathcal{H}(r, z, t)) \quad (3)$$

Here, t is time, and $\mathcal{H}(r, z, t)$ is a Heaviside function such that,

$$\mathcal{H}(r, z, t) = \begin{cases} 1 & (r, z, t) \text{ in the bulk,} \\ 0 & (r, z, t) \text{ in the bubble} \end{cases}. \quad (4)$$

As previously mentioned, blood has been treated as a continuous incompressible medium here since the diameter of the vessel ($40\mu\text{m}$) is much larger than the thickness and diameter of a RBC. Individual interactions of the bubble with each RBC has not been modeled. The behavior of the bulk liquid has been modeled as a two-layer fluid of density ρ_l consisting of a cylindrical core of concentrated red blood cell (RBC) suspension, surrounded by a cell-free layer. This assumption is a limitation of this model. The cell-free layer is modeled as a Newtonian fluid of constant viscosity μ_{layer} [48] while the RBC suspension is modeled as a shear-thinning Casson fluid of viscosity μ_c [14]. The viscosity of the liquid μ_l as a function of the radial position in a bubble-free tube is thus,

$$\mu_l = \begin{cases} \mu_c, & 0 \leq r \leq (1 - \delta)R \\ \mu_{\text{layer}}, & (1 - \delta)R < r \leq R \end{cases}, \quad (5)$$

where δ is the non-dimensional thickness of the cell-free layer normalized with R . The evaluation of this thickness and the two viscosities μ_{layer} and μ_c have been discussed in detail in [31]; following [31] and [40], we write,

$$\mu_c = \left[\sqrt{\mu_\infty} + \sqrt{\frac{\tau_y}{|\gamma|}} \left(1 - e^{-\sqrt{m}|\gamma|} \right) \right]^2, \quad (6)$$

where μ_∞ is the asymptotic Newtonian viscosity, τ_y is the yield stress, γ is the prevalent local shear rate and m is the Casson viscosity regularization exponent. In equation 6, the expressions for μ_∞ and τ_y as functions of core hematocrit H_C are given by [7] as:

$$\mu_\infty = \frac{\mu_p}{(1 - H_C)^{C_1}}; \tau_y^{1/2} = C_2 \left[\left(\frac{1}{1 - H_C} \right)^{C_1/2} - 1 \right]. \quad (7)$$

Here, C_1 , C_2 are constants whose values for human blood are given as 2.0 and 0.3315, respectively. The evaluations of the equations require a knowledge of H_C , δ , and β . In regard to the hematocrit, the discharge hematocrit H_D is usually a known quantity. For $\delta > 0$, the core hematocrit H_C , which is based upon the core volume, is larger than H_D . For a given vessel size, the relationships between H_D , H_C , δ , and β are nonlinear. For vessels of diameter in the range $20\mu\text{m} \leq d \leq 300\mu\text{m}$, Sharan and Popel [48] have described methods that are based on non-linear coupled differential equations supplemented by experimental data. These methods establish relationships between H_D , H_C , δ , and β for known values of d and H_D . We have previously solved these equations for $d = 40\mu\text{m}$ (small arteriole) and $100\mu\text{m}$ (large arteriole) for $H_D = 0.45$ [31], and have documented values for H_C , δ , and β . In [31], we have also examined a vessel size $d = 2000\mu\text{m}$ (small artery). At such a large radius, $\delta \rightarrow 0$ and $H_C \sim H_D$. The discharge hematocrit is taken to be equal to 0.45 in all our calculations which is the usual value for normal humans. The core hematocrit and viscosity are calculated for the vessel under consideration as described. μ_{layer} which usually varies as a function of the discharge hematocrit is thus a constant (for a given vessel size). The surface tension of the interface, separating the continuous and dispersed phases, varies with the surfactant concentration, Γ , on the interface, according to the equation of state given by the Langmuir isotherm [24]:

$$\sigma = \sigma_s + RT\Gamma_\infty \ln \left(1 - \frac{\Gamma}{\Gamma_\infty} \right), \quad (8)$$

where σ_s is the surface tension of a surfactant-free clean interface, $\mathfrak{R}$ is the ideal gas constant, T is the absolute temperature and Γ_∞ is the maximum monolayer interface surfactant concentration. Alternately, the equation of state can also be given by the Frumkin isotherm

$$\sigma = \sigma_s + \mathfrak{R}T\Gamma_\infty \left(\ln \left(1 - \frac{\Gamma}{\Gamma_\infty} \right) + \frac{\xi}{2} \left(\frac{\Gamma}{\Gamma_\infty} \right)^2 \right), \quad (9)$$

where ξ is the Frumkin interaction parameter. The evolution of the surfactant concentration at the interface is given by [51] as

$$\frac{\partial \Gamma}{\partial t} + \nabla_s \cdot (\mathbf{u}_s \Gamma) + \Gamma (\nabla_s \cdot \mathbf{n}_f) (\mathbf{u} \cdot \mathbf{n}_f) = D_s \nabla_s^2 \Gamma + j_n, \quad (10)$$

with j_n being the diffusional flux at the interface given by Fick's law: $j_n = D_l (\mathbf{n}_f \cdot \nabla) C$. Also, $\mathbf{u}_s$ and $\mathbf{u} \cdot \mathbf{n}_f$ are the tangential and normal components of the velocity on the interface, respectively, D_s is the surface diffusion coefficient, D_l is the bulk diffusion coefficient, C is the bulk concentration, and, $\nabla_s = \nabla - n_f(n_f \cdot \nabla)$ is the gradient operator along the interface. The diffusional flux on the interface, $D_l (\mathbf{n}_f \cdot \nabla) C$, is balanced by the adsorption and desorption terms as,

$$D_l (\mathbf{n}_f \cdot \nabla) C = k_a C_s \left(1 - \frac{\Gamma}{\Gamma_\infty} \right) - k_d \Gamma, \quad (11)$$

in which k_a and k_d are the adsorption and desorption coefficients, respectively, and C_s is concentration in the sublayer adjacent to the interface. The governing equation for the bulk concentration C then becomes,

$$\frac{\partial C}{\partial t} + (\mathbf{u} \cdot \nabla) C = \nabla \cdot (D \nabla C) - \int_{S(t)} \left[k_a C_s \left(1 - \frac{\Gamma}{\Gamma_\infty} \right) - k_d \Gamma \right] \widehat{\delta}(\mathbf{x} - \mathbf{x}_f) dS, \quad (12)$$

where the diffusion coefficient D may be written as,

$$D = D_l \mathcal{H}. \quad (13)$$

These governing equations are coupled with suitable initial and boundary conditions. At the inlet boundary $z = 0$, the velocity profile is a fully developed two-layer Casson profile. This velocity profile and the associated pressure gradient have to be numerically evaluated for each vessel size using the Casson two layer model (equations 5,6) and applicable boundary conditions (see [31] for details). This evaluation is based on the maximum flow velocity at the centerline of a blood vessel of a given size, in the absence of a bubble, which is known [1]. The velocity profile and the associated pressure gradient so calculated are then used as the inlet boundary conditions. At the outlet boundary, $z = L$, the outflow condition,

$$\frac{\partial \mathbf{u}}{\partial z}(r, L, t) = 0, \quad (14)$$

is used. The reflective boundary conditions, at $r = 0$ are given as:

$$\begin{aligned}v_r(0, z, t) &= 0, \\ \frac{\partial v_z}{\partial r}(0, z, t) &= 0, \\ \frac{\partial C}{\partial r}(0, z, t) &= 0.\end{aligned}\quad (15)$$

The wall no-slip, no flux boundary conditions at $r = R$ are,

$$\begin{aligned}\mathbf{u}(R, z, t) &= 0, \\ \frac{\partial C}{\partial r}(R, z, t) &= 0.\end{aligned}\quad (16)$$

The initial surfactant concentration in the bulk is taken to be

$$C(r, z, 0) = C_0 \mathcal{H}(r, z, 0). \quad (17)$$

3 Non-dimensionalization and time scales

Consider the non-dimensional quantities (denoted by superscripted *): $s^* = s/d$, $r^* = r/d$, $z^* = z/d$, $\rho^* = \rho/\rho_l$, $\mathbf{u}^* = \mathbf{u}/U_{max}$, $\mathbf{u}_s^* = \mathbf{u}_s/U_s$, $t^* = tU_{max}/d$, $p^* = p/\rho U_{max}^2$, $C^* = C/C_0$, $\Gamma^* = \Gamma/\Gamma_\infty$, $\mathcal{H}^* = d\mathcal{H}$ and $\hat{\delta}^* = d^3\hat{\delta}$. Here, C_0 (mol/cm³) is the far field bulk concentration and Γ_∞ (mol/cm²) is the maximum monolayer interface surfactant concentration. U_s is a representative surface velocity. Here we assume $U_s \sim U_{max}$ (see, for example, [46] pp 117 for relation between surface and bulk velocities for creeping flows). Recasting the governing equations 2, 10 and 12 in terms of these non-dimensional parameters (and dropping the superscript star for convenience) yields:

$$\frac{\partial \mathbf{u}}{\partial t} + \nabla \mathbf{u} \cdot \mathbf{u} = -\nabla p + \frac{1}{\text{Re}} \nabla \cdot \mu (\nabla \mathbf{u} + \nabla^T \mathbf{u}) + \frac{1}{\text{We}} \int_s \left[\sigma \mathcal{H} \mathbf{n}_f + \frac{\partial \sigma}{\partial s} \mathbf{t}_f \right] \widehat{\delta}(\mathbf{x} - \mathbf{x}_f) ds + \frac{1}{\text{Fr}^2} \rho \mathbf{g}, \quad (18)$$

$$\frac{\partial \Gamma}{\partial t} + \nabla_s \cdot (\mathbf{u}_s \Gamma) + \Gamma (\nabla_s \cdot \mathbf{n}_f) (\mathbf{u} \cdot \mathbf{n}_f) = \frac{1}{\text{Pe}_s} \nabla_s^2 \Gamma + \frac{1}{\alpha \text{Pe}} (\mathbf{n}_f \cdot \nabla) C, \quad (19)$$

$$\frac{\partial C}{\partial t} + (\mathbf{u} \cdot \nabla) C = \frac{1}{\text{Pe}} \nabla \cdot (D \nabla C) - \int_s [\text{St}_d C_s (1 - \Gamma) - \alpha \text{St}_d \Gamma] \widehat{\delta}(\mathbf{x} - \mathbf{x}_f) ds, \quad (20)$$

in which the relevant non-dimensional parameters are defined as, Reynolds number $\text{Re} = \rho U_{max} d / \mu$, Weber number $\text{We} = \rho_l U_{max}^2 d / \sigma$, Froude number $\text{Fr} = U_{max} / \sqrt{gd}$, surface Péclet number $\text{Pe}_s = U_{max} d / D_s$, desorption Stanton number $\text{St}_d = k_d d / U_{max}$, dimensionless adsorption depth $\alpha = \Gamma_\infty / C_0 d$, bulk Péclet number $\text{Pe} = U_{max} d / D_l$, and adsorption Stanton number $\text{St}_a = k_a / U_{max}$. The capillary number $\text{Ca} = \mu U_{max} / \sigma$ is the ratio of Re and We .

Based on these non-dimensional numbers, the important time scales relevant to this problem are: convection time scale d/U_{max} , momentum diffusion time scale $\rho d^2/\mu$, and mass diffusion time scales d^2/D_l and d^2/D_s .

Equations 1, 2, 10, 11 and 12, subject to the appropriate initial and boundary conditions (equations 14, 15, 16 and 17) are solved using a front-tracking method coupled with a level contour reconstruction procedure. This procedure and the validation of the numerical model has been described in detail in [31], [62] and [55], and will not be repeated here for the sake of brevity. We have performed some simple experiments to observe the rise velocities of air bubbles in human blood plasma. In appendix A we have further compared our experimental results with the values from our numerical method.

4 Results

The effects of various soluble surfactant-parameters on the motion of a nearly occluding bubble in a blood vessel of circular cross section have been computed. The bubble is introduced axisymmetrically at the base of a vertical vessel. Fluid flow direction is from the bottom towards the top and occurs at a fixed pressure gradient. The bubble rises in the vessel under the action of body forces (due to gravity) and surface forces (fluid motion), and deforms as it moves. Its motion from release as well as its steady state characteristics are evaluated. For the conditions investigated here, the motion in horizontal tubes does not offer different results and will not be discussed here.

Surfactant parameters affecting the behavior of the bubble are varied over a range, to evaluate their effects. The values of parameter ranges have been summarized in Table 2 and the variation of the parameters has been broadly chosen from [6],[55] and [39], and the corresponding diffusion properties are available in literature [13,50,30].

As noted earlier, it is not possible to design a surfactant with all the desirable properties for use with gas embolism. This necessitates the study of surfactants with parameters grouped into logical sets wherein we vary one parameter at a time while holding all others constant. For illustration, individual parameters such as k_a/k_d , and D_l are not related. For example, if we were to compare the two surfactants sodium dodecyl sulfate (properties noted from [6] and [50]) and hexaethylene monododecyl ether (properties from [6] and [30]), although there is large difference in the values of k_a/k_d ($\mathcal{O}(10^7)$), the difference in the values for D_l is relatively small ($\mathcal{O}(10^2)$). While diffusion coefficients are mostly determined by the molecule (micelle) size, the adsorption and desorption coefficients additionally are also strongly dependent on the chemical properties. These observations justify our basis for varying k_a/k_d while holding D_l fixed in this comparison. In a similar fashion, other parameters have been varied.

4.1 Flow features

The flow features of a nearly occluding finite sized gas bubble in a pressure driven Casson fluid has been described in detail for a clean bubble in [31] and for a surfactant-coated bubble in [55]. In this section, we briefly recap the relevant results.

Figure 2 shows the steady state streamlines for flow over a clean bubble in a reference frame attached to the bubble for $\lambda = 1.0$ and $Re = 0.2$. The bubble is deformed with a slight bulge at the rear primarily due to the imposed pressure gradient. At a certain location along the interface, a very narrow layer of fluid separates the bubble from the wall. This proximity of the bubble to the vessel wall is of particular interest in this problem. The drainage flow squeezes through this narrow gap and is mainly responsible for the surface mobility of the bubble. This in turn gives rise to internal vortical motions as seen in figure 2(b). A secondary internal vortex is also noted. The sense of rotation of the secondary vortex is opposite to that of the primary. Two distinct recirculatory bolus formations are discerned, one at the front region of the bubble and the other at the rear. Two stagnation rings, a convergent ring at the rear and a divergent ring at the front, exist on the bubble surface where the back flow adjacent to the wall (drainage

flow) meets the recirculating boluses. These flow features have significant effects on the distribution of the shear stress and its gradients at the vessel wall.

When a soluble surfactant is present in the fluid, upon the introduction of the bubble, diffusive and convective mechanisms in the bulk phase bring the surfactant from the bulk medium to the gas-liquid interface. Here, adsorption and desorption mechanisms are initiated. Although the vortical motions inside the bubble are essentially similar in their dynamic characteristics to the clean bubble case, they are considerably weaker in strength. Diffusion and advection of the adsorbed surfactant occur at the interface, the latter due to surface mobility. Consistent with the bulk concentration and interfacial capacity for adsorption and desorption of the surfactant, a steady state mass transfer profile is eventually established describing a non-uniform distribution of the surfactant at the interface. A representative steady state concentration profile at the interface for $\lambda = 1.0$ and $Re = 0.2$ is shown in figure 3. The internal motion has not been shown.

Bubble motion causes temporal and spatial gradients of shear stress at the cell surface lining the blood vessel wall as the bubble approaches the cell, passes over it and departs. Rapid reversals occur in the sign of the shear stress imparted to the cell surface during this motion. A comparison of the shear stress experienced by a point on the vessel wall for various concentrations of $C_{12}E_6$, is shown in figure 4. The properties of the surfactant hexaethylene glycol dodecyl ether ($C_{12}E_6$), are obtained from [39]. All surfactant properties, except for the diffusivity (which will be higher in blood than in glycerol-water mixture), are assumed to be identical to those obtained for the 70:30 glycerol-water mixture listed therein. In these simulations, C_0 is the bulk concentration (this is assumed to be less than the critical micelle concentration, reported as 0.209 mol/m^3 in [39]), Γ_∞ is $5 \times 10^{-6} \text{ mol/m}^2$, both D_l and D_s are $1.3 \times 10^{-10} \text{ m}^2/\text{sec}$ (this value is from [6]), k_d is $9 \times 10^{-3} \text{ sec}^{-1}$ and k_a is $5 \times 10^{-5} \text{ m/sec}^{-1}$. The parameter ξ is 5.47 in our simulation [39].

As the bubble moves, the entrained fluid surrounding it causes rapid changes in the magnitude and the sign of the shear stresses experienced by the wall. For a given point on the wall, the changes in shear stress manifest as a solitary wave. When the bubble is far upstream from the point under consideration, it has negligible effect on this point and the shear stress is at its basal value. As the bubble moves closer to the point, the local fluid velocity is increased. Both the local pressure gradient and the flow rate at the location of this point attain higher values and there is a corresponding increase in the shear stress. As the bubble moves over the point, the flow decelerates due to entrainment and the shear stress gradually reduces to zero. The local pressure gradient reverses from being favorable to adverse during this period. As the maximum bulge in the bubble passes over the point, a local flow reversal occurs due to the presence of the recirculating vortex (see figure 2(a)). This vortex arises due to the drainage flow interacting with the forward flow. These interactive effects are ascribable due to the finite size of the bubble and the resultant physical interplay of the trailing gas-liquid interface and the presence of the wall. In particular, the sign of the shear stress becomes negative. Beyond this, as the maximum bulge of the bubble departs the location, there is fluid flow recovery and a significant increase in local fluid velocity in the direction of motion of the bubble. This causes the shear stress to become positive and attain a value that is higher than its basal value. As the bubble moves farther away from the point, the entrainment effects become progressively weaker and the shear stress gradually returns to the basal value staying there for the remainder of the motion of the bubble. Further details of this solitary wave can be found in [31] and [55]. This solitary wave has major potential physiological implications including induction of a complex pattern of endothelial cell membrane stretch and compression, activation of mechanotransduction pathways, loss of plasma membrane integrity and plasma membrane stress failure [60, 4, 17, 26, 28]. As would be expected, an increase in the surfactant concentration in the bulk reduces the magnitude of the shear stress variation imparted to the cell surface.

Shear stress gradients together with sign reversals are associated with a recirculation vortex at the rear of the bubble. Presence of the surfactant in the bulk and the interface reduces the level of the shear stresses imparted to the cell surface and the strengths of the vortical motions as compared to an equivalent clean system (no surfactant present). Furthermore, the shape of the bubble, and consequently the gap between the bubble and the vessel wall changes in the presence of the surfactant. The net effect of the presence of the soluble surfactant in the bulk phase is to reduce the level or eliminate the mechanically driven injury to the cell surface.

4.2 Variations in surfactant concentration and adsorption/desorption ratio

In figure 5, we display the normalized total interface surfactant mass, $\mathcal{M}$, as a function of $\mathcal{K}$ ($= k_a/k_d d = St_d/St_d$) for varying values of α ($= \Gamma_\infty/C_0 d$). The quantity Γ_∞ is a property that depends on the nature of the particular surfactant and its value is obtainable from published sources (e.g. see, [6]). Since we have presented results in terms of dimensionless parameters, variations in α could be ascribed to variations in Γ_∞ for a fixed C_0 or to variations in C_0 for a fixed Γ_∞ . In the following we choose to regard variations in α as changing C_0 at fixed Γ_∞ . Pe ($= U_{max}d/D_l$) and Pe_s ($= U_{max}d/D_s$) have been held constant (at 1.49×10^3). The range of $\mathcal{K}$ investigated, characterize various surfactants. For a given C_0 , $\mathcal{M}$ increases with the $\mathcal{K}$. This would be as expected, because at a given C_0 , increase in k_a/k_d would amount to increased net adsorption. Next, at a given $\mathcal{K}$, denoting a particular surfactant, $\mathcal{M}$ increases with increasing C_0 . For $\mathcal{K} > \mathcal{O}(10^{-6})$, $\mathcal{M}$ approximately scales with

$$\frac{St_d/\alpha St_d}{1+St_d/\alpha St_d}, \quad (21)$$

as expected from the Langmuir isotherm [6]. In figure 5, for $\alpha = 9.5 \times 10^{-2}$ and $\alpha = 9.5 \times 10^{-4}$ and varying values of $\mathcal{K}$, we have plotted this equation (dotted lines) and the increasing characteristics are in accordance with the scaling law.

Next, we examine the effect of the surfactant on the shape of the bubble. The bubble shape directly determines the proximity of the bubble and the tube wall. This proximity will impact the flow field near the wall and the magnitude of the shear stress experienced by the cells lining the interior of the vessel wall, and is an important parameter in the gas embolism problem. Closeness between the gas bubble and the vessel wall is known to induce the initiation of cellular responses such as intracellular calcium (Ca^{2+}) signaling. In general, there are three primary surface forces which affect the shape of the nearly occluding bubble. The first is the surface tension on the interface of the bubble and this tends to make the bubble spherical. The second is a result of the prevailing pressure gradient driving the flow. This force will tend to “flatten” the bubble in the rear causing it to be an oblate spheroid in shape. The third force arises due to the presence of the wall. As the bubble gets closer to the wall, the drainage flow generates a force which acts to push the sides of the bubble radially inward, away from the wall causing it to elongate in the direction of its motion. The final shape of the bubble is the result of a balance of these three forces. The body force (due to buoyancy) does not play a major role in this problem, as shown in [55]. For our choice of Reynolds number (0.2), the capillary effects dominate over the inertial and viscous effects. For $\lambda = 0.9$, the bubble remains close to spherical in shape, while for $\lambda \geq 1.0$, the bubble nearly occludes the vessel. Reduction in the value of the surface tension due to the surfactant results in increased departure from sphericity and the bubble shape is more responsive to fluid flow induced deformation forces. Further details of the effect of the surfactant on the change in shape of a bubble are discussed in [55].

The change in bubble shape is evaluated in terms of the minimum gap between the bubble and the tube wall (distance to the wall from the point on the bubble that is closest to the wall). The

variation of this gap as a function of $\mathcal{K}$ and α is shown in figure 6. For $\mathcal{K} < \mathcal{O}(10^{-8})$, the bubble shape is such that the minimum gap between the bubble and the wall is lesser than that for the corresponding clean bubble. As $\mathcal{K}$ increases, more surfactant is present on the interface reducing its surface mobility. This reduction causes an increase in the radially inward force from the drainage flow. As a result, there is an increase in the minimum gap size (elongated bubble). Around $\mathcal{K} \sim \mathcal{O}(10^{-5})$, this elongation is drastic with the result that the gap size relative to that of a clean bubble is nearly doubled. However beyond $\mathcal{K} \sim \mathcal{O}(10^{-4})$, for all values of α and all surfactants, the gap size essentially plateaus. Thus surfactants with properties such that $\mathcal{K} \geq \mathcal{O}(10^{-5})$ and $\alpha \geq 9.5 \times 10^{-4}$ would be most preferable from the point of view of increased gap between the bubble and the vessel wall mitigating cell injury.

In figure 7 the jump in the value of the shear stress, $\Delta\tau = \tau_{max} - \tau_{min}$, where τ_{max} is the maximum (positive) of the shear stress while τ_{min} is the minimum (negative), has been plotted as a function of $\mathcal{K}$ for various α . The normalization of the shear stress is done with the corresponding basal value [55]. The corresponding clean bubble results are also given for comparison.

The shear stress level, $\Delta\tau$, increases above the clean bubble value for lower values of $\mathcal{K}$. In this range, the surfactant decreases the “minimum” gap between the bubble and the vessel wall (see figure 6) causing the maximum shear stress levels experienced by the wall to increase. However, at much higher values of $\mathcal{K}$, the increased surfactant coating on the interface significantly decreases the mobility of the interface. There is a decrease in the strength of the recirculating vortex, resulting in an increased τ_{min} . At this limit, even though both the minimum and maximum values of the shear stress are higher, the difference between the two, $\Delta\tau$, is lower than that for the clean bubble.

The variation in the bulk concentration has little effect for surfactants having a small $\mathcal{K}$. At these values, even if a large amount of surfactant is present in the bulk, the interface concentration is adsorption limited. However, if $\mathcal{K}$ exceeds $\mathcal{O}(10^3)$, the interface concentration and subsequently the shear stress variation is dominated by the bulk concentration of the surfactant present. This indicates that addition of a large amount of low adsorption surfactant to the bulk flow does not mitigate gas embolism effectively. On the other hand, once $\mathcal{K}$ reaches a given value, it is more effective to increase the bulk concentration rather than trying to increase the adsorption coefficient. It should also be noted that in general the bulk concentration cannot be increased indefinitely owing to physiological constraints.

4.3 Bulk and surface diffusion effects

Next, we examine the effect of varying the bulk and surface Péclet numbers, which are varied by changing the values of the bulk and surface diffusivities. The other parameters are fixed at $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$. It is noted that in general bulk and surface diffusivities may be different. First we consider a range of values where $Pe = Pe_s$. The distribution of the surfactant on the interface is displayed in figure 8. For $Pe = Pe_s \geq \mathcal{O}(10)$, the diffusive effects are much smaller than convective effects. The highest and lowest surfactant concentrations on the interface occur in the vicinity of the convergent and divergent rings, respectively (from figure 8 the maximum corresponds to about 0.35 of the normalized arc length). However for $Pe = Pe_s = \mathcal{O}(1)$, diffusive mechanisms become relevant compared to convective mechanisms and the concentration profile is essentially even over the interface. The distribution profiles at the highest and lowest values of the Péclet numbers considered in this study are shown in figure 9.

Compared to figure 9(a), in figure 9(b), the profile is more evenly distributed with a higher concentration at the rear of the bubble. The variation of the total interface surfactant mass, $\mathcal{M}$, as a function of Pe and Pe_s is shown in figure 10. At a given Pe_s , there is very little variation in $\mathcal{M}$ with Pe (less than 20%). With increasing Pe , $\mathcal{M}$ initially increases slightly and then

plateaus. The initial increase is ascribable to a decrease in the bulk diffusivity and consequently, a lesser amount of surfactant is diffusively removed from the interface for otherwise identical conditions. Beyond $Pe > \mathcal{O}(10^2)$, diffusion in the fluid is negligible compared to convection and thus further lowering of the diffusivity has minimal effect.

At a given Pe , interfacial surfactant mass is lower when Pe_s becomes $\mathcal{O}(1)$ and the surface diffusive mechanisms compete with the convective mechanisms. The amount of surfactant on the interface decreases because surface diffusion leads to higher desorption from otherwise low concentration areas on the bubble interface. At higher values of Pe_s , there is very little change in the surfactant mass on the interface. Compared to figure 5, however, there is very little variation in $\mathcal{M}$ as Pe and Pe_s change, indicating that the surface diffusivity, while affecting the overall distribution on the interface, does not significantly change the total mass.

Next, the variation of the minimum gap between the vessel wall and the bubble as a function of Pe and Pe_s is shown in figure 11. For a given Pe_s , the change in the minimum gap as a function of Pe is very small (less than 5%). The minimum gap for $Pe_s < \mathcal{O}(10)$ is smaller than that for the other cases. There is a more uniform coating of the surfactant due to the higher surface diffusivity in this case (see figure 9(b)). This reduces the surface tension and makes the bubble more responsive to the deformations (increased deformation) from the fluid forces resulting in a reduction in the minimum gap size.

Next, we display the variation of the jump in the shear stress experienced by a point on the vessel as a function of Pe and Pe_s in figure 12. Similar to characteristics in figures 10 and 11, at a given Pe_s , a change in Pe has very little effect on $\Delta\tau$ experienced by the vessel wall. Owing to the proximity to the vessel wall and a lower surfactant interface mass, a higher $\Delta\tau$ occurs at $Pe_s = \mathcal{O}(1)$.

4.4 Aspect ratio effect

In this section, we discuss the effects of the various parameters (Pe_s , α and $\mathcal{K}$) with bubbles of various sizes (λ). The bubble aspect ratio, λ varies between 0.9 and 1.05. As previously stated, one of the most important effects to examine, in gas embolism studies, is the shear stress impulse experienced by a cell on the blood vessel as the bubble passes over it. In this study, this impulse has been measured as the difference between the maximum and minimum values of the shear stress. Here we consider the variation in $\Delta\tau$ as a function of different parameters for four different of aspect ratios.

The first plot, figure 13 shows the variation in normalized $\Delta\tau$ as a function of α for various λ . An increase in α denotes lowering of the bulk concentration. The values on the right hand side of the figure correspond to an essentially clean bubble motion. There is a sharp decrease in the values of $\Delta\tau$ at higher values of the bulk concentration of the surfactant. This is due to decreased surface mobility and weakening of the recirculating vortex that causes the variations in the shear stress profile at any point on the vessel wall. For $\lambda < 1.0$, we also see that addition of the surfactant (lowering of α) may, in some ranges, increase $\Delta\tau$. This is explained by noting that bubble deformation in these cases result in a decrease in the minimum gap between the bubble and the vessel wall. This is an unusual feature.

Next, figure 14 shows the variation in $\Delta\tau$ as a function of the surface Péclet number. For the values of the various parameters chosen, we note that the lowest $\Delta\tau$ occurs the highest value of Pe_s , while the highest $\Delta\tau$ is associated with the lowest Pe_s . These indicate that increasing the surface diffusivity results in a lowering of the minimum gap while not significantly changing the vortex strength.

Finally, the variation of $\Delta\tau$ with $\mathcal{K}$ for various aspect ratios is shown in figure 15. At a higher $\mathcal{K}$, there is a reduction in the value of $\Delta\tau$ for all λ . This trend is due to a decrease in surface mobility. However at $\lambda < 1.0$ this reduction is not as steep due to the two competing mechanisms: reduction in vortex strength causing a decrease in $\Delta\tau$ while an increased deformation causing an increase in $\Delta\tau$. At higher λ the role of reduced surface mobility is the dominant effect.

5 Conclusions

In this paper we have evaluated the effectiveness of various surfactants for reducing the shear stress level imparted to an endothelial cell by a finite sized gas bubble moving past it. This has been achieved by evaluating the roles of various surfactant properties and the associated shear stress levels. This analysis allows for a better understanding of exogenous surfactant-based intervention of gas embolism and allows us to optimize the desirable characteristics of such surfactants. The main observations include:

- The non-dimensional adsorption depth, α and the ratio of adsorption to desorption coefficients, k_a/k_d , have a profound impact on the shear stress levels experienced by a cell on the vessel wall as the bubble moves past it in the surfactant laden bloodstream. At small values of $\mathcal{K}$ (meaning low adsorption to desorption ratio), α has very little effect on the shear stress jump. However once $\mathcal{K}$ is greater than $\mathcal{O}(10^3)$, decreasing α , i.e. increasing the bulk concentration or decreasing the maximum interface concentration, has a profound effect. Surfactants with $\mathcal{K} > \mathcal{O}(10^5)$ and $\alpha > 9.5 \times 10^{-4}$ are noted to be preferable from the point of view of increased gap between the bubble and vessel wall and a corresponding reduction in the shear stress level.
- The bulk and surface diffusivities do not play a major role in determining wall shear stress characteristics. Higher values of Péclet number distribute the surfactant more evenly on the interface but do not drastically change the total amount present, $\mathcal{M}$. An increased total amount on the interface is preferable since it corresponds to a reduced $\Delta\tau$.
- The shear stress characteristics of larger bubbles, $\lambda \geq 1.0$, are affected most by the introduction of a surfactant. The overall dependence of the shear stress on $\mathcal{K} = St_d / St_d$, α and the Péclet numbers is generally the same for various values of λ .

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Appendices

Appendix A Validation

In addition to the validation of the numerical scheme done previously, in this appendix, we compare the rise velocity of an air bubble in human blood plasma by performing experiments and numerical calculations. The bubble motion and bubble shape cannot be visualized adequately using whole blood. Thus we examine terminal bubble rise velocity using freshly prepared human blood plasma. Following an approved Institutional Review Board protocol, whole blood was obtained by venipuncture from healthy adult volunteer donors. Samples were immediately citrated (9 parts blood to 1 part citrate) and spun in a Sorvall Super T21 centrifuge (Thermo Electron Corporation, Asheville, NC, USA) at 2600 rpm (1500 g) for 15 minutes to obtain platelet poor plasma [8]. Plasma was used to fill a 180cm length of TYGON®R-3603 AAC00003 tubing (Saint-Gobain Performance Plastics Akron, OH, USA) having an inner

diameter of 1.5875mm. The tubing, which was affixed tightly alongside a ruler onto a vertical frame, was open to atmosphere on top and closed via a blunt-tip connector attached to a three-way stopcock on the bottom. Bubbles were introduced into the liquid by slow injection using a microsyringe (Hamilton Company, Reno, NV, USA) and allowed to rise freely under buoyancy.

Bubbles were viewed in the upper-most (last) 20cm of tubing using a video imaging system consisting of a high resolution black and white video camera (JE12H MV, Javelin Systems, Torrance, CA), a video image marker-measurement system (Model VIA-170, Boeckeler Instruments, Tucson, AZ, USA), monitor (Model PVM-1343MD, Sony, Tokyo, Japan), and video cassette recorder (Sony SVO-9500 MD S-VHS, Sony Corporation, Tokyo, Japan) operating at a standard 30 frames per second[9,10,38,5,3]. Post-experiment measurements of bubble dimensions and terminal rise velocity were made by reviewing the videotape calibrated for distance with the ruler included in the video image and by counting the number of video frames elapsed for a minimum vertical bubble displacement of 20mm.

A comparison of the rise velocity of bubble under identical conditions is shown in figure 16. The diameter of the bubble (d_{bubble}) has been normalized with the diameter of the tube (d_{tube}) and the velocity has been normalized with the Mendelsen equation[27]

$\sqrt{2\sigma/\rho_l d_{tube} + g d_{tube}/2}$. For the numerical simulation, the evaluation of surface tension in [22], gives the value of σ for the air-plasma interface as ~54mN/m. The viscosity of plasma is obtained from [48] as 1.2cP. The predicted numerical results compare with our experimental. It can be seen that the experimental and numerical results agree well (<15% error), noting that our experiments are carried out in a very long open tube. This comparison thus serves to additionally validate our numerical procedure.

References

1. Berger, SA.; Goldsmith, W.; Lewis, ER. Introduction to Bioengineering. New York, USA: Oxford University Press; 1996.
2. Branger AB, Eckmann DM. Theoretical and experimental intravascular gas embolism absorption dynamics. Journal of Applied Physiology 1999;87:1287–1295. [PubMed: 10517754]
3. Branger AB, Eckmann DM. Accelerated arteriolar gas embolism reabsorption by an exogenous surfactant. Anesthesiology 2002;96(4):971–979. [PubMed: 11964607]
4. Butler PJ, Tsou TC, Li JYS, Usami S, Chien S. Rate sensitivity of shear-induced changes in the lateral diffusion of endothelial cell membrane lipids: a role for membrane perturbation in shear-induced mapk activation. FASEB Journal 2001;15:216–218. [PubMed: 11744620]
5. Cavanagh DP, Eckmann DM. Interfacial dynamics of stationary gas bubbles in flows in inclined tubes. Journal of Fluid Mechanics 1999;398:225–244.
6. Chang C-H, Franses EI. Adsorption dynamics of surfactants at the air/water interface: a critical review of mathematical models, data, and mechanisms. Colloids Surfaces A: Physicochem. Eng. Aspects 1995;100:1–45.
7. Das B, Johnson PC, Popel AS. Computational fluid dynamic studies of leukocyte adhesion effects on non-Newtonian blood flow through microvessels. Biorheology 2000;37(3):239–258. [PubMed: 11026943]
8. Eckmann DM, Armstead SC, Mardini F. Surfactant reduces platelet-bubble and platelet-platelet binding induced by *in vitro* air embolism. Anesthesiology 2005;103:1204–1210. [PubMed: 16306733]
9. Eckmann DM, Cavanagh DP. Bubble detachment by diffusion-controlled surfactant adsorption. Colloids and Surfaces A: Physicochem. Eng. Aspects 2003;227:21–33.
10. Eckmann DM, Lomivorotov VN. Microvascular gas embolization clearance following perfluorocarbon administration. Journal of Applied Physiology 2003;94:860–868. [PubMed: 12571123]

11. Eggleton CD, Pawar YP, Stebe KJ. Insoluble surfactant on a drop in an extension flow: a generalization of the stagnated surface limit to deformable interfaces. *Journal of Fluid Mechanics* 1999;385:79–99.
12. Eggleton CD, Tsai TM, Stebe KJ. Tip streaming from a drop in the presence of surfactants. *Physical Review Letters* 2001;87(4) Art. No. 048302.
13. Ferri, James K.; Stebe, Kathleen J. Which surfactants reduce surface tension faster? A scaling argument for diffusion-controlled adsorption. *Advances in Colloid and Interface Science* 2000;85(1):61–97. [PubMed: 10696449]
14. Fung, YC. *Biomechanics: Circulation*. New York, USA: Springer-Verlag; 1997.
15. Ghadiali SN, Gaver DP. The influence of non-equilibrium surfactant dynamics on the flow of a semi-infinite bubble in a rigid cylindrical capillary tube. *Journal of Fluid Mechanics* 2003;478:165–196.
16. Hammon JW, Stump DA, Butterworth JB, Moody DM. Approaches to reduce neurologic complications during cardiac surgery. *Seminars in Thoracic & Cardiovascular Surgery* 2001;13(2): 184–191. [PubMed: 11494210]
17. Huang HD, Kamm RD, Lee RT. Cell mechanics and mechanotransduction: pathways, probes, and physiology. *American Journal of Physiology-Cell Physiology* 2004;287:C1–C11. [PubMed: 15189819]
18. Jacqmin D. Calculation of two-phase Navier-Stokes flows using phase-field modeling. *Journal of Computational Physics* 1999;55:96.
19. James AJ, Lowengrub J. A surfactant-conserving volume-of-fluid method for interfacial flows withinsoluble surfactant. *Journal of Computational Physics* 2004;201:685–722.
20. Johnson, Robert A.; Borhan, Ali. Pressure-driven motion of surfactant-laden drops through cylindrical capillaries: effect of surfactant solubility. *Journal of Colloid and Interface Science* 2003;261:529–541. [PubMed: 16256565]
21. Kobayashi S, Crooks SD, Eckmann DM. Surfactant mitigation of has bubble contact-induced endothelial cell death. *Undersea and Hyperbaric Medicine*. 2010 (in Press).
22. Lampe JW, Liao Z, Dmochowski IJ, Ayyaswamy PS, Eckmann DM. Imaging macromolecular interactions at an interface. *Langmuir* 2010;26(4):2452–2459. [PubMed: 20085337]
23. Lee L, Leveque R. An immersed interface method for incompressible Navier-Stokes equations. *SIAM Journal of Scientific Computing* 2003;25:832.
24. Levich, VG. *Physicochemical Hydrodynamics*. Prentice Hall; 1962.
25. Li XF, Pozrikidis C. The effect of surfactant on drop deformation and on the rheology of dilute emulsion in stokes flow. *Journal of Fluid Mechanics* 1997;341:165–194.
26. McNeil PL, Steinhardt RA. Loss, restoration, and maintenance of plasma membrane integrity. *Journal of Cell Biology* 1997;137:1–4. [PubMed: 9105031]
27. Mendelson HD. The prediction of bubble terminal velocities from wave theory. *AIChE Journal* 1967;13:250.
28. Mendez JL, Rickman OB, Hubmayr RD. Plasma membrane stress failure in ventilator-injured lungs - a hypothesis about osmoregulation and the pharmacologic protection of the lungs against deformation. *Biology of the Neonate* 2004;85:290–292. [PubMed: 15218285]
29. Milliken WJ, Leal LG. The influence of surfactant on the deformation and breakup of a viscous drop. *Journal of Colloid and Interface Science* 1994;166:275–285.
30. Morales D, Solans C, Gutierrez JM, Garcia-Celma MJ, Olsson U. Oil/water droplet formation by temperature change in the water/c16e6/mineral oil system. *Langmuir* 2006;22(7):3014–3020. [PubMed: 16548551]
31. Mukundakrishnan K, Ayyaswamy PS, Eckmann DM. Finite-sized gas bubble motion in a blood vessel: Non-newtonian effects. *Physical Review E* 2008;78 036303(1–15).
32. Mukundakrishnan K, Ayyaswamy PS, Eckmann DM. Bubble motion in a blood vessel: Shear stress induced endothelial cell injury. *Journal of Biomechanical Engineering* 2009;131(7) 074516.
33. Mukundakrishnan K, Eckmann DM, Ayyaswamy PS. Bubble motion through a generalized power-law fluid flowing in a vertical tube. *Annals of the New York Academy of Sciences* 2008;1161:256–267. [PubMed: 19426324]

34. Mukundakrishnan K, Quan S, Eckmann DM, Ayyaswamy PS. Numerical study of wall effects on buoyant gas-bubble rise in a liquid-filled finite cylinder. *Physical Review E* 2007;76 036308(1–15).
35. Muradoglu, Metin; Tryggvason, Gretar. A front-tracking method for computation of interfacial flows with soluble surfactants. *Journal of Computational Physics* 2008;227:2238–2262.
36. Oguz HN, Sadhal SS. Effects of soluble and insoluble surfactants on the motion of drops. *Journal of Fluid Mechanics* 1988;194:563–579.
37. Osher S, Fedkiw R. Level set methods: an overview and some recent results. *Journal of Computational Physics* 2001;169:463.
38. Cavanagh DP, Eckmann DM. The effects of a soluble surfactant on the interfacial dynamics of stationary bubbles in inclined tubes. *Journal of Fluid Mechanics* 2002;469:369–400.
39. Palaparthi R, Papageorgiou DT, Maldarelli C. Theory and experiments on the stagnant cap regime in the motion of spherical surfactant-laden bubbles. *Journal of Fluid Mechanics* 2006;559:1–44.
40. Papanastasiou TC. Flows of materials with yield. *Journal of Rheology* 1987;31(5):385–404.
41. Park CW. Influence of soluble surfactant on the motion of a finite bubble in a capillary tube. *Phys. Fluids A* 1992;4(11):2335–2347.
42. Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke* 1994;25:1393–1399. [PubMed: 8023354]
43. Quan S, Schmidt DP. A moving mesh interface tracking method for 3d incompressible two-phase flows. *Journal of Computational Physics* 2007;221:761–780.
44. Rodrigue D, De Kee D, Chan Man Fong CF. An experimental study of the effect of surfactants on the free rise velocity of gas bubbles. *Journal of Non-Newtonian Fluid Mechanics* 1996;66(3):213–232.
45. Rodrigue D, De Kee D, Chan Man Fong CF, Yao J. The slow motion of a single gas bubble in a non-newtonian fluid containing surfactants. *Journal of non-Newtonian Fluid Mechanics* 1999;86:211–227.
46. Sadhal, SS.; Ayyaswamy, PS.; Chung, JN. Transport phenomena with drops and bubbles. New York, USA: Springer-Verlag; 1997.
47. Scardovelli R, Zaleski S. Direct numerical simulation of free surface and interfacial flow. *Annual Review of Fluid Mechanics* 1999;31:576.
48. Sharan M, Popel AS. A two-phase model for blood flow in narrow tubes with increased viscosity near the wall. *Biorheology* 2001;38:415–428. [PubMed: 12016324]
49. Shin S, Juric D. Modeling three-dimensional multiphase flow using a level contour reconstruction method for front tracking without connectivity. *Journal of Computational Physics* 2002;180:427–470.
50. Stigter D, Mysels KJ. Tracer electrophoresis. ii. the mobility of the micelle of sodium lauryl sulfate and its interpretation in terms of zeta potential and charge. *Journal of Physical Chemistry* 1955;59(1):4551.
51. Stone HA. A simple derivation of the time-dependent convective-diffusive equation for surfactant transport along a deforming interface. *Physics of Fluids A* 1990;2:111–112.
52. Sussman M, Almgren AS, Bell JB, Colella P, Howell L, Welcome M. An adaptive level set approach for incompressible two-phase flows. *Journal of Computational Physics* 1999;148:81.
53. Sussman M, Puckett EG. A coupled level set and volume-of-fluid method for computing 3D and axisymmetric incompressible two-phase flows. *Journal of Computational Physics* 2000;162(2):301–337.
54. Suzuki A, Armstead SC, Eckmann DM. Surfactant reduction in embolism bubble adhesion and endothelial damage. *Anesthesiology* 2004;101:97–103. [PubMed: 15220777]
55. Swaminathan TN, Mukundakrishnan K, Ayyaswamy PS, Eckmann DM. Effect of a soluble surfactant on a finite sized bubble motion in a blood vessel. *Journal of Fluid Mechanics* 2010;642:509–539. [PubMed: 20305744]
56. Torres DJ, Brackbill JU. The point-set method: front tracking without connectivity. *Journal of Computational Physics* 2000;165:620.

57. Tsai TM, Miksis MJ. Dynamics of a drop in a constricted capillary tube. *Journal of Fluid Mechanics* 1994;274:197–217.
58. Udaykumar HS, Tran L, Belk DM, Vanden KJ. An eulerian method for computation of multimaterial impact with ENO shock-capturing and sharp interfaces. *Journal of Computational Physics* 2003;186:136–177.
59. Unverdi SO, Tryggvason G. A front-tracking method for viscous incompressible, multi-fluid flows. *Journal of Computational Physics* 1992;100(1):25–37.
60. Vlahakis NE, Hubmayr RD. Invited review: plasma membrane stress failure in alveolar epithelial cells. *Journal of Applied Physiology* 2000;89:2490–2496. [PubMed: 11090606]
61. Yon S, Pozrikidis C. A finite volume/boundary-element method for flow past interfaces in the presence of surfactants, with application to shear flow past a viscous drop. *Computational Fluids* 1998;27:879–902.
62. Zhang J, Eckmann DM, Ayyaswamy PS. A front tracking method for a deformable intravascular bubble in a tube with soluble surfactant transport. *Journal of Computational Physics* 2006;214:366–396.

Figure 1.
Schematic of a finite sized nearly occluding bubble in vertical and horizontal vessel configurations.

Figure 2. Streamlines for flow over a clean bubble. The aspect ratio (λ) is 1.0 and the Reynolds number is 0.2.

Figure 3.

Representative distribution of surfactant concentration at the interface. $\lambda = 1.0$, $Re = 0.2$. Very weak internal motion is not shown. Γ/Γ_∞ at the maximum thickness is 4.9×10^{-2} and Γ/Γ_∞ at the minimum thickness is 4.4×10^{-2} . Γ_{max} and Γ_{min} illustrate the angles (ϕ_{max} and ϕ_{min}), measured from the rear stagnation point, to the maximum and minimum surfactant concentration location on the surface.

Figure 4.

Variation of the shear stress at a point on the vessel wall as the bubble passes over it with and without the presence of the surfactant $C_{12}E_6$. The normalization of the shear stress is done with the corresponding basal value. $\lambda = 1.0$ and $Re = 0.2$.

Figure 5.

Variation of the normalized total interface surfactant mass as a function of the ratio of the adsorption and desorption Stanton numbers for various dimensionless adsorption depths. Pe_s and Pe are fixed at 1.49×10^3 . λ is 1.0. The normalization of the total interface surfactant mass is done with the quantity $\pi d^2 \Gamma_\infty$.

Figure 6. Variation of the normalized minimum gap between the bubble and the vessel wall as a function of $\mathcal{R}$ for various α . $Pe_s = Pe = 1.49 \times 10^3$, $\lambda = 1.0$. The gap is normalized with the vessel radius.

Figure 7. Variation of the difference between the maximum and minimum shear stress experienced by a point on the vessel wall as a function of $\mathcal{K}$ for various α . $Pe_s = Pe = 1.49 \times 10^3$, $\lambda = 1.0$.

Figure 8.

Distribution of the surfactant concentration at the interface. The normalized arc lengths along the surface of the bubble is measured from the rear stagnation point to the front stagnation point ($0 \rightarrow \pi$). $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 9.

Distribution of surfactant concentration at the interface. $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 10.

Variation of the normalized total interface surfactant mass $\mathcal{M}$ as a function of the bulk Péclet number for various surface Péclet numbers. $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 11. Variation of the normalized minimum gap between the bubble and the vessel wall as a function of Pe for various Pe_s , $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 12.

Variation of the difference between the maximum and minimum shear stress experienced by a point on the vessel wall as a function of Pe for various Pe_s . $\mathcal{K} = 4.5 \times 10^{-5}$, $\lambda = 1.0$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 13.

Variation of the difference between the maximum and minimum shear stress experienced by a point on the vessel wall as a function of the dimensionless adsorption depth, α , for various aspect ratios. $\mathcal{K} = 4.5 \times 10^{-5}$. $Pe_s = Pe = 1.49 \times 10^3$

Figure 14.

Variation of the difference between the maximum and minimum shear stress experienced by a point on the vessel wall as a function of the surface Péclet number, Pe_s , for various aspect ratios. $\mathcal{H} = 4.5 \times 10^{-5}$, $Pe = 1.49 \times 10^3$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 15.

Variation of the difference between the maximum and minimum shear stress experienced by a point on the vessel wall as a function of $\mathcal{K}$, for various aspect ratios. $Pe_s = Pe = 1.49 \times 10^3$ and $\alpha = 9.5 \times 10^{-4}$.

Figure 16. Comparison of the numerical results of the rise of an air bubble in a tube containing human blood plasma with that of our experimental results. Here $d_{tube} = 1.5875mm$ is the tube diameter.

Table 1

Parameters relevant to the estimation of Reynolds number in various vessels.

Vessel	Re	diameter(μm)	Centerline velocity(cm/s)
Small arteriole	0.2	40	1.75
Large arteriole	2.0	100	7.0
Small artery	200	2000	35.0

Table 2

Range of variation of various parameters along with their base values. These parameters have been defined in section 3.

Parameter	Symbol	Fixed/Variable	Range
Reynolds number	Re	Fixed	0.2
Capillary number (clean bubble)	$Ca = \mu U_{max}/\sigma$	Fixed	1.225×10^{-3}
Aspect ratio	λ	Variable	0.9 – 1.05
Surface Péclet number	$Pe_s = U_{max}d/D_s$	Variable	$1.49 \times 10^0 - 1.49 \times 10^4$
Bulk Péclet number	$Pe = U_{max}d/D_l$	Variable	$1.49 \times 10^0 - 1.49 \times 10^6$
Dimensionless adsorption depth	$\alpha = \Gamma_x/C_0d$	Variable	$9.5 \times 10^{-2} - 9.5 \times 10^{-4}$
Ratio of adsorption to desorption Stanton number	$\mathcal{K} = St_a/St_d = k_a/k_d d$	Variable	$4.5 \times 10^{-13} - 4.5 \times 10^{-3}$