Air and blood fluid dynamics: at the interface between engineering and medicine

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Abstract. The flows in the human upper airway and human heart during open heart surgery are considered. Beginning with idealized models of the human upper airway, current methods to extract realistic airway geometries using a novel implementation of optical coherent tomography modality are introduced. Complementary direct numerical simulations are considered that will assist in pre-surgery planning for obstructive sleep apnea. Cardiac air bubbles often arise during open heart surgery. These bubbles are potential emboli that can cause neurological impairment and even death. An experimental programme is outlined that uses acoustic sound to instil bubble surface oscillations that result in bubble breakup. A novel algorithm is introduced that enables a surgical team to obtain real-time in-vivo bubble data to aid cardiac de-airation procedures.

1. Introduction

Human bodies have multiple systems that rely on fluid transport; here, the pulmonary and arterial systems are considered with specific attention on the upper airway and the heart. In the case of the former, the fluid dynamics of air from the entrance of the oral cavity to at least the first bronchus is important because portions of it act as a vehicle for the delivery of nutrients and air as well as to enable speech. In the case of arterial systems, the heart is the major organ and during open-heart surgery air bubbles maybe introduced that have the potential to embolise. These emboli have been shown to be strongly correlated with neurological dysfunction and even death. In this paper, the fluid dynamics associated with these two physiologically critical systems are explored using theory, experiment and computations.

Note that given the breadth of the subject matter considered here, many details are not included and a reader is directed to the relevant literature.

The paper is laid out in the following manner. The human airway is first considered. Here, the research conducted in our laboratory is traced from introducing an idealized human upper airway and how we investigated the flow both computationally using lattice Boltzmann methods and RANS and experimentally using flow visualization, hot wire anemometry and particle image velocimetry. Current efforts are introduced to explore realistic upper airway geometries and a new endoscopic-type tool called long distance optical coherency tomography (OCT) that is under development by a group at the University of California, Irvine to help characterize the geometry of specific human upper airways. The images obtained can then be translated into a stereo-lithographic file (.stl), which, when imported into a grid-generator enables fluid
modelling and direct numerical simulations to be performed. Importantly, OCT includes the ability to image paediatric patients who may have breathing difficulties due to pathological issues (Down’s syndrome etc.). The second part of the paper considers the bubbles that are often encountered during cardiac surgery and developments in our laboratory, with reference to clinical practice, are introduced to both characterize the number and sizes of these bubbles in real time as well as to introduce a novel bubble destruction approach. This destruction depends on initiating air/liquid interfacial instabilities so as to cause larger bubbles to disintegrate into a cloud of smaller bubbles with the desire to make such bubbles less than 40 µm in diameter so they can pass harmlessly through the arterial system.

2. Fluid Dynamics in both idealised and real forms of the upper human airway

The human airway, defined here to include only the oral cavity, the non-nasal pharynx, the larynx and trachea, is a complex geometry. The rather tortuous pathway leading from the mouth to the lower trachea, however, provides lower resistance than breathing through the nasal orifice and thus greater volumes of oxygen/carbon dioxide can be exchanged during the inhalation-exhalation breathing cycle. Reynolds numbers within the human airway can vary $650 \leq \text{Re} \leq 13,000$ depending on inhalation flow rate (typically between 10 and 120 litres per minute) and location in the airway, see [21].

The fluid mechanics in the nasal passages is complicated by the turbinates, which maximise exposure of these tissues to the incoming air, thereby enabling the air to be raised in temperature, humidified and cleansed prior to exiting the nasal-pharynx, which then passes over the epiglottis and through the larynx before entering the trachea and eventually the lungs. The Reynolds number in the nasal passages is of order 1000. Doorly et al. [8]; while this suggests inertial dominance, there are regions in the turbinates where the flow velocities are very much lower so that diffusion controlled mass transfer takes place to the olfactory glands. In this work, the flow in the nasal passages is referred to, but is otherwise ignored; interested readers may consult that literature (see for example, Doorly et al. [8, 9]; Shi et al. [40]; Xi and Longest [47].

Physiologically, the upper respiratory tract is important because it serves as the sole route for nutrient delivery (oxygen is carried to the lungs, food is diverted through “swallowing”, which engages the epiglottis, from the pharynx to the stomach via the oesophagus) as well as speech. The lower airway helps maintain homeostasis (through oxygen/carbon-dioxide exchange, acid-base balance, etc.), while guarding against infection (moist mucous membranes and nasal hairs trap large particles, the mucociliary escalator removes small particles, and the pharyngeal lymphoid ring guards against pathogens). Finally, it is an important site for delivery of medications (oral, sub-lingual, intra-nasal, and inhaled).

In the past, the majority of efforts have been directed to understand the basic fluid mechanics in the airway to eventually improve drug delivery to the lungs. A new, emerging driver is even more challenging: improve breathing patterns in clinically abnormal airways. This is an interdisciplinary research objective to integrate novel experimental modalities with fluid dynamic simulations to effect rapid resolution of these breathing difficulties by guiding a surgical team to maximize the benefits while minimizing failure, see for example, [22] and [46]. However, before these new directions are considered, the basic fluid dynamics of the human upper airway will be surveyed.

The human airway, as with all physiology, evolves with time. The sizes and flexibility of the airway passages change with age and disease. For example, Heenan et al. [17] obtained MRI scans of two subjects and due to their physiological differences, refer to them as big nose-small mouth and small nose-big mouth due to their presentation. In addition, delivery of aerosols to the lungs from an inhaler often results in poor drug delivery either by the user from improper use, particulate impaction in the throat or in the case of pathological/physiological condition, asymmetric delivery to the lungs [25].
Historically, and because of the huge variability in human airway physiology, many simplifications have been introduced when the human airway fluid dynamics are explored, which include simple curved tubes to current work on an idealised model geometry. The idealised geometry continues to be used to help establish some of the basic fluid dynamic mechanisms that should be expected in realistic geometries. Once understood, then perhaps the variations encountered from replacing idealised with real geometries will assist in our broader understanding of the effects of, for example, tissue compliance, mucus, oxygen/carbon dioxide exchange etc. as will be explored shortly.

2.1. Idealised Geometry
Stapleton et al. ([13]) were the first to introduce an idealised geometry that encompassed all the basic attributes of a human airway. Heenan et al. [17] and others (see for example [24], [5]) continue to use this idealised model, or slight variants of it to explore the rich flow features. In my group, we have considered both computational and experimental investigations using a slight variant of the University of Alberta model (Stapleton et al.) and a brief summary of major findings are now provided.

Johnstone et al. [21] performed initial flow visualization and hot wire anemometry (and endoscopic PIV, [20]) studies using steady flow over inhalation rates \(10 \leq m \leq 120\) litres per minute (lpm), which are encountered physiologically. Their flow visualisation revealed complex secondary flows both in the sagittal and cross sagittal (that is transverse and coronal) planes. The hot wire data, taken only at the sagittal plane, indicated significant changes to the turbulence intensities and Reynolds stresses as flow traversed the large oral cavity and through the naso-pharynx due to the curvature and constriction of the airway. Once the epiglottis is encountered, these quantities reflected the emergence of a shear layer that gives rise to a laryngeal jet. Within these sections, from the oral cavity to beyond the larynx, flow recirculation regions that are oriented parallel to the main flow in the airway, and identified from the flow visualisation, produced data that were deemed questionable because of the directional insensitivity of the hot wires. Ball et al. performed RANS [2] and direct numerical simulation [3] using the same idealized geometry as Johnstone et al., but only for inhalation flow rates of 10 litres per minute. RANS predictions were tolerably good compared with the hot wire data, while the DNS, which used the lattice Boltzmann method DNS provided better agreement with those same data. Subsequently, Pollard et al. [34] provided an overview of the flow in the idealized airway, and drew attention to the need for careful correlation between experiments and simulation due to the inherent resolution and uncertainty issues from both simulations, modelling and experiment.

Interestingly, what emerged from Ball et. al. [3] was the complex flow around the epiglottis. The flow around the epiglottis is preceded by its passage upstream, which had negotiated curvature and flow acceleration in the naso-pharynx region. The flow is then intercepted by the sharp, flap-like Bourda-like mouth-piece of the epiglottis that then creates a shear layer, from which the flow then evolves into what had been previously observed as a laryngeal jet. However, what had not been previously observed was the resulting complex axial helical motion of the flow distal to the epiglottis that then created an asymmetric flow that enters the first bronchus. This means that it is incorrect to assume fully developed pipe-flow both in the mean and time dependent flow structure if computational studies of flow to the lungs is contemplated.

Shinneeb et al. [42], [41] performed the first particle image velocimetry using a clear silicon version of the idealized model. Their data were taken in both the sagittal and trans-sagittal planes, and focussed particularly on the epiglottal region, see figure 2. They used a water-glycerin mixture with the flow rate adjusted to give the equivalent of 10 litres per minute in the airway. They determined that the epiglottis produces significant vortex shedding, see figure 3 and determined “The flow contains a large number of counter-rotating vortical structures that are distributed throughout the pharynx/larynx region at all times particularly whose axes are
normal to the sagittal (x-y) plane. These structures are very energetic and subject to deformation by other structures that present in that region; and sic, that the pharynx/larynx region is characterised by bursting events (e.g. ejection, sweep, and interaction events) particularly in the epiglottal region. These events appear to be responsible for deforming and/or tearing apart the vortical structures. In addition, the limited space of the flow field in the epiglottal region as well as the relatively large number and size of the structures that present there appear to enhance the occurrence of the merging process.7

Figure 1. Sagittal view of human airway geometry, including nasal passages

The most recent work on the idealized geometry is due to Kleinstreuer et al. ([24]) and has provided a review of flow in the idealized airway, and complemented existing data using results from large eddy simulation.

2.2. Real geometries

The actual geometry of the human airway is highly variable because of patient specific physiology, age-dependent and pathological conditions. As referred to previously, Heenan et al. (2004) [17] considered two realistic geometries, derived from magnetic resonance imaging (MRI), computerized tomography (CT) to explore deposition of aerosol in the airway. These two geometries were referred to as large mouth (small nose) and small mouth (large nose) are examples of the high variability that is encountered, see figures 4 and 5. In fact, these were from healthy subjects; in the case of diseased airways, these geometries may be even more complex. More recently, de Rochefort et al. [7] noted in their study of the lower human airway “Finally, this combined numerical and experimental approach of flow assessment in realistic in vivo-based human airway geometries confirmed the strong dependence of airway flow patterns on local and global geometrical factors”. While this statement confirms the expected observation that flow feature variations should be expected between subjects, the authors

Figure 2. Sagittal view of idealized human airway geometry used for PIV measurements, without nasal passages. Planes of interest in epiglottal region fields of view (FOV) [42]

Figure 4. Small mouth geometry obtained by MRI [17].

Figure 5. Large mouth geometry obtained by MRI [17].
Figure 3. Four examples of POD-reconstructed fluctuation velocity fields (a), (b), (c), and (d) show vortical structures identified on the x-y plane along z/D=0. The turbulent kinetic energy recovered in these fields is 62.1% using 3 modes. Slice is from FOV1 of figure 2 [42]

seem to not appreciate the diminishing local effects of the time dependent inlet conditions, distal to the larynx and upstream from the first bronchus, with descent from the first to the fourth bronchial branch.

2.2.1. Computational and experimental investigations of flow in real geometries While Ball et al. [2], [3] performed both RANS and direct numerical simulation (through the use of the lattice Boltzmann method) inside the idealized geometry, recent work has shifted to real geometries. Clearly, the complex geometries and relatively low flow rates and local Reynolds numbers suggest the use of DNS, many others continue to apply RANS as well as large eddy simulation, see for example Wootton et al. [46] and Mihaescu et al. [31]. The most recent application of DNS to real geometries has been the work of Nicolaou and Zaki [32] and Wong and Elghobashi [45]. In the former, the realistic geometries used by [17] and Grgec et al. [18], see figures 4 and 5, were incorporated into a structured finite-volume code, while in the latter, the lattice Boltzmann
method was applied to two subjects one healthy and the other with an obstructed airway. In the geometries considered, a main conclusion was that the flow features in these geometries are more complicated than those encountered in idealized geometries while many of the main features of the flow remain unchanged.

A novel experimental method that has emerged to help interrogate flows in the airway is an adaptation of magnetic resonance imaging (MRI) to magnetic resonance velocimetry or MRV, see [12], [11]. MRI uses the frequency of excited hydrogen nuclei when they are exposed to intense magnetic fields. This technique should be able to provide the same type of data obtained using holographic PIV. However, it does not require either optical access, seeding or post processing. While the method has been considered for use as a flow investigative tool, it is limited to the use of non-magnetic models and can only, at this time, provide time average velocities. While hyperpolarised $^3$He has been used in-vitro for lower airway velocity characterization, [7], it remains to be seen if this approach can be incorporated into the arsenal of modalities for rapidly assisting a surgical team. However, as will be noted below, there maybe more optimal and convenient modalities available.

2.2.2. Pre-surgery planning The human airway is also subject to disease and obstruction, which leads to breathing and nutrient delivery difficulties. Common issues include tonsillitis, adenoiditis (hypertrophy of the pharyngeal tonsils) and other types of inflammation. Sleep apnea is also readily encountered in the general population (about 5%), with obstructive sleep apnea (OSA) being an additional unpleasant complication (e.g. snoring). As noted above, CT and MRI maybe used to obtain images of the airway. However, these modalities have drawbacks when applied to OSA, especially for paediatric subjects. Moreover, these cannot identify the pathogenesis of the obstruction.

A new tool has emerged to help decrease the difficulty in acquiring requisite images. This is called optical coherence tomography (OCT), and long range OCT in particular, Jing et al. [22]. It uses near infrared light to obtain high resolution (of order 10 microns) images of tissue. A recent evolutionary step in this technology has enabled the frequency of image capture to be increased from between 1 to 5 frames per second to about 25. It uses an flexible endoscope (as opposed to the fixed, single fibre endoscope used by Heenan et al. [21]). Laser light is fed through an optical fibre to a mirror with a 45° surface, which rotates at 25 Hz. The diameter of the unit is less than 1 mm. The LROCT is positioned in vivo through the nasal passage. Once in position, it is slowly withdrawn all the while scanning the inner surface of the subject with an axial resolution of about 10 microns. These scans are then spliced together to give a high resolution geometry. Examples for both pre- and post operative airways are provided in figures 6 and 7.

A major issue with OSA is to find a quantifiable method to identify the obstruction that is the cause of the apnea while also ensuring that removal of the obstruction will provide the expected
diminution in breathing difficulty. With this in mind, Wang and Elghobashi [45] working with Jing et al. [22] mentioned above, took the LROCT images and imported them into a lattice Boltzmann code to perform DNS. LBM was first applied to the idealised human airway by Ball et al. [3] with up to 144 million control elements/volumes wherein it was demonstrated to provide superior predictions to a variety of RANS approaches. The large number of CV’s was required to resolve the Kolmogorov scale regions where the local Re was high. Jing et al., using upwards of 210 million control volumes/elements, considered the flow entering the airway through the nasal cavity, rather than the oral cavity, for both a healthy 8 year old and a 7 year old with adenotonsillar hypertrophy (enlarged tonsils and adenoids) obstructed upper airway. They compared the time dependent velocity (see figures 10 and 11) and pressure signals at a variety of locations in the airway during both inhalation and exhalation and these computational simulations of the full breathing cycle are, to the authors’ knowledge, the first of its kind in realistic airways. They could uniquely identify the obstructed region by calculating the $\partial p/\partial z$ and $\partial^2 p/\partial z^2$, where $p$ is the mean pressure and $z$ is the direction of the main flow. They concluded that where $\partial^2 p/\partial z^2$ became positive and was maximum correlated very well with the known location of the obstruction.

The challenge now is to move this capability into the hands of an otolaryngology and simulation team to enable reasonable turnaround between patients entering a clinic, being assessed by LROCT, incorporating the geometry into a DNS code and in an interactive environment, recompute the flow after the "team" has virtualized the removal of the obstruction to ensure the pressure drops meet physiological requirements and post-operative assessment/validation.

![Figure 8. Instantaneous velocity contours at various cross section in normal airway [45]](image)

![Figure 9. Instantaneous velocity contours at various cross section in obstructed airway [45]](image)

2.3. Summary and prospectus for human airway research

The human upper airway presents a rich research environment for fluid dynamists providing they appreciate the constraints of the medical environment they enter. The link between clinical and computational fluid dynamic simulations using DNS continues to strengthen, but there remains many exciting opportunities and challenges, including fluid-structure interaction, incorporation of mucous onto a flexible and pliable tissue and introduction of heat and mass transfer to and from these surfaces.
3. Cardiac emboli

Attention is now turned to the heart and some of the fluid dynamic issues of the introduction of air (and i.e. nitrogen in particular) into the cardiac cavities during open heart surgery. Skipping the surgical details, during for example heart valve replacement, the open chest and cardiac cavity is often bathed in carbon dioxide, which is readily absorbed by blood, but more importantly assists to ensure that nitrogen absorption is minimized. Even so, during and after “de-airation” when gases in the heart cavity are expelled through a variety of non-standard methods, gaseous bubbles remain. When viewed through an ultrasound probe (trans-esophageal echocardiography (TEE)) that is positioned in the esophagus and scans the cardiac cavity to detect inter-facial surfaces, the potential gaseous emboli may appear as a “snow-storm”. These bubbles vary in diameter. As blood corpuscles must be $\leq 40 \mu m$ to negotiate the capillaries that link the arterial to venous systems, any potential emboli that is greater than $40 \mu m$ in diameter are candidates to lodge in the body with a variety of consequences, most of which place the patient at some level of risk. Complications such as neurological impairment from bubbles being transported through the carotid arteries to lodge perhaps in the brain [1, 19, 37], myocardial dysfunction [10], and even death [19] may result.

Gases trapped within the heart are assisted to escape by a variety of non-standardized techniques, which include venting, altering the patient’s position to permit the air to escape or to be directed into the lower extremities of the body etc. Also, external pressure could be also applied to the carotid arteries to prevent cerebral embolism [23]. Interestingly, embolic signals have been detected in patients with a wide variety of potential embolic sources, including symptomatic and asymptomatic carotid stenosis [30, 39], atrial fibrillation [6, 43] and prosthetic cardiac heart valves [35]. They also have been detected during and after many surgical procedures, including carotid endarterectomy [15, 44] and cardiopulmonary bypass [14].

While there have been methods and appliances devised to monitor embolic activity in blood, many of these methods are used post-operatively [4]. Some systems even use a multifrequency trans-cranial Doppler (TCD) to detect the differences between solid and gaseous emboli [38]. With Doppler micro-emboli signals obtained using TCD it is not possible to distinguish two or more emboli per frame. This is not a disadvantage for most of the applications for which TCD monitoring is used; however, for the period during heart surgery prior to weaning from the cardiopulmonary bypass machine where there are numerous air emboli per frame it would
be extremely difficult for Doppler ultrasonography to accurately distinguish between all emboli. Also, gas emboli post cardiac surgery are not just micro-emboli, which are considered to be ≤40\(\mu m\) in diameter, with gaseous potential emboli being up to 2\(mm\) or greater in diameter. All TCD systems are set up to acquire mid-cranial embolic signals but are unsuitable if emboli have diameters ≥40\(\mu m\) and therefore TCD is not suitable for immediate post-CPB separation. Therefore, detection of heart cavity resident potential emboli, where both large quantities and size distributions of air bubbles are encountered, will require a new method.

3.1. Emboli Bubbles and Surface Interference

As noted, gaseous potential emboli, or bubbles in blood that are ≥40\(\mu m\) are problematic. One possible method to ameliorate the negative effects of these larger bubbles is to break them apart. It is to this subject that attention is now turned.

3.1.1. Dimensional analysis

The literature on bubbles is extensive, and will not be reviewed here; rather, the relevant material will be introduced as needed. As potential gaseous emboli tend to move through the human body using the cardiac systole - diastole wave form, it is simpler, in the first instance, to assume that the blood to be stationary and permit bubbles to rise against the gravity vector. The bubble shape is then determined from the well-known plot of the Morton number (\(M\)) as a function of the Reynolds (\(Re\)) and Eotvos (\(Eo\)) numbers (see [16])

\[
Eo = \frac{g\Delta\rho D^2}{\sigma} \quad M = \frac{\mu^4 \Delta\rho}{\rho l^2 \sigma^3} \quad Re = \frac{\rho l D_o U}{\mu l} \tag{1}
\]

where the meaning of the symbols should be self-evident. In the problem considered here, the log of the Morton number is between -8 and -11, but the Eotvos number is ≤0.3 so that spherical bubbles are expected although excursions into a wobbling mode maybe encountered.

3.1.2. Bubble surface oscillations - Lamb and Rayleigh-Plesset

Lamb [26] considered a spherical drop that was subjected to small oscillations about its spherical form with only surface tension effects considered. He introduced a spherical harmonic approximation to describe the small oscillations about the mean radius of the drop:

\[
r = R_o + \sum_{n,m} a_{nm} Y^m_n \tag{2}
\]

where \(r = r(\theta, \phi, t)\) is the bubble radius as a function of sphere angular coordinates, \(R_o\) is the initial bubble radius and time, \(a_{nm} = a_{nm}(t)\) are the amplitudes of the spherical harmonic component of order \(n\) and degree \(m\), and \(Y^m_n = Y^m_n(\theta, \phi)\) is the normalized spherical harmonic function. The shapes so obtained are illustrated in figure 12. In these images, the colours red and blue indicate positive and negative values of the function \(Y^m_n\), for \(R_o = 0\) and \(a_{nm} = 1\) from equation 2. In figure 13, the images are for an initial bubble radius \(R_o = 0.6\) and \(a_{nm} = 0.4\).

Lamb used the Young-Laplace equation that describes the capillary pressure difference across the interface between two fluids at rest:

\[
\Delta p = \sigma \left( \frac{1}{R_1} + \frac{1}{R_2} \right) \tag{3}
\]

where \(\Delta p\) and \(\sigma\) are the pressure differences across a bubble surface and the surface tension, respectively. \(R_1\) and \(R_2\) are the maximal and minimal radii of curvatures of the surface,
respectively (also known as the principal radii of curvature). Lamb employed velocity potentials and solid geometry and the spherical harmonic approximation with equation 3 to obtain the frequencies at which a bubble or drop will oscillate, this frequency being called the modal frequency. The modal frequencies are the natural frequencies of the bubble when given a particular mode of vibration (analogous to the natural frequency for a spherical bubble):

$$\omega_n = \frac{1}{2\pi R_o} \sqrt{\frac{n(n+1)(n-1)(n+2)}{((n+1)p_g + n\rho_l)R_o}} \left(\frac{\sigma}{\rho_l} + \frac{\sigma}{\rho_l R_o} \right) \left(\frac{\rho_l}{\rho_g} + \frac{\rho_l}{\rho_g R_o} \right)$$

(4)

where $\omega_n$ is the modal surface perturbation frequency of order $n$, $R_o$ is the initial bubble radius and $\rho_l$ and $\rho_g$ are the densities of the liquid and gas, respectively. From equation 4 the modal frequency is only dependent on the order $n$ and initial radius, $R_o$. Therefore, given an applied frequency the bubble will prefer to oscillate with a mode in accordance with equation 4. However, to oscillate the bubble with maximum amplitude with minimal power the natural frequency of the bubble must be used. Other frequencies other than the natural will tend to damp out and cause no stimulated growth of the amplitude. Attention is now directed towards the dynamics of the problem to determine the natural frequency of a bubble.

To introduce the dynamics of bubble motion, Rayleigh [36] described the pressure inside a collapsing spherical bubble and Plesset [33] extended this work to account for the stability of the interface and the following is now referred to as the Rayleigh-Plesset equation:

$$\ddot{R} R + \frac{3}{2} \dot{R}^2 + \frac{4\nu_l}{R} \dot{R} + \frac{2\sigma}{R \rho_l} = \left(\frac{p_o}{\rho_l} + \frac{2\sigma}{R \rho_l} \right) \left(\frac{R_o}{R} \right)^{3\kappa} - \frac{p_\infty}{\rho_l}$$

(5)

where $\dot{R}$ and $\ddot{R}$ are the acceleration and velocity of the bubble radial surface of radius $R$ and $\kappa$ is the polytropic index that accounts for isothermal or adiabatic compression; the other symbols should be obvious as to their meaning. This equation reduces to Rayleigh’s equation when $p_\infty = P_o$ (a constant external pressure), $p_g = 0$ (empty cavity) and the surface tension and viscosity are neglected. If, however, the external pressure is not constant, but fluctuating in a prescribed manner, then the bubble radius will oscillate. The natural frequency of the 0th mode (or of spherical motion) can be derived from the Rayleigh-Plesset as:

$$\omega_0 = \frac{1}{2\pi R_o} \sqrt{\frac{3\kappa p_o}{\rho_l R_o} + \frac{6\kappa \sigma}{\rho_l R_o} - \frac{2\sigma}{\rho_l R_o}}$$

(6)
Figure 14 presents the natural frequency and the modal frequencies as a function of bubble radius. Ideally, the shape that a bubble will take is dependent upon its original radius and the applied frequency, although the bubble will only respond to the natural frequency which leads to the discussion of the preferred mode.

The intercept of the natural and modal frequencies in figure 14 leads to the preferred modes of a bubble (figure 15). As a bubble is subject to it’s natural frequency the bubble will not only oscillate in the spherical direction but also with a modal shape as described by the preferred mode, see figure 13.

Note, however, that equation (5) is accompanied with the proviso, stated by Plesset [33] “While the stability question is thereby answered, the results cannot be applied to the determination of the rate of development of interface distortions of significant amplitude.” It is postulated here that with increased interfacial amplitude, however caused, will create sufficient “violent” perturbations that surface tension forces should enable pinch-off between the mother bubble and its daughters thereby causing a diminution in the size of the mother. Obviously, the change in diameter of the mother bubble will alter its oscillation natural frequency and it is hoped the daughter bubble diameter will be small enough to pass through the human arterial system without consequence.

From the preceding, it is evident that any approach that uses a single frequency will be of limited utility, which therefore requires the development of a methodology that is based on applying an adaptable spectrum of disturbances on bubbles to effect continuous mother-daughter evolution. It is both the current limitation in theory and the requirement to expose bubbles to a multifrequency environment that has caused us to explore this phenomenon using experiments.
The experimental rig is displayed in figure 16. This rig permits two types of experiments to be performed: (a) automatically generate single bubbles into still water permitting them to rise against the gravity vector, activate a speaker with a variety of different sound wave frequency types and obtain high speed video of each bubble evolution and (b) automatically generate bubbles and then provide cross correlation of these bubble to validate ultrasound transducers against visual records (see next section). To date, 6 Tbytes of data have been acquired, which transforms into about 700 events per day that each produces about 100 Gbytes. The frequency types include single continuous, pulsed and ramped frequencies.

The images obtained were analysed using in-house developed image processing software. Simply put, the images captured by the high speed camera were analysed. Analysis included the number and size distribution of the bubble fragments and the geometrical centre of the initial bubble. The geometric centre of the initial bubble was used to check the data to determine if the initial bubble travelled outside of the test section, in which case, those data were rejected.

Figure 17. Sequence of bubbles: The single bubble was radiated with a frequency sweep from 1000 to 1500 Hz over 0.5 sec at 0.6 psi. For the image sequence shown, the frequency ranged from 1400 to 1427.0 Hz. over 13.5 ms

An example of the images obtained are provided in figure 17. The single bubble was radiated
with a frequency sweep from 1000 to 1500 Hz over 0.5 sec. at a pressure of 0.6 psi. The pressure was determined using a hydrophone located in the centre of the speaker at the same distance from it as the bubble release point. The images from a frequency ramp between 1400 and 1427 Hz capture the modes of the breakup of one bubble in 1.5ms intervals. The mother bubble is seen to undergo simple harmonic oscillation for 1.5 ≤ t ≤ 3 before the lower lobe undergoes an azimuthal instability that in the next image ((t=4.5 ms) can be clearly discerned as a roughening of the lower surface of the bubble. With increased time, the whole bubble evolves into a multimodal instability. By t=9 ms surface tension forces pinch off multiple daughter bubbles of varying size, but which are very much smaller that the mother bubble.

### 3.2. Operating room implementation of DETECTS

We have developed a novel algorithm to detect heart resident potential emboli; it is called Detection of Emboli using Transesophageal Echocardiography for Counting, Total volume, and Size estimation or DETECTS. This software maybe used in the operating theatre during cardiac de-airation to provide real-time bubble information (as the name implies). The experimental rig, see figure 16, is equipped to validate the ultrasound images by correlating the US to high speed video images. Our work is to the best of our knowledge the first validation of information that is presented to a cardiac team and it is important to note that typical TEE or foot-print US transducers have relatively poor resolution. A three-dimensional reconstruction of the raw data was preformed to consolidate the measurement slices of the optical and ultrasound, figure 18. Bubbles from the optical data were then matched to the ultrasound bubble to minimize the error between the radius, centre of geometry and time. An example of the congruence between the optical and sound images is provided in figure 19.

![Figure 18. Comparison of optical using DETECTS (violet) and ultrasound (light blue) extracted data.](image)

![Figure 19. DETECTS extracted bubble radii vs. radii obtain from optical images. Lines indicate 1:1 correlation and ± 95% confidence levels.](image)

### 3.3. Summary and prospectus for cardiac potential emboli research

There are many routes available to the fluid dynamics researcher who specialize in bubble dynamics. Clearly, there are interesting theoretical solutions to be considered that must be
complemented by computational simulations that include fluid-structure interaction, where of course the “structure” here is the bubble interface. And, there is the need to introduce blood properties, rather than the “simple” approximation of air in water considered here. In the context of cardiac surgery, implementation of bubble destruction technology into the cardio-pulmonary system, either in-vitro (via the perfusion portion of the cardiac team) or preferably in-vivo directly, has many thermo-fluid challenges. A major obstacle for in-vivo application is the thermal impact on blood and tissue of what ever method that emerges as an optimal modality for bubble break-up. Additionally, a significant challenge faced by engineers is to deal with the resistance of the medical community to the introduction of non-standard procedures into their regimes.

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