

CLIMATE CHANGE, DOLPHINS, SPACESHIPS AND ANTIMICROBIAL RESISTANCE - THE IMPACT OF BUBBLE ACOUSTICS

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Bubbles couple to sound fields to an extraordinary extent, generating and scattering sound, and changing the chemical, physical and biological environments around them when excited to pulsate by an appropriate sound field. This paper accompanies a plenary lecture, opening with the way that the sound emitted by bubbles, when they are injected into the ocean by breaking waves, helps track the >1 billion tonnes of atmospheric carbon that transfers between atmosphere and ocean annually. However, compared to carbon dioxide, atmospheric methane has at least 20 times the ability, per molecule, to generate ‘greenhouse’ warming. Worldwide there is more than twice the amount of carbon trapped in the seabed in the form of methane hydrate than the amount of carbon worldwide in all other known conventional fossil fuels. Acoustics can track the release of bubbles of seabed methane as this hydrate dissociates in response to increasing ocean temperatures, an effect cited by some as a possible climate apocalypse. Continuing the methane theme, this paper discusses the sounds of methane/ethane ‘waterfalls’ on Titan, Saturn’s largest moon, before returning to Earth’s oceans to discuss how whales and dolphins might use the interaction between sound and bubbles when hunting. This in turn suggests possibilities for radar in the search for improvised explosive devices. The paper closes with consideration of another apocalypse, discussing the role that bubbles and acoustics have in mitigating the ‘antibiotic apocalypse’, when in response to the increasing use of antimicrobials (antibiotics to combat bacterial infections; anti-virals for viral infections; anti-fungals for fungal infections; and targeted chemicals to combat parasites) the four classes of microbes all naturally evolve resistance, such that by 2050 Anti-Microbial Resistance will be killing more people than cancer, and will have cost the world economy more than the current size of the global economy.

Keywords: bubbles, acoustics, climate, Anti-Microbial Resistance.

1. Introduction

A gas bubble injected into, or fragmenting within, a liquid, will generate a natural acoustic frequency that is inversely proportional to its size, because the act of injection causes the bubble to pulsate. This acoustic signal can be remotely detected by passive hydrophones and used to monitor the amount of gas that is injected into the natural bodies of water by waterfalls [1], breaking ocean waves (Fig. 1a) [2-5], or the leaks of gas from the seabed, deep-sea pipelines, or carbon capture and storage facilities (Fig. 1b) [6].

When driven by an imposed acoustic field that has a frequency close to the bubble’s natural frequency, resonance can occur, significantly increasing scatter [7]. This can add active methods for bubble detection, to support or replace the passive detection techniques mentioned above. These active techniques can be further enhanced when the bubble is driven with an amplitude that is large enough, and sufficiently close to resonance, to cause nonlinear scattering to occur, generating harmonics, subharmonics and ultraharmonics of the incident acoustic field [8], enabling the bubbles to

be distinguished from scatterers (such as suspended solids [9]) which are not able to generate nonlinear signals when driven by the same sound field. At even higher amplitudes, the bubble pulsations are sufficiently great to cause biological [10], chemical [11] and physical [12] changes to their local environment, which can be unwanted to desirable, depending on the application [13].

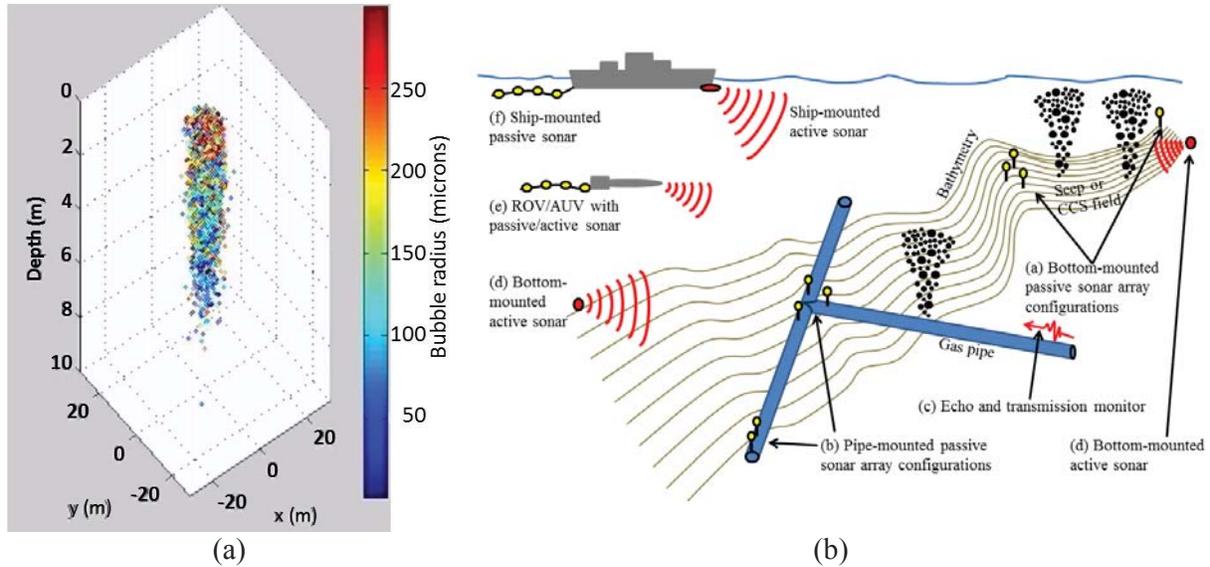


Figure 1: (a) Model of the spatial distribution of bubbles formed under a breaking wave, where the colour scale indicates the bubble radius (for details see [14, 15]). (b) Schematic of how passive (yellow) and active (red) acoustics might be used to detect bubble leaks from deep sea pipelines and carbon capture and storage facilities, and from natural seeps from the seabed [6].

2. The coupling between the submerged gas bubble and the acoustic field

A submerged bubble of gas couples extraordinarily well with sound fields. A submerged pocket of gas is a target that has a huge acoustic impedance mismatch at the bubble wall, because the acoustic impedance of the gas differs so much from that of the liquid [16]. However (except for large bubbles) this impedance mismatch is a secondary contributor to the strong coupling between bubbles and sound fields. This is because the stiffness of the gas (which resists expansions and contractions as the bubble pulsates) and the inertia of the liquid (which must move in and out as the wall of the bubble moves) combine to make an oscillator. Surface tension (the energy required to form a unit area of new surface) makes bubbles tend to the spherical (with greater effectiveness as the bubble size decreases), because a spherical wall takes least surface area energy to encapsulate [17]. Oscillations of the bubble can be broken down into a set of spherical harmonic perturbations, but only the zeroth order spherical harmonic (the pulsation) changes the bubble volume to first order: the second order (the oscillatory shape change of the bubble between ‘pancake’ and ‘needle’ shape [17]) and higher orders, and the first-order ‘translation’ of the bubble, do not change the volume of the gas, and so do not perturb the pressure in the gas in an oscillatory manner. However the zeroth (‘pulsation’) order component of the bubble oscillation does change the gas pressure on the inner boundary of the bubble wall, which is matched by an oscillatory pressure in the liquid. This signal can propagate acoustically away (and towards) the bubble. Injected bubbles therefore can take all manner of shapes, and ‘wobble’ in all manner of ways, but hidden in among these many oscillations is a pulsation component which radiates an acoustic wave into the liquid at the natural frequency of the bubble (as given by the square root of the ratio of the stiffness of the gas to the inertia of the liquid).

In similar vein, a low-amplitude acoustic wave directed at a bubble, if it is close to the pulsation resonance frequency of the bubble, can generate bubble pulsations with characteristic resonance-type variations in amplitude and phase determined by the ratio of the acoustic frequency to the pulsation resonance frequency. The bubble scatters the sound field close to resonance because of that pulsation. When the bubble is driven by frequencies that are much higher than its pulsation resonance frequency (which is equivalent to using, as a target, a bubble which has a radius much larger than that which would be resonant at the driving frequency, since the bubble resonance frequency is inversely proportional to the bubble radius), the bubble barely pulsates, and the scatter is due to the impedance mismatch at the bubble wall [16]. At driving frequencies much less than resonance, although the bubble is far from resonance, the timescale of the compressions and rarefactions of the acoustic wave in the liquid are long compared to the natural frequency of the bubble: the bubble has plenty of time to grow and contract, so even though it is far from resonance, the bubble can, for example, dramatically reduce the sound speed at low frequencies [18]. Sound speed changes, attenuation, and scatter are (with some exceptions), greater the closer one is to resonance.

When strong sound fields are used close to resonance, the bubble pulsation becomes nonlinear, because the stiffness of the gas depends on the displacement of the bubble wall and so varies through the oscillatory cycle [19]. This can create harmonics, subharmonics and ultraharmonics, and if the bubble is insonified with two frequencies (ω_1 and ω_2), it can generate combinations of those frequencies ($\omega_1 \pm \omega_2$; $\omega_1 \pm 2\omega_2$; $\omega_1 \pm 3\omega_2$; $\omega_1 \pm \frac{\omega_2}{2}$; $\omega_1 \pm \frac{3\omega_2}{2}$; etc. [8, 20]). These can be used to detect and size the bubbles, separating them out from other scatterers [2].

At still higher pulsation amplitudes, the bubble can change the environment: simple characterizations have discussed how the compressed gas can attain temperatures of thousands of degrees, causing the production of highly reactive chemical species, which in turn can affect species in the gas or liquid, including DNA. In fact, shock waves can occur in the bubble gas and liquid, particularly if the bubble involutes during collapse, such that a high speed liquid jet passes through the bubble and impacts the far bubble size, causing GPa blast waves [21-23]. These can cause physical damage, which can be detrimental (e.g. erosion to propellers [24]) or beneficial (e.g. in the destruction of kidney stones [23, 25, 26]).

3. Oceans and climate change

The power of acoustics to detect and characterize bubble populations brings obvious benefits to the petrochemical industry (Fig. 1b). However, there are also significant implications for climate science. The oceans act as a significant sink of anthropogenic carbon dioxide [27, 28], yet most historical calculations have assumed that the ocean is an unbroken surface [29, 30]. Bubbles not only increase the effective surface area of transfer for atmospheric gas to dissolve into, and exsolve out of, the oceans – they also remove the process from chemical equilibrium conditions because the excess pressure in the bubble gas (caused by the effects of surface tension and hydrostatic pressure) tends to favour dissolution.

To quantify the climatically-important carbon transfer mediated by bubbles trapped through breaking ocean waves, we can assess the number of bubbles (and their size) injected into the ocean using passive acoustics. However, it is not sufficient simply to know how many bubbles are injected into the ocean by breaking waves. One must also know how many are left some time after the wave has broken, after some bubbles have risen to the surface, and others have dissolved. To do this, we project sound at the bubble clouds [3, 15, 31, 32], and from the scatter we quantify how this undersea bubble population evolves, producing models of the shape and size of the undersea bubble clouds [Fig. 1a]. Such models [33-35] allow us to quantify the effect of bubbles on the transfer of carbon between atmosphere and ocean.

The transport of atmospheric carbon in the form of carbon dioxide is well known to have climatic significance. However methane has the ability to generate ‘greenhouse’ warming per molecule of methane gas that is at least 20 times greater than that of each CO₂ molecule [36], and any assessment

of marine gas reserves should also factor in the potential contribution from hydrate dissociation, which will be promoted through warming associated with climate change [37]. The assessment of Dillon [38] is that the global reserve of methane in the form of hydrate is more than twice the worldwide amount of carbon to be found in all known conventional fossil fuels on Earth. Therefore in the past decade, significant attention has been paid to the acoustics of the seabed near natural seeps of methane and carbon dioxide, and to the regions where CO₂ (anthropogenically trapped from the atmosphere) might be stored in depleted seabed oil and gas reservoirs. The world's first gas injection tests, to test acoustic (and other) methods of detecting gas leaks from such sources, and their impact, have recently been conducted [39, 40].

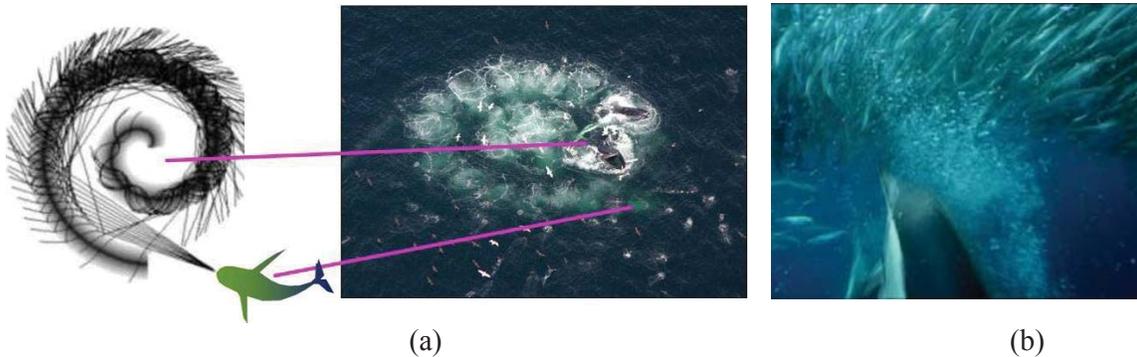


Figure 2: (a) Model (left) of acoustic rays based on a photographed spiral bubble net (modelling from Leighton *et al.* [41, 42]; photo by T. Voorheis of Gulf of Maine Production). (b) Image of a dolphin blowing bubbles to catch fish (Image courtesy of The Blue Planet. BBC).

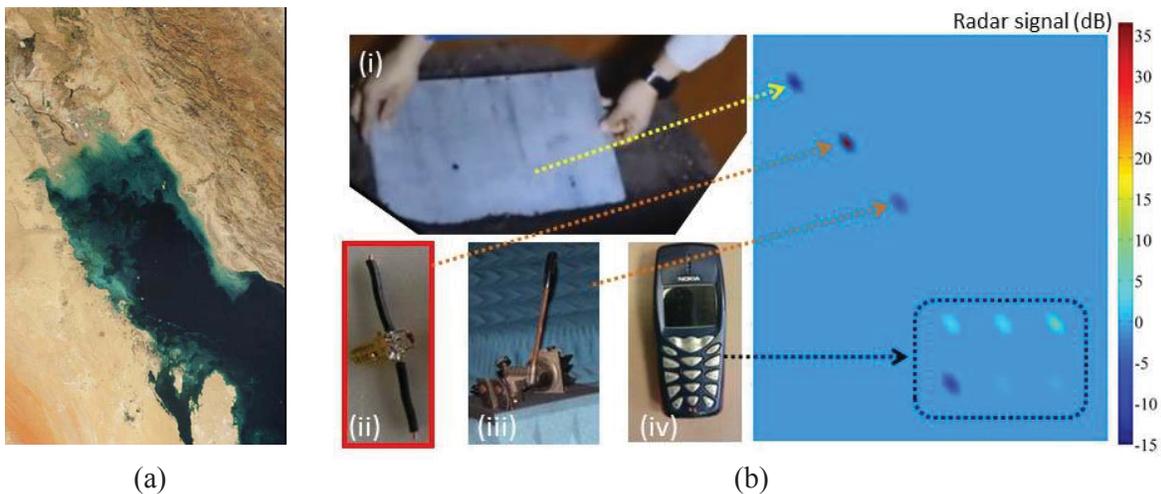


Figure 3: (a) Aerial image of Persian Gulf (mage courtesy J. Desclotres, MODIS Land Rapid Response Team at NASA GSFC). (b) TWIPR Radar signal from (i) an aluminium plate, (ii) a circuit resembling components of a bomb trigger; (iii) a rusty bench clamp; (iv) mobile phones in various states (on, off, or with invalid SIM cards) See [48] for details.

4. Marine mammals and bubbles

Our ability to model the scattering of sound by undersea bubbles allowed us to postulate the mechanism by which humpback whales trap prey within spiral bubble nets. Although it had been known for decades that whales blow bubbles to do this, the reason why the prey do not escape the trap was not known [14]. Our models [Fig. 2(a)] showed that the spiral bubble net traps the loud calls emitted by whales to produce an impassable ‘wall of sound’, whilst simultaneously creating a quiet zone in

which the prey would congregate, this zone appearing to occur (in the limited data available) in the model at the exact location where the rising whales feed [as photographed in Fig. 2(a)] [41-43].

However, unlike humpback whales, dolphins use high frequency sonar to find prey, and the bubble nets they create [Fig. 2(b)] would confound their sonar. Rather than accept that such dolphins would ‘blind’ their most spectacular sensory apparatus when hunting, we set about proving that a previously unknown type of sonar processing (TWIPS) could detect prey in bubble nets [19, 44]. This was shown to work with dolphin sonar calls [45], although the question of whether odontocetes use such a method or not is still open to question [46, 47]. Industry is now developing this to protect shipping in coastal regions such as the Persian Gulf, where clouds of bubbles and particles in the near-shore waters make mine detection difficult [Fig. 3(a)]. Realizing that this new processing system could work with radiations other than just sonar, we used it to develop a radar system (TWIPR) where the scattering off circuitry from a bomb trigger was more than 30 dB more powerful than the scattering off other targets [Fig. 3(b)] [48]. With the ability selectively to detect mobile phones as readily as bomb triggers, TWIPR can help finding buried targets of interest (bombs, people carrying phones buried by collapsed buildings or avalanches) where normal radar would not be able to identify the genuine target from other debris [typified in Fig. 3(b) by (i) & (iii)].

5. Extraterrestrial bubble acoustics

The ability to infer the bubble sizes generated from the sounds of waterfalls and breaking waves (as discussed above) was used to create [14, 49] the possible sound of ‘methanefalls’ (waterfalls made up of liquid methane and ethane) on Saturn’s largest moon, Titan. As the Cassini-Huygens mission approached Titan in 2004, no-one knew what the surface would be like because Titan is shrouded in a thick fog. However, one body of opinion held that, with a 93 K surface temperature, the cold conditions and dense atmosphere would allow for the existence of lakes and possibly methanefalls.

Prior to Huygens’ landing, we simulated the sound that would be made were Huygens to splash-down in a lake, and the sound that a probe on the surface of Titan might detect if it landed with its camera facing away from the methanefall. Huygens was very successful, and although its images from its landing site revealed a barren landscape (Fig. 4(a)), during descent some indication of topography that might have been carved by flowing surface liquid was revealed (Fig. 4(b)), and later radar observations by Cassini revealed lakes (Fig. 4(c)).

The objective of our research was to provide material for outreach, but also to explore the extent to which we might start to construct the soundscapes of other worlds. Despite all the planetary probes that have been sent out, we have not yet heard the soundscape of another world [50]. Consequently, this work was conducted for the purpose of:

- enabling better design of microphones and sound sources for use on future planetary probes, with respect to improving signal to noise ratios, more reliably interpreting any detected signals, and enabling and maintaining an appropriate calibration given the differences between Earth’s environmental parameters and the deployment environments (which can vary hugely even over a single world like Venus or Jupiter) [51-55];
- improving the design of missions exploiting acoustics in planetary exploration (for example, by correcting the analysis used to predict the correct placement of detectors on ice-covered moons like Jupiter’s moon Europa, with the purpose of using sound to explore the vast water oceans beneath the ice [56-58]);
- eliminating errors in mission planning introduced by use of familiar Earth-based acoustics to extraterrestrial environments [53];
- exploring the extent to which we might interpret sounds picked up by planetary probes to ascertain key features about the world the probe is exploring [59,60].

For this latter objective, in designing the algorithms to simulate the sounds of worlds, we were able to provide a device, licensed to planetaria [59], which not only allows the audience to hear the

simulated sound of the world under discussion, but in live presentations allows the presenter to use the voice they would have on a given planet (if they could live and speak), when telling schoolchildren about that planet [61]. More details on this topic are available on the Internet [62].

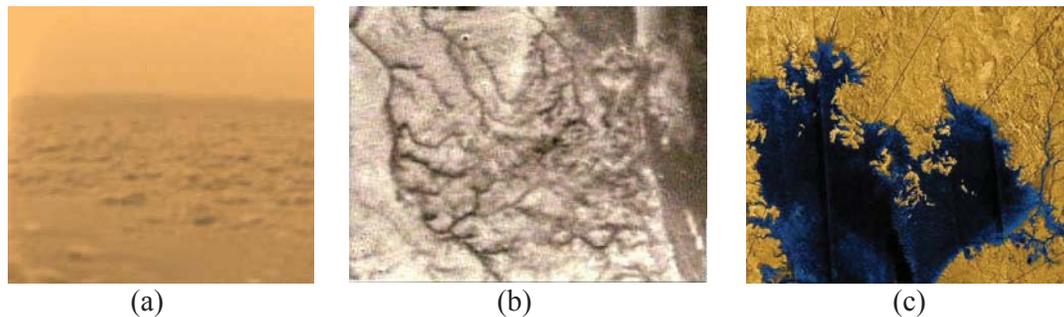


Figure 4: *Cassini-Huygens* images of Titan. (a) Titan's surface at Huygens' landing site. (b) Titan's surface imaged by *Huygens* during descent. (c) False-colour Cassini radar image of Titan's surface. Blue colouring indicates low radar reflectivity, attributed to hydrocarbon seas, lakes and tributary networks of liquid ethane/methane. Credit: NASA/JPL/Caltech.

6. A role for bubble acoustics to mitigate the 'antibiotic apocalypse'

The 'antibiotic apocalypse' is in fact a broader problem than simply our 'running out of antibiotics': within a decade we will encounter increasing failure of current interventions to combat infections and parasites, as an unstoppable consequence of evolution.

AntiMicrobial Resistance (AMR) is the increasing resistance of microbes to the drugs that treat them: the ability of bacteria to resist antibiotics, the ability of viruses to resist antiviral agents, the ability of fungi to resist antifungal agents, and the ability of parasites (such as those which cause malaria) to resist the drugs used against them.

We steer our global policy, and teach our children, around the predictions that, by the end of the century, climate change will bring in changes in sea level and ice coverage, extreme weather and flooding. These in turn affect human migration and disease, food and water supplies, and generate conflict, instability and market perturbations. Some of the grandparents living then, will never have met their mothers, because those women (our grandchildren) will have died of a 'superbug' infection following routine childbirth. As those children grow up, from 2050 to the end of the century, the inability to treat infection will have increased, because of AMR.

In 2050 we will pass the so-called Antibiotic Apocalypse, when the rise of drug-resistant superbugs will be killing more people than cancer, and after that things will become worse. The UK Government-commissioned O'Neill report [63] states "by 2050, 10 million lives a year and a cumulative 100 trillion USD of economic output are at risk due to the rise of drug-resistant infections if we do not find proactive solutions now to slow down the rise of drug resistance. Even today, 700,000 people die of resistant infections every year... If [antibiotics] lose their effectiveness, key medical procedures (such as gut surgery, caesarean sections, joint replacements, and treatments that depress the immune system, such as chemotherapy for cancer) could become too dangerous to perform. Most of the direct and much of the indirect impact of AMR will fall on low and middle-income countries" (LMICs). The report sets out a 10 point plan for action which it states will only succeed through a "global coalition for action on AMR". The recent 'Wilton Meeting' organised by the Foreign and Commonwealth Office (FCO) looked at the issue of AMR in LMICs, stating [64] "The relative lack of population data regarding the level, complex spread and patterns of resistance in human, animal and agricultural contexts prevents many countries from recognising the true extent of the problem and also prevents the formulation of evidence-based intervention design and monitoring."

What has been the response to the above authoritative reports [63, 64] on AntiMicrobial Resistance? – a consensus to act from the UN [65], intermittent coverage by the media when they find the ‘answer to antibiotic resistance’ [66], and the allocation of research funds. However, the allocation of funds is not a strategy. Wisdom is needed, because the above responses all contain the improbably optimistic implicit assumptions that:

- ‘someone’ will produce an antibiotic replacement that is effective and to which resistance will never develop faster than we can produce replacements;
- behaviour of the public, prescribers, retailers and food producers will change from current levels of antimicrobial guardianship [67] to a sustainably responsible level.

Should we not have a dedicated parallel plan resourced for a future where the steps to proper guardianship were implemented too late, with insufficient effectiveness or global coverage, and where any new antibiotic replacements were only a stopgap against their own imminent resistance issues? That is to say, should we not plan for a world without antibiotics? That is the role of NAMRIP (the Network for Anti-Microbial Resistance and Infection Prevention) [68]. NAMRIP considers the wider picture beyond the simple action of a clinician giving a patient a therapeutic drug once the infection has become established (a small portion of the top right quadrant of Fig. 5).

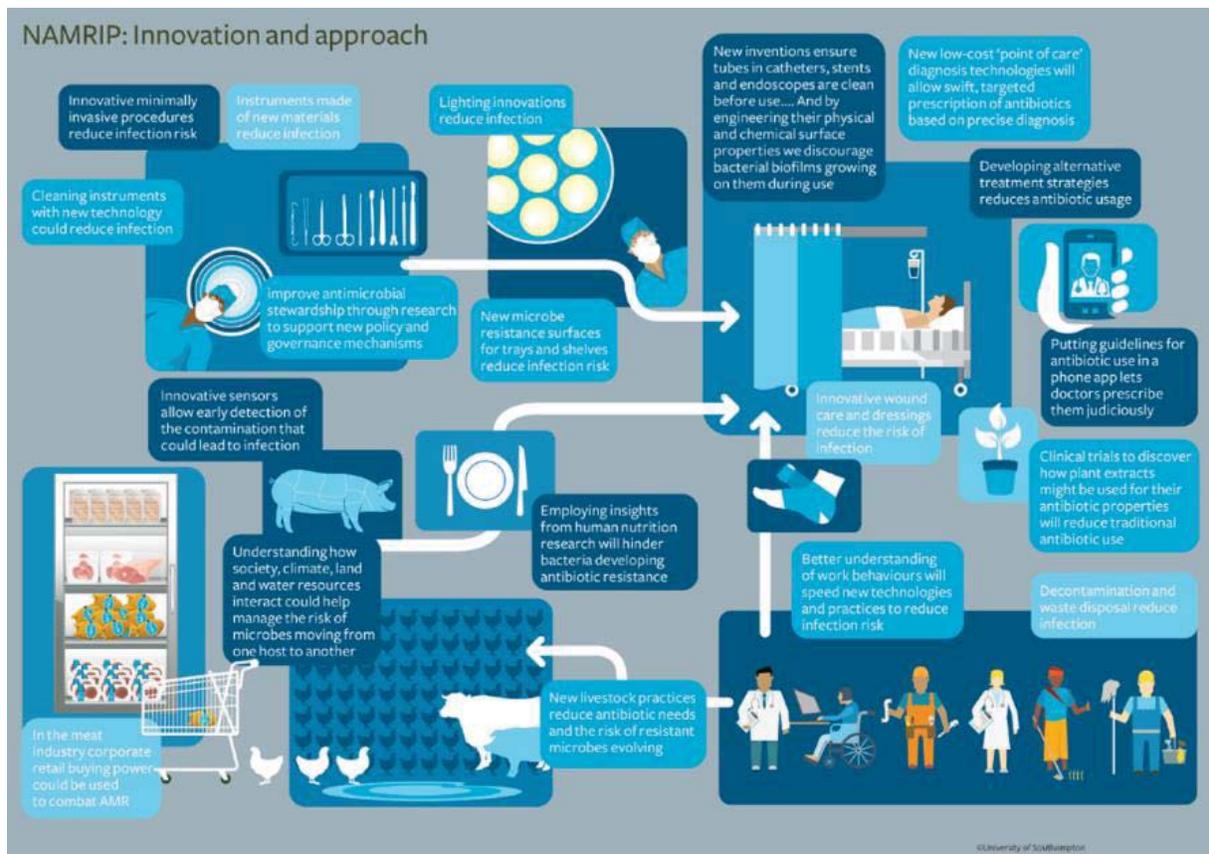


Figure 5: NAMRIP’s approach (for further details see [68]).

One aspect is to look at prevention, rather than cure: if we can prevent the microbe entering the body, we need never apply the anti-microbial drug. The picture is however complex. For example, an under-rated protection against AMR is healthy skin. For many (but not all) microbes, healthy skin is an effective barrier. This can lead to a discussion of the roles in AMR of wound treatment and new minimally invasive surgical procedures. However skin can also be a potent vehicle for transporting unwanted microbes, e.g. when hands carry microbes to eyes, mouth, nose etc. Handwashing reduces such hazard, but can degrade skin integrity [69], which might lead to infection. Gloves protect the wearer, but their use can sometimes lead to behaviour that increase the chance of cross-infection [70].

Cleaning can therefore be effective, but multifaceted. Inadequate cleaning produces severe public health issues in hospitals [71, 72] and food preparation. From major factories in the industrialized world to the local abattoir in the developing world, the mismatch between the volumes of water and additives used, and the robustness of the water supplies on which we depend, is failing to do its part in mitigating against future crises in water supplies, food production, and healthcare [73].

One particular innovation was the Ultrasonically Activated Stream (UAS, invented at the University of Southampton and now in production by Ultrawave Ltd. under the name StarStream™), which enhances the cleaning ability of liquids, and in particular enables cold water cleaning. The UAS system, like the ultrasonic cleaning bath, bases its cleaning action on the speed of the bubble wall motion, and not (like pressure washers) on the speed of the flow. As such it will be less damaging than pressure washers. UAS produces a free flowing liquid stream, each nozzle generating flows of around 2 litres min⁻¹. Here the cleaning action of bubbles, excited with a suitable ultrasonic field, is generated at the end of a fluid stream. In addition, low flow rates of fluid within this approach are useful in releasing the contaminant from the surface and avoiding re-deposition at another location (a further possible limitation in bath geometries). Using higher frequencies and generating lower amplitudes of ultrasound in air than cleaning baths, StarStream has not had any reports of the ‘subjective’ adverse effects (headaches, nausea, tinnitus, migraine etc.) anecdotally attributed to some other sources of ultrasound in air, by, for example, some (but by no means the majority of) users of ultrasonic cleaning baths [74, 75]. The low velocity stream approach has many advantages; however, two basic criteria are necessary for this strategy to be successful. First, the sound field must be sufficient to generate bubble activity at the solid/liquid interface of the material to be cleaned. Second, a suitable bubble population must also be present on the surface of the target that needs cleaning. This population can then be driven by the sound field deployed and act on the contaminant at the interface in question (through suitable oscillation [76-79] and shear forces). These two requirements are by no means simple to create within a flowing stream but this has successfully been achieved in the UAS system.

The ultrasonic cleaning bath causes cavitation, whereby bubbles collapse under pressure fields to generate extreme conditions [80-82], which can include the generation of free radicals [11, 83] and strong pressure waves [84-85] from the gas compression, although significantly more powerful ones can occur in the blast waves launched when collapsing bubbles involute to form microjets [21-23]. Pressure waves and jet impact can remove material from surfaces [10, 24]. In contrast, the UAS system projects sound down a column of water [86] in order to excite surface waves [87] on the walls of microscopic bubbles on the surface to be cleaned. These surface waves can generate convection [88-91] and shear forces [92, 93] in the liquid close to the bubble wall, and so produce a cleaning effect, altering the way material deposits onto surfaces [12].

A Mark I StarStream prototype was compared on paper against two commercial washing/disinfecting systems (see Appendix) and shown would make: 79-97% of energy savings (primarily through not having to heat the water, which brings the additional benefit of making it suitable for targets that cannot withstand hot water – fig. 6); 100% of additive savings; and 83-99% of water savings (note however that a Mark I StarStream recycles water, and these water savings would become losses in a non-recycling mode – see Appendix). Because a single UAS nozzle treated instruments one at a time, and was being compared to batch processors, the duration of the treatment was 150-300% worse. Using multiple nozzles to treat instruments simultaneously would reduce the savings in energy and water commensurately. Therefore the most efficient use of UAS would be to substitute it for an identical process, e.g. when instruments are first rinsed under a normal tap immediately after use, one at a time, before being entered into the batch processor washer/disinfectant chain.

The basic principle of the UAS device is that cold water is fed into a hollow horn that contains an ultrasonic transducer operating in excess of 100 kHz. The ultrasound and microbubbles in the flow both travel down the stream of water to the target that is to be cleaned. If the bubbles are ultrasonically activated when they are on the target, the cleaning ability of the liquid is enhanced in four ways:

(i) The bubbles are attracted to the surface to be cleaned by Bjerknes radiation forces [17, 94], and are not as rapidly washed away by the flow as they would be in the absence of ultrasound. (ii) The

bubbles are particularly attracted into crevices by secondary Bjerknes radiation forces [17, 94]; such crevices are traditionally more difficult to clean by wiping or brushing. (iii) Surface waves on the walls of the bubble, excited by the ultrasound, produce enhanced convection in the liquid and enhanced shear in the contaminant, causing its removal. (iv) The progress of the bubble into the crevices would, if the liquid contained additives (e.g. detergent or biocide) cause that additive to penetrate the crevice far more rapidly than would reliance on simple diffusion, so that cleaning can potentially be achieved more rapidly, and with lower concentrations of additives.

The effectiveness of the UAS system has been demonstrated in controlled tests on particularly difficult problems, specifically on: the cleaning of brain tissue and prions from surgical steel, the removal of contaminating material from bone transplants [95]; the removal of biofilms of dental bacteria [95, 96]; the cleaning of skin models [95, 97]; the cleaning of marine biofoulant [98]; the cleaning of railway track [99]; the cleaning of hands, kitchen surfaces, tools, glue from jar labels, contaminated tubes, and components of railway locomotives [94, 100].



Figure 6: One half of a lettuce is cleaned with cold water, and the other half is cleaned with the same cold water to which bubbles and ultrasound have been added using the StarStream technology (for video see [101]).

Some targets, of course, can only be cleaned with cold water and, preferably, with no detergents or biocide added. Figure 6 shows the removal of soil from lettuce using StarStream (for video see [101]). This might at first sight seem a straight, non-medical illustration for AMR, an example of cleaning from the food retail sector. However AMR is a multidisciplinary issue, and opening up a new food retail link between two countries will open up a route to spread drug resistance across continents, making it an issue for food scientists, transportation scientists, microbe detectors, cleaning and refrigeration engineers, economists and lawyers. AMR is spreading (Fig. 7) and in 15 years what we see now as usually mild gastric upsets from food poisoning, will be fatalities. This makes it, in addition, an issue for social scientists studying handwashing, and sewage engineers, and of course makes the effect of AMR on the food retail sector (and vice versa) a healthcare issue.

Furthermore, we must look beyond our first world solutions to AMR, because the spread of AMR (Fig. 7) means that measures to mitigate against its development and spread must be effective for the billions of people worldwide, and their livestock. Much of the world does not have adequate access to clean water, and a given low/middle income country (LMIC) might see inadequate access to drugs in rural areas, and yet over-the-counter access to inappropriate antibiotics in other areas [102].

Here too, UAS might have a role to play. A healthcare worker in a rural LMIC (or an army medic, or mountain rescue or catastrophe zone worker) might carry a limited amount of drinking water, but appreciate having the ability (when the need arises) to pass his/her remaining drinking water reserves through a battery-powered StarStream nozzle in order to clean a wound for a few minutes [94]. Battlefield and catastrophe zone wounds can be extremely hazardous, and sepsis can set before the victim arrives at hospital. Cleaning the wound first can reduce that hazard, a procedure equally important for rural clinics (including maternity services) [103].

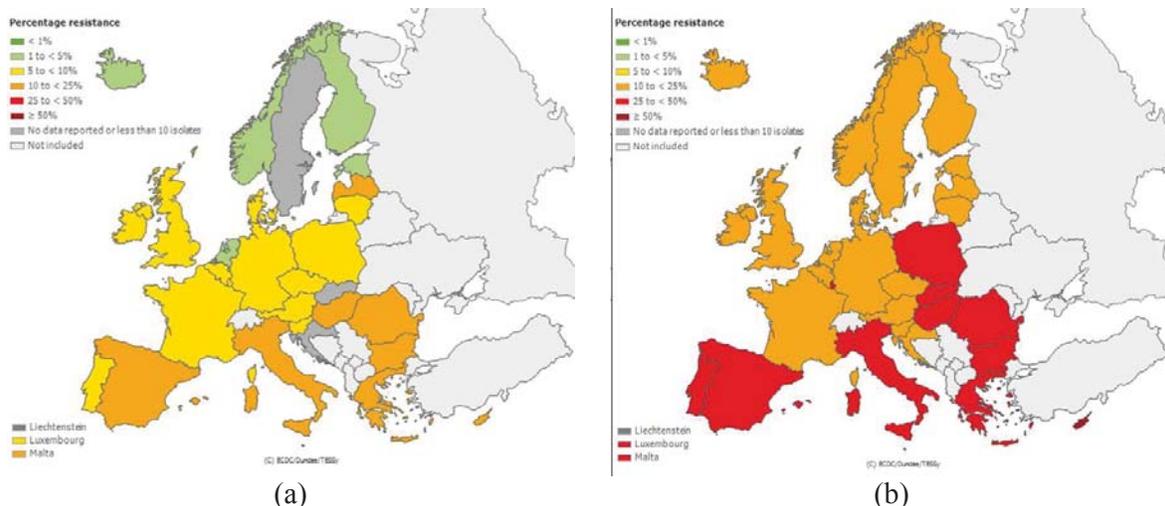


Figure 7: The distribution of E. Coli resistant to cephalosporins in (a) 2009 and (b) 2013 [104].

7. Conclusions

The interaction of bubbles with acoustic fields provides a route by which fundamental research, covering physics, engineering, zoology, biophysics and biomedicine can be conducted and translated through to benefit society.

A key opportunity for bubble acoustics is in cold water cleaning, and its potential to address AMR. Unless preventative measures are found (and no-one in the world currently knows what those will be), AMR will (through the colloquial ‘rise of superbugs’) by 2050 be killing more people than cancer, and cost the world economy more than the current size of the global economy. We will not be able to feed the world unless we wean our food production industry off its dependence on antibiotics; common medical procedures (minor surgery, childbirth) will become significantly more hazardous; and advances in treatments (such as those for childhood leukaemia) will become reversed.

To offset this doom, the benefits for finding these preventative measures now would revolutionise current healthcare and food production, and in these too bubble acoustics might have a role to play.

8. Appendix

A performance test of a new cleaning technology is insufficient to assess its practicality. The requirement for operator training must be taken into account. In this UAS fares well, as the prototype was not difficult to operate, and did not require extensive training. Running costs are also an issue, and so an estimate was made of resource usage, and compared to that of a commercial washer-disinfector, which can wash up to 500 instruments in the decontamination cycle given in Table 1. Table 2 compares resource requirements of the UAS system used in the paper, and the commercial washer-disinfector system, to clean 500 instruments. It must be stressed that both were paper exercises.

The UAS system saves energy (primarily because it does not have to heat the water), and uses no additives. The saving on water shown in Table 2 is marked with an asterisk to indicate that it needs to be treated with caution. The Mark I StarStream was designed to be portable, and usually (as here) operates by recycling the water. That is to say, water spilling from the item to be cleaned is caught in a tray and pumped back through the device, so that the system only uses 1.5 litres of water. Whilst an attractive feature for some uses (e.g. reducing the amount of contaminated run-off that must be disposed of, or operating in a catastrophe where water is scarce), it is unappealing to clean in this way. If the device were to have been continually fed with fresh water, it would have consumed 375 litres of water, 74% more than the washer-disinfector.

Table 2 shows that, in this like-for-like comparison, the Mark I StarStream was three time slower than the washer disinfector. A like-for-like comparison sets up for the optimum conditions of the

washer-disinfector, and a sequentially-washing UAS system would not be intended to replace a bulk-washing system like this. However the results suggest that the incorporation of a pre-wash immediately after instrument use is not impractical in terms of resource usage.

One estimate (Table 1) gives limited information, and therefore a second paper exercise was conducted to compare the use of the UAS system used in this paper with another bulk-washing system, the use of a modern ultrasonic cleaning bath intended for cleaning dental instruments (and equipped with an automated system to ensure the bath is used properly, e.g. by locking the bath for the duration of a full wash and issuing a record of the wash). Table 3 gives data for the resource usage by Hygea 2. Detergent is added at start up. When loaded to maximum capacity it washes 45 instruments per cycle. The Hygea 2 uses two 50 W ultrasonic transducers, so there is 100 W power usage for ultrasonics, plus more for heating (data taken from Hygea 2 Instruction Manual & ECN product database).

Table 1: Usage of power and water in the state-of-the-art washer-disinfector, showing that: Total energy used heating water = 49.2 MJ; Total water used = 216 litres; Max time (not including drying) = 85 mins. Data from [105].

Stage	Water Description	Time (mins) [max from cycle description]	Temperature (°C) [mid-value from cycle description]	Water consumption (litres) [106]	Energy (MJ) to heat water, assuming 7.3°C for water from the cold tap [107].
Pre-wash	Cold water	15	Max 21 °C	36	2.0
Enzyme	Hot tap water + enzyme	15	65 °C	36	8.7
Wash	Hot tap water + detergent	15	65 °C	36	8.7
Neutralise	Hot tap water + neutraliser	15	65 °C	36	8.7
Rinse	Hot tap water	15	65 °C	36	8.7
Thermal rinse	Hot pure water	10	90 °C	36	12.4

Table 2: Because the washer-disinfector of Table 1 cleans 500 instruments at a time, a side-by-side comparison is done between the resource needed for that, and the resource needed to clean 500 instruments one after another, spending 30 s on each instrument, using the UAS system described in this paper. See text re *.

Row	Device	Energy (MJ)	Additives	Water (litres)	Time taken (s)
α	Washer-disinfector	49.2	enzyme, detergent & neutraliser	216	5100
β	Mark I StarStream	1.5	none	1.5 *	15,000
% difference	$\frac{\alpha - \beta}{\alpha} \times 100\%$	-97%	-100%	-99% *	+294%

Table 3: The resource usage of the Hygea 2 ultrasonic cleaning bath (Ultrawave Ltd.).

Stage	Water Description	Time (mins) [max from cycle description]	Temperature (°C) [mid-value from cycle description]	Water consumption (litres) [106]	Energy to heat water and power ultrasound (kJ) [assuming 7.3°C for water from the cold tap [107]].
Wash	Hot tap water + detergent	10	25 °C	8	653
Rinse	Tap water	2	At tap	1	0

Table 4: Because the washer-disinfector of Table 1 cleans 500 instruments at a time, a side-by-side comparison is done between the resource needed for that, and the resource needed to clean 500 instruments one after another, spending 30 s on each instrument, using the UAS system described in this paper. See text re *.

Row	Device	Energy (kJ)	Additives	Water (litres)	Time taken (s)
α	Hygea 2	653	detergent	9	810
β	Mark I StarStream	135	none	1.5 *	1350
% difference	$\frac{\alpha - \beta}{\alpha} \times 100\%$	-79%	-100%	-83% *	+166%

Since a fully loaded Hygea 2 washes 45 instruments, Table 4 compares the resource it takes with that which would be used if the UAS system mentioned in this paper were used to clean 45 instruments one after another, spending 30 s on each one.

As before, the UAS system used saves 100% on additives and uses only 21% of the energy used by the Hygea 2. The saving in water must be taken in the context that this paper's UAS system was used in recycling mode, and if it had been connected to a supply of clean water it would have consumed around 34 litres, nearly 4 times as much as the Hygea 2. Again, as before, the UAS system is nearly twice as slow, because the Mark I StarStream can only clean items sequentially and it is being compared to a bulk cleaner operating in its optimal conditions.

Clearly therefore if advantage is to be taken of the opportunities (cold water, low training requirements, little resource equipment, low space footprint, no additive requirement) that UAS systems potentially offer, it is likely to be in the pre-wash or rinse immediately after use, where the instruments are treated one at a time.

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REFERENCES

- 1 Leighton, T. G. and Walton, A. J. An experimental study of the sound emitted from gas bubbles in a liquid, *European Journal of Physics*, **8**, 98-104, (1987).
- 2 Phelps, A. D., Ramble, D. G. and Leighton, T. G. The use of a combination frequency technique to measure the surf zone bubble population, *J. Acoust. Soc. Am.*, **101**(4), 1981-1989, (1997).
- 3 Phelps, A. D. and Leighton, T. G. Oceanic bubble population measurements using a buoy-deployed combination frequency technique, *IEEE Journal of Oceanic Engineering*, **23**(4), 400-410, (1998).
- 4 Pascal, R. W. *et al.* A spar buoy for high-frequency wave measurements and detection of wave breaking in the open ocean, *Journal of Atmospheric and Oceanic Technology*, **28**(4), 590-605, (2011).
- 5 Brooks, I. M. *et al.* Physical Exchanges at the Air Sea Interface: UK SOLAS Field Measurements, *Bulletin of the American Meteorological Society*, **90**, 629-644, (2009).
- 6 Leighton, T. G. and White, P. R. Quantification of undersea gas leaks from carbon capture and storage facilities, from pipelines and from methane seeps, by their acoustic emissions, *Proc. Roy. Soc. A*, **468**, 485-510, (2012).
- 7 Clarke, J. W. L. and Leighton, T. G. A method for estimating time-dependent acoustic cross-sections of bubbles and bubble clouds prior to the steady state, *J. Acoust. Soc. Am.*, **107**(4), 1922-1929, (2000).
- 8 Leighton, T. G., Ramble, D. G. and Phelps, A. D. The detection of tethered and rising bubbles using multiple acoustic techniques, *J. Acoust. Soc. Am.*, **101**(5), 2626-2635, (1997).
- 9 Richards, S. D., Leighton, T. G. and Brown, N. R. Visco-inertial absorption in dilute suspensions of irregular particles, *Proc. Roy. Soc. A*, **459**(2038), 2153-2167, (2003).
- 10 Pickworth, M. J. W., Dendy, P. P., Twentyman, P. R. and Leighton, T. G. Studies of the cavitation effects of clinical ultrasound by sonoluminescence: 4. The effect of therapeutic ultrasound on cells in monolayer culture in a standing wave field, *Physics in Medicine and Biology*, **34**(11), 1553-1560, (1989).
- 11 Birkin, P. R., Power, J. F. and Leighton, T. G. Electrochemical evidence of H• produced by ultrasound, *J. Chem. Soc. Chemical Communications*, **21**, 2230-2231, (2001).
- 12 Offen, D. G., Birkin, P. R. and Leighton, T. G. Electrodeposition of copper in the presence of an acoustically excited gas bubble, *Electrochemistry Communications*, **9**(5), 1062-1068, (2007).
- 13 Leighton, T. G. What is ultrasound? *Progress in Biophysics and Molecular Biology*, **93**(1-3), 3-83, (2007).

-
- 14 Leighton, T. G. From seas to surgeries, from babbling brooks to baby scans: The acoustics of gas bubbles in liquids, *International Journal of Modern Physics B*, **18**(25), 3267-3314, (2004).
 - 15 Leighton, T. G., Meers, S. D. and White, P. R. Propagation through nonlinear time-dependent bubble clouds and the estimation of bubble populations from measured acoustic characteristics, *Proc. Roy. Soc. A*, **460**(2049), 2521-2550, (2004).
 - 16 Leighton, T. G. How can humans, in air, hear sound generated underwater (and can goldfish hear their owners talking)? *J. Acoust. Soc. Am.*, **131**(3 Pt 2), 2539-2542, (2012).
 - 17 Leighton, T. G. *The Acoustic Bubble*, Academic Press, 640pages (ISBN 0124419208) (1994).
 - 18 Leighton, T. G. and Robb, G. B. N. Preliminary mapping of void fractions and sound speeds in gassy marine sediments from subbottom profiles, *J. Acoust. Soc. Am.*, **124**(5), EL313-EL320, (2008).
 - 19 Leighton, T. G., Finfer, D. C., Chua, G. H., White, P. R. and Dix, J. K. Clutter suppression and classification using Twin Inverted Pulse Sonar in ship wakes, *J. Acoust. Soc. Am.*, **130**(5), 3431-3437, (2011).
 - 20 Leighton, T. G., Ramble, D. G., Phelps, A. D., Morfey, C. L. and Harris, P. P. Acoustic detection of gas bubbles in a pipe, *Acustica with Acta Acustica*, **84**(5), 801-814, (1998).
 - 21 Turangan, C. K., Jamaluddin, A. R., Ball, G. J. and Leighton, T. G. Free-Lagrange simulations of the expansion and jetting collapse of air bubbles in water, *Journal of Fluid Mechanics*, **598**, 1-2, (2008).
 - 22 Jamaluddin, A.R., Ball, G.J., Turangan, C.K. and Leighton, T.G. The collapse of single bubbles and calculations of the far-field acoustic emissions for cavitation induced by shock wave lithotripsy, *J. Fluid Mech.*, **677**, 305-334, (2011).
 - 23 Leighton, T. G., Turangan, C. K., Jamaluddin, A. R., Ball, G. J. and White, P. R. Prediction of far-field acoustic emissions from cavitation clouds during shock wave lithotripsy for development of a clinical device, *Proc. Roy. Soc. A*, **469**(2150), 20120538, (2013).
 - 24 Birkin, P. R., Offin, D. G. and Leighton, T. G. Electrochemical measurements of the effects of inertial acoustic cavitation by means of a novel dual microelectrode, *Electrochemistry Communications*, **6**(11), 1174-1179, (2004).
 - 25 Leighton, T. G., Fedele, F., Coleman, A., McCarthy, C., Ryves, S., Hurrell, A., De Stefano, A. and White, P. R. A passive acoustic device for real-time monitoring the efficacy of shockwave lithotripsy treatment, *Ultrasound in Medicine and Biology*, **34**(10), 1651-1665, (2008).
 - 26 Leighton, T. G. and Cleveland, R. O. Lithotripsy, *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, **224**(2), 317-342, (2010).
 - 27 Ciaia, P. *et al.* Carbon and other biogeochemical cycles. In: *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change* (Stocker, T.F *et al.* eds.) Cambridge University Press, (2013).
 - 28 Rhein, M. *et al.* Observations: Ocean. In: *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change* (Stocker, T.F *et al.* eds.) Cambridge University Press (2013).
 - 29 Takahashi, T. *et al.* Climatological mean and decadal change in surface ocean pCO₂, and net sea-air CO₂ flux over the global oceans, *Deep-Sea Res. II*, **56**, 554-577, (2009).
 - 30 Watson, A. J. *et al.* Tracking the Variable North Atlantic Sink for Atmospheric CO₂, *Science*, **326**, 1391-1393, (2009).
 - 31 Farmer, D. M. and Vagle, S. Waveguide propagation of ambient sound in the ocean-surface bubble layer. *J. Acoust. Soc. Am.*, **86**, 1897-1908 (1989).
 - 32 Breitz, N. D. and Medwin, H. Instrumentation for in situ acoustical measurements of bubble spectra under breaking waves, *J. Acoust. Soc. Am.*, **86**, 739-743, (1989).
 - 33 Blomquist, B. W., Fairall, C. W., Huebert, B. J., Kieber, D. J. and Westby, G. R. DMS sea-air transfer velocity. Direct measurements by eddy covariance and parameterization based on the NOAA/COARE gas transfer model, *Geophys. Res. Lett.*, **32**, 10.1029/2006GL025735, (2006).
 - 34 Thorpe S. On the clouds of bubbles formed by breaking wind-waves in deep water, and their role in air-sea gas transfer, *Philos. Trans. R Soc London A*, **304**, 155-210, (1982).
 - 35 Jeffery, C. D., Robinson, I. S. and Woolf, D. K. Tuning a physically-based model of the air-sea gas transfer velocity, *Ocean Modelling*, **31**, 28-35, (2010).

-
- 36 Khalil, M. A. K. and Rasmussen, R. A. The changing composition of the Earth's atmosphere. In *Composition, chemistry, and climate of the atmosphere* (ed. H. B. Singh), pp. 50–97. New York, NY: Van Nostrand Reinhold, (1995).
- 37 Westbrook, G. K. *et al.* Escape of methane gas from the seabed along the West Spitsbergen continental margin, *Geo. Res. Lett.* **36**, L15608, (2009).
- 38 Dillon, W. *Gas (methane) hydrates: a new frontier*. US Geological Survey, Marine and Coastal Geology Program Fact Sheet, OCLC No.: ocm40490917. Coastal and Marine Geology Program (Geological Survey), US Geological Survey, US Department of the Interior, Woods Hole, MA, (1995).
- 39 Berges, B. J. P., Leighton, T. G. and White, P. R. Passive acoustic quantification of gas fluxes during controlled gas release experiments, *International Journal of Greenhouse Gas Control*, **38**, 64-79, (2015).
- 40 Blackford, J., *et al.* Detection and impacts of leakage from sub-seafloor deep geological carbon dioxide storage, *Nature Climate Change* **4**(11), 1011-1016, (2014).
- 41 Leighton, T. G., Finfer, D., Grover, E. and White, P. R. An acoustical hypothesis for the spiral bubble nets of humpback whales and the implications for whale feeding, *Acoustics Bulletin*, **22**(1), 17-21, (2007).
- 42 Leighton, T. G., Finfer, D. C. and White, P. R. Cavitation and cetacean, *Revista de Acustica*, **38**(3/4), 37-81, (2007).
- 43 Leighton, T. G. and White, P. R. Dolphin-inspired target detection for sonar and radar, *Archives of Acoustics*, **39**(3), 319-332, (2014).
- 44 Leighton, T. G., Finfer, D. C., White, P. R., Chua, G. H. and Dix, J. K. Clutter suppression and classification using Twin Inverted Pulse Sonar (TWIPS), *Proc. Roy. Soc. A*, **466**, 3453-3478, (2010).
- 45 Leighton, T. G., Chua, G. H. and White, P. R. Do dolphins benefit from nonlinear mathematics when processing their sonar returns? *Proc. Roy. Soc. A*, **468**, 3517-3532, (2012).
- 46 Chua, G. H., White, P. R. and Leighton, T. G. Use of clicks resembling those of the Atlantic bottlenose dolphin (*Tursiops truncatus*) to improve target discrimination in bubbly water with biased pulse summation sonar, *IET Radar Sonar & Navigation*, **6**(6), 510-515, (2012).
- 47 Finfer, D. C., White, P. R., Chua, G. H. and Leighton, T. G. Review of the occurrence of multiple pulse echolocation clicks in recordings from small odontocetes, *IET Radar Sonar & Navigation*, **6**(6), 545-555, (2012).
- 48 Leighton, T. G., Chua, G. H., White, P. R., Tong, K. F., Griffiths, H. D. and Daniels, D. J. Radar clutter suppression and target discrimination using twin inverted pulses, *Proc. Roy. Soc. A*, **469**(2160), 20130512, (2013).
- 49 Leighton, T. G. and White, P. R. The Sound of Titan: A role for acoustics in space exploration, *Acoustics Bulletin*, **29**(4), 16-23, (2004).
- 50 Leighton, T. G. and Petculescu, A. Sounds in space: The potential uses for acoustics in the exploration of other worlds, *Hydroacoustics*, **11**, 225-238, (2008).
- 51 Jiang, J., Baik, K. and Leighton, T. G. Acoustic attenuation, phase and group velocities in liquid-filled pipes II: Simulation for spallation neutron sources and planetary exploration, *J. Acoust. Soc. Am.*, **130**(2), 695-706, (2011).
- 52 Leighton, T. G. Fluid loading effects for acoustical sensors in the atmospheres of Mars, Venus, Titan and Jupiter, *J. Acoust. Soc. Am.*, **125**(5), EL214-EL219, (2009).
- 53 Ainslie, M. A. and Leighton, T. G. Sonar equations for planetary exploration, *J. Acoust. Soc. Am.*, **140**(2), 1469–1480, (2016).
- 54 Ainslie, M. A. and Leighton, T. G. Near resonant bubble acoustic cross-section corrections, including examples from oceanography, volcanology, and biomedical ultrasound, *J. Acoust. Soc. Am.*, **126**(5), 2163-2175, (2009).
- 55 Robb, G. B. N. *et al.* Absolute calibration of hydrophones immersed in sandy sediment, *J. Acoust. Soc. Am.*, **125**(5), 2918-2927, (2009).
- 56 Leighton, T. G., Finfer, D. C. and White, P. R. The problems with acoustics on a small planet, *Icarus*, **193**(2), 649-652, (2008).
- 57 Leighton, T. G., White, P. R. and Finfer, D. C. The opportunities and challenges in the use of extra-terrestrial acoustics in the exploration of the oceans of icy planetary bodies, *Earth Moon and Planets*, **109**(1-4), 91-116, (2012).
- 58 Leighton, T. G. The use of extra-terrestrial oceans to test ocean acoustics students, *J. Acoust. Soc. Am.*, **131**(3 Pt 2), 2551-2555, (2012).
- 59 Petculescu, A. and Leighton, T. G. Guest editorial: Acoustic and related waves in extraterrestrial environments, *J. Acoust. Soc. Am.*, **140**(2), 1397–1399, (2016).

-
- 60 Leighton, T. G., Banda, N., Berges, B., Joseph, P. F. and White, P. R. Extraterrestrial sound for planetaria: a pedagogical study, *J. Acoust. Soc. Am.*, **140**(2), 1400-1419, (2016).
- 61 Leighton, T. G. and Petculescu, A. The sound of music and voices in space, *Acoustics Today*, **5**(3), 17-29, (2009).
- 62 Leighton, T. G. The sounds of voices and waterfalls on other planets, *University of Southampton* <http://tinyurl.com/znx4rve>, (publ. Dec 13 2014; accessed Feb 21, 2016), (2014).
- 63 O'Neill, J. *et al.* Tackling drug-resistant infections globally: final report and recommendations, *Final report of the Review of AntiMicrobial Resistance*, (May 2016), <http://tinyurl.com/horfr8d>, (2016).
- 64 Foreign and Commonwealth Office Antimicrobial resistance in humans and animals in low and middle income countries - How can knowledge and action be strengthened at national level?, (March 2015), <http://tinyurl.com/h2a27fu>, (2015).
- 65 United Nations. Draft political declaration of the high-level meeting of the General Assembly on antimicrobial resistance, <https://tinyurl.com/gqf2qdp>, (2016).
- 66 MacDonald, F. The Science World Is Freaking Out Over This 25-Year-Old's Answer to Antibiotic Resistance. Could this be the end of superbugs? *Science Alert*, <https://tinyurl.com/h36ocxd>, (2016).
- 67 O'Neill, J. *et al.* Rapid Diagnostics - Stopping unnecessary use of antibiotics. *Final report of the Review of AntiMicrobial Resistance* (May 2016), <https://tinyurl.com/gnr37bo>, (2016).
- 68 NAMRIP. Network for AntiMicrobial Resistance and Infection Prevention, <http://www.southampton.ac.uk/namrip/index.page>, (2017).
- 69 NAMRIP Ambassadors, <https://tinyurl.com/zl3s8w9>, (2017).
- 70 NAMRIP. Mapping microbes, <https://mappingmicrobes.wordpress.com/about/>, (2017).
- 71 Cohen, E. Deadly superbug-related scopes sold without FDA approval, *CNN News Website*, <https://tinyurl.com/jz3dyvo>, (published March 5, 2015; accessed Feb 21, 2016), (2015).
- 72 Shaw, M. C. Who's Watching The Watchers: Big problems with ERCP Scopes, *Health News Digest*, <https://tinyurl.com/ztut92q>, (published Sep 13, 2015; accessed Feb 21, 2016), (2015).
- 73 Leighton, T. G. We need more than just new antibiotics to fight superbugs, *The Conversation*, <https://tinyurl.com/js6ebye>, (published 15 July 2015; accessed Feb 21, 2016), (2015).
- 74 Leighton, T. G. Are some people suffering as a result of increasing mass exposure of the public to ultrasound in air?, *Proc. Roy. Soc. A*, **472**(2185), 20150624, (2016).
- 75 Leighton T. G. Comment on 'Are some people suffering as a result of increasing mass exposure of the public to ultrasound in air?' *Proc. Royal Soc. A*, 473(2199), 20160828, (2017).
- 76 Maksimov, A. O. and Leighton, T. G. Transient processes near the threshold of acoustically driven bubble shape oscillations, *Acta Acustica*, **87**(3), 322-332, (2001).
- 77 Maksimov, A. O., Leighton, T. G. and Birkin, P. R. Self focusing of acoustically excited Faraday ripples on a bubble wall, *Physics Letters A*, **372**(18), 3210-3216, (2008).
- 78 Birkin, P. R., Offin, D. G., Vian C J B, Leighton, T. G. and Maksimov, A. O. Investigation of non-inertial cavitation produced by an ultrasonic horn, *J. Acoust. Soc. Am.*, **130**(5), 3297-3308, (2011).
- 79 Maksimov, A. O. and Leighton, T. G. Pattern formation on the surface of a bubble driven by an acoustic field, *Proc. Roy. Soc. A*, **468**, 57-75, (2012).
- 80 Leighton, T. G. , Ho, W. L. and Flaxman, R. Sonoluminescence from the unstable collapse of a conical bubble, *Ultrasonics*, **35**, 399-405, (1997).
- 81 Leighton, T. G., Phelps, A. D., Cox, B. T. and Ho, W. L. Theory and preliminary measurements of the Rayleigh-like collapse of a conical bubble, *Acustica with Acta Acustica*, **84**(6), 1014-1024, (1998).
- 82 Leighton, T. G., Cox, B. T. and Phelps, A. D. The Rayleigh-like collapse of a conical bubble, *J. Acoust. Soc. Am.*, **107**(1), 130-142, (2000).
- 83 Birkin, P. R., Power, J. F., Leighton, T. G. and Vincotte, A. M. L. Cathodic electrochemical detection of sonochemical radical products, *Analytical Chemistry*, **74**, 2584-2590, (2002).
- 84 Birkin, P. R., Offin, D. G., Joseph, P. F. and Leighton, T. G. Cavitation, shock waves and the invasive nature of sonoelectrochemistry, *J. Physical Chemistry B*, **109**, 16997-17005, (2005).

-
- 85 Birkin, P. R., Offin, D. G., and Leighton, T. G. Experimental and theoretical characterisation of sonochemical cells. Part 2: Cell disruptors (ultrasonic horn) and cavity cluster collapse, *Physical Chemistry Chemical Physics*, 530-537, (2005).
- 86 Birkin, P. R., Leighton, T. G., Power, J. F., Simpson, M. D., Vincotte, A. M. L. and Joseph, P. Experimental and theoretical characterisation of sonochemical cells. Part 1. Cylindrical reactors and their use to calculate the speed of sound in aqueous solutions, *J. Physical Chemistry A*, **107**, 306-320, (2003).
- 87 Faraday, M. On the forms and states assumed by fluids in contact with vibrating elastic surfaces, *Phil. Trans. Roy. Soc. London*, **121**, 319-340, (1831).
- 88 Watson, Y. E., Birkin, P. R. and Leighton, T. G. Electrochemical detection of bubble oscillation, *Ultrasonics Sonochemistry* **10**, 65-69, (2003).
- 89 Elder, S. A. Cavitation microstreaming, *J. Acoust. Soc. Am.*, **31**, 54-64, (1958).
- 90 Nyborg, W. L. Acoustic streaming near a boundary, *J. Acoust. Soc. Am.*, **30**, 329-339, (1958).
- 91 Birkin, P. R., Watson Y E, Leighton, T. G. and Smith, K. L. Electrochemical detection of Faraday waves on the surface of a gas bubble, *Langmuir Surfaces and Colloids*, **18**, 2135-2140, (2002).
- 92 Rooney, J. A. Hemolysis near an ultrasonically pulsating gas bubble, *Science*, **169**, 869, (1970).
- 93 Lewin, P. A. and Bjørnø, L. Acoustically induced shear stresses in the vicinity of microbubbles in tissue, *J. Acoust. Soc. Am.*, **71**, 728, (1982).
- 94 Leighton, T. G. The acoustic bubble: Ocean, cetacean and extraterrestrial acoustics, and cold water cleaning, *IOP Journal of Physics: Conference Series*, **797**, 012001, (2017).
- 95 Birkin, P. R., Offin, D. G., Vian, C. J. B., Howlin, R. P., Dawson, J. I., Secker, T. J., Herve, R. C., Stoodley, P., Oreffo, R. O. C., Keevil, C. W. and Leighton, T. G. Cold water cleaning of brain proteins, biofilm and bone - harnessing an ultrasonically activated stream, *Physical Chemistry Chemical Physics*, **17**, 20574-20579, (2015).
- 96 Howlin, R. P., Fabbri, S., Offin, D. G., Symonds, N., Kiang, K. S., Knee, R. J., Yoganantham, D. C., Webb, J. S., Birkin, P. R., Leighton, T. G. and Stoodley, P. Removal of dental biofilms with a novel ultrasonically-activated water stream, *J. Dental Research*, **94**(9), 1303-1309, (2015).
- 97 Birkin, P. R., Offin, D. G., Vian, C. J. B. and Leighton, T. G. Electrochemical "bubble swarm" enhancement of ultrasonic surface cleaning, *Physical Chemistry Chemical Physics* **17**(33), 21709-21715, (2015).
- 98 Salta, M., Goodes, L., Mass, B., Dennington, S., Secker, T. and Leighton, T. G. Bubbles vs. biofilms: A novel method for the removal of marine biofilms attached on antifouling coatings using an ultrasonically activated water stream, *Surface Topography: Metrology and Properties*, **4**(3), 034009, (2016).
- 99 Goodes, L., Harvey, T., Symonds, N. and Leighton, T.G. 2016 A comparison of ultrasonically activated water stream and ultrasonic bath immersion cleaning of railhead leaf-film contaminant, *Surface Topography: Metrology and Properties*, **4**(3), 034004, (2016).
- 100 Leighton, T. G. 2015 The acoustic bubble: Oceanic bubble acoustics and ultrasonic cleaning, *Proceedings of Meetings on Acoustics (POMA)*, *Acoustical Society of America*, **24**(1) doi: 10.1121/2.0000121, (2015).
- 101 Leighton, T. G. StarStream (2007-2015) - Cleaning with low volumes of cold water, <http://www.southampton.ac.uk/engineering/research/projects/starstream.page>, (2016).
- 102 Harford, T. How economics killed the antibiotic dream, BBC World Service <http://www.bbc.co.uk/news/business-38828079>, (2017).
- 103 Kyomuhendo, G. B. Low use of rural maternity services in Uganda: Impact of women's status, traditional beliefs and limited resources, *Reproductive Health Matters*, **11**(21), 16-26, (2003).
- 104 European Centre for Disease Prevention and Control (ECDC). Antimicrobial resistance surveillance in Europe 2015, Surveillance report, <https://tinyurl.com/zomfn9w>, (2016).
- 105 Steris. Washing and decontamination systems, <https://tinyurl.com/j28bwkj> (accessed Mar 14 2017), (2017).
- 106 Calculations assume water use is evenly split between stages
- 107 BBC news. Record low for water temperature, <https://tinyurl.com/hgayu2p> (accessed Mar 14 2017), (2010).