

Bulk Nanobubbles Unveiled: Insights into Their Formation, Characteristics, and Applications

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Abstract

Nanobubbles, particularly bulk nanobubbles, are gas-filled cavities suspended within a liquid. Recently, bulk nanobubbles have garnered significant interest due to their distinctive nanoscale physical properties. While traditional gas diffusion theories and Laplace pressure suggest that nanobubbles should dissolve within a few microseconds, experimental observations have shown that they can persist in solution for hours or even days. This exceptional stability and extended lifespan have made bulk nanobubbles a focal point for numerous research groups globally. In this paper, we explore the historical development of research on bulk nanobubbles, examine their characteristics along with current techniques for their generation and detection, and assess the validity of stability theories related to bulk nanobubbles. Additionally, we highlight key applications of bulk nanobubbles across various fields.

Keywords

Bulk nanobubbles, stability, applications.

1. INTRODUCTION

In nature, the dissolving of gas molecules in water or other liquids is a frequent occurrence. What state do gas molecules exist in when they are in liquids is a fundamental question that needs to be addressed. Generally speaking, the states of gas molecules in liquid are divided into three states: dissolved state, bubble state and molecular cluster state. However, it is still unclear whether there are nanoscale gas molecule clusters or nanobubbles in the solution. It was proposed in the 1940s that small gas nuclei, or small gas masses, would appear in animal tissues and blood at low pressures and could be eliminated by boiling, filtering, centrifuging, and applying high hydrostatic pressures. These cavitation nuclei are theoretically stable because they adhere to the sidewalls of hydrophobic conical crevices [1]. This shows that nano-scale bubbles may be ubiquitous in nature, but due to the limitations of detection technology at the time, they were not directly observed by people. In 1950, a theoretical model for the dissolution of gas bubbles in liquids was created by Epstein and Plesset using the Laplace equation and diffusion theory as foundations. It has been demonstrated that this hypothesis is rather effective at understanding the behavior of microbubbles in liquids [2]. A bubble with a radius of 100 nm will have an interior pressure that is approximately 14.4 times that of the atmosphere, according to the Epstein-Plesset hypothesis, and it will not be able to live for less than one millisecond. This seemed to refute the stable existence of nanoscale gas bubbles in liquids, and as a result, only a few studies on this topic were reported afterward. However, in order to provide a satisfying explanation for the inexplicable long-range attractive forces detected between the two hydrophobic surfaces submerged in aqueous solutions, Parker et al., proposed the idea of nanobubbles again in 1994 [3]. More significantly, the initial direct observations of surface nanobubbles were reported by the research teams of Hu[4] and Higashitani[5] in the

2000s. Their research demonstrated that the nanobubbles exhibited significant stability on surfaces in aqueous solutions [6-11].

Nanobubbles (NBs) are currently classified into two main types: "surface nanobubbles (SNBs)", which are attached to solid surfaces and "bulk nanobubbles (BNBs)", which are dispersed in water. Additionally, other forms of nanobubbles have also been reported, such as nano pancakes and multilayer structures [12,13]. Despite ongoing debates surrounding nanobubbles (NBs) since their study began, and the unresolved discrepancy between the short lifespan predicted by Epstein-Plesset theory and the observed prolonged stability of NBs in water [14-18], it is acknowledged that the stable presence of NBs could have considerable impacts on various critical processes. These include protein folding, peptide self-assembly [19], electrochemical reaction activities [20-22], and boundary slip [23].

Conversely, the practical applications of nanobubbles, particularly bulk nanobubbles (BNBs), have not been limited by the ongoing debates in fundamental research. In the past several years, nanobubbles (NBs) have found widespread use across various fields, including water treatment, aquaculture, agriculture, health care, mineral flotation, and many others [24-27]. The number of published articles and citations related to nanobubbles is rapidly increasing each year. Given the significance and broad range of applications for bulk nanobubbles (BNBs), this paper aims to provide a concise overview of BNBs, covering their historical research, methods for generation and detection, and discussions on stability mechanisms.

2. THE HISTORY OF BNBS RESEARCH

Bulk nanobubbles are commonly described as gas-filled cavities in water or solutions with a typical diameter of less than 1 μm [28]. Figure 1 illustrates the historical evolution of research on surface nanobubbles and bulk nanobubbles, highlighting the significant events and breakthroughs over the past half century. In this paper, we focus on reviewing the research history of bulk nanobubbles.

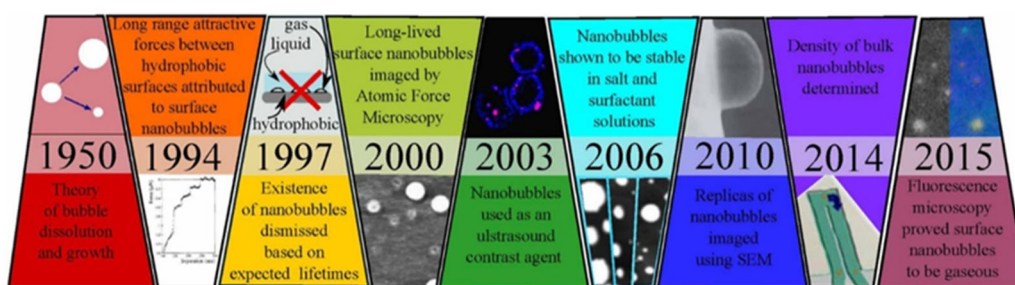


Figure1. A timeline highlighting key publications in the area of surface nanobubbles and bulk nanobubbles [9].

During the early 1950s, Donald A. Glaser found that when charged particles traversed a superheated liquid inside a glass chamber, the liquid along the path of the particles would vaporize, resulting in a visible trail of microsized bubbles [29]. Since the 1980s, stable microbubbles and submicron bubbles have been identified in both seawater and distilled water [28]. These bubbles have been used to explain various phenomena, including significant anomalies in acoustic data collected by navy sonar, decompression sickness experienced by scuba divers, and the presence of gas nuclei in classical nucleation processes [30]. The stability of these small bubbles was attributed to the reduced gas diffusion caused by impurities or surfactants coating their surfaces.

With the rapid advancements in light scattering techniques and charge-coupled devices (CCDs) since the 1980s, it became feasible to detect small particles in suspensions. In 1992, studies showed that clusters of ion-stabilized submicron bubbles, also known as bubstons, could exist in aqueous salt systems like NaCl solutions [31,32], although control experiments to confirm the gaseous nature of these submicron bubbles were largely lacking. Other research groups also reported detecting bulk nanobubbles (BNBs) in aqueous solutions using various methods, such as ultrasonic cavitation [33], mixing gas and liquid, or passing the solution through a porous membrane [34]. It was further noted that BNBs remained stable in alkaline solutions but became unstable in solutions with higher ionic strength [35,36]. Raman spectroscopy revealed the presence of gaseous N-N stretching vibrations in N₂ nanobubbles [37]. Electron microscopy revealed spherical structures with radii of several hundred nanometers in freeze-fractured replicas of nanobubble solutions [38]. Subsequently, an increasing number of studies on bulk nanobubbles (BNBs) were published.

3. THE PROPERTIES OF BNBS

Bulk nanobubbles exhibit many unique properties in aqueous solutions due to their nanoscale size. Figure 2 presents some fundamental characteristics of bulk nanobubbles.

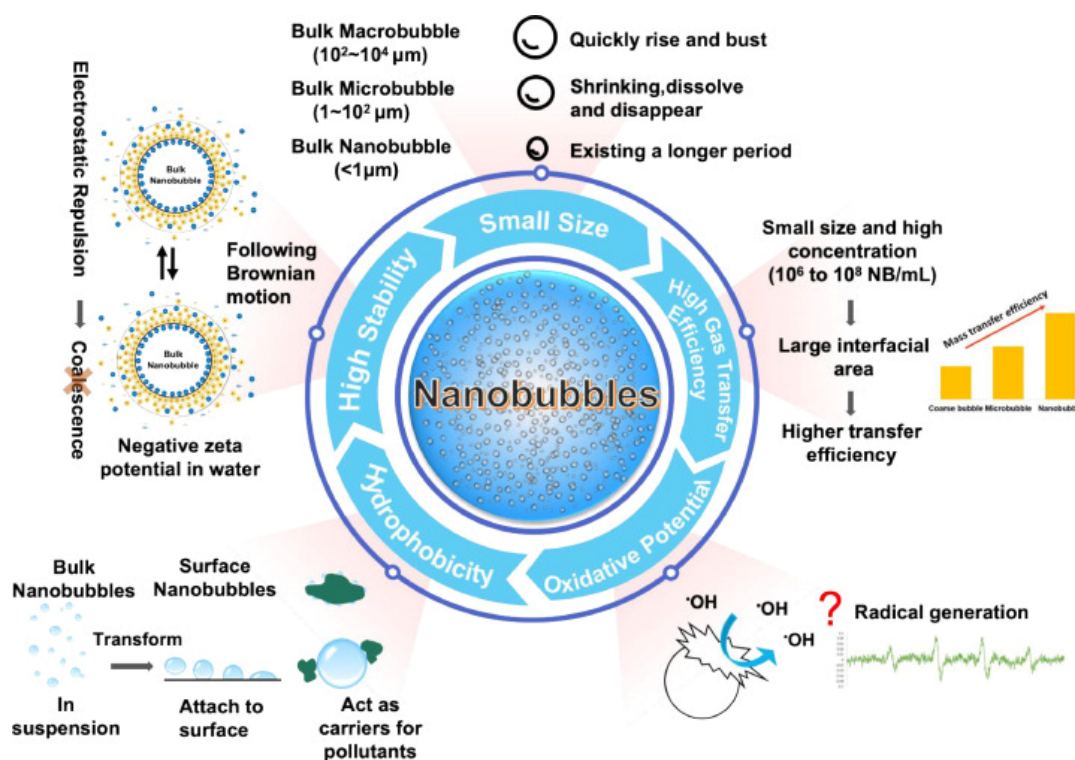


Figure 2. Several essential features of bulk nanobubble[39].

Bulk nanobubbles exhibit several notable characteristics, such as prolonged residence times and remarkable resistance to merging [40,41]. They also have large specific surface areas [42], increased gas solubility in water [42,43], high zeta potentials [40], and are capable of generating free radicals and releasing significant amounts of energy through bubble rupture or collapse [41,44]. Additionally, bulk nanobubbles, due to their large specific surface area, exhibit high mass transfer efficiency [45], and the free radicals generated upon their collapse also possess strong oxidative properties [46].

4. METHODS FOR GENERATING BULK NANOBUBBLES

The mechanisms for generating bulk nanobubbles in a solution are based on two distinct processes. The first process involves the nucleation of bubbles from the liquid phase, a phenomenon that has been thoroughly investigated since Gibbs' initial description in the 19th century. The second process pertains to the collapse or reduction in size of microbubbles, with its precise mechanisms still not fully understood and subject to ongoing debate. This paper primarily addresses methods for producing bulk nanobubbles through the first process.

4.1. Cavitation methods

Cavitation is a widely recognized method for generating small gas-filled bubbles [47,48]. Typically, cavities form when a uniform liquid undergoes a phase transition triggered by a rapid decrease in pressure below a specific critical threshold. Pressure reduction can occur through two primary mechanisms: hydrodynamic cavitation and acoustic cavitation.

When using the hydrodynamic cavitation method, gas and liquid are simultaneously transported through a Venturi tube. As the mixed fluid enters the converging section of the Venturi tube, the pipe diameter narrows, causing a significant increase in flow velocity and a rapid decrease in local pressure. This pressure drop induces cavitation in the dissolved gas within the liquid, leading to the generation of bulk nanobubbles [47,49].

The hydraulic cavitation technique is recognized as one of the most affordable and energy-efficient methods for generating bulk nanobubbles, thanks to its benefits like straightforward equipment and minimal maintenance expenses. Additionally, the Venturi generator, which operates on this cavitation principle, is commonly employed due to its ability to facilitate large-scale production and ease of operation [42,47,50].

The principle of acoustic cavitation to produce nanobubbles is that when ultrasound propagates in a liquid, a high-pressure and low-pressure alternating wave region is formed. In the low-pressure region of the ultrasound, the pressure in the liquid is reduced to a certain extent, causing the gas dissolved in the liquid to gradually form bubbles. By applying ultrasonic waves with a 50% amplitude in the lactose solution, Xun, Truong, and Bhandari generated CO₂ bubbles ranging from nanometers to micrometers in size [51].

4.2. Electrolysis methods

Electrolysis is one type of chemical process that can produce bulk nanobubbles [52-55]. The primary mechanism for generating bulk nanobubbles through electrolysis involves the formation of gas near the electrode during the electrolysis process. In an electrolyzer, two electrodes (anode and cathode) are inserted into an electrolyte, which is usually water containing electrolytes. When an electric current passes through the electrodes, the electrolysis reaction occurs on the electrode surfaces. Oxygen bubbles will form on the surface of the anode (positive electrode). Hydrogen bubbles will form on the surface of the cathode (negative electrode). Bulk nanobubbles can form when the gases (hydrogen and oxygen) created by electrolysis are released into the liquid and allow it to attain a supersaturated condition [55].

4.3. Solvent exchange methods

The solvent exchange method for producing bulk nanobubbles relies on altering gas solubility through the process of exchanging solvents. When one solvent in a liquid is gradually replaced by another solvent, the gas solubility of the solution will change. The new solvent may reduce the solubility of the gas, and when the solubility of the gas drops to a certain level, the gas begins to precipitate from the liquid and form bubbles. The solvent exchange method has now been proven to be an effective method for generating bulk nanobubbles [56-59]. Chen et al., while employing the solvent exchange method, used light scattering technology to observe the

ethanol-water replacement process. They discovered that the average size of the formed objects progressively decreased until it stabilized, leading them to speculate that these objects could be gas nanobubbles [60].

5. METHODS FOR DETECTING BULK NANOBUBBLES

In order to deeply study the formation mechanism of bulk nanobubbles and the reasons for their long-term existence, the detection of bulk nanobubbles becomes increasingly important. In this article, we will introduce several common instruments and methods for detecting bulk nanobubbles, including atomic force microscopy (AFM) [61,62], dynamic light scattering (DLS)[60] and nanoparticle tracking analysis (NTA) [63,64].

The detection of bulk nanobubbles with atomic force microscopy (AFM) relies on the analyzing the interaction between the AFM probe and the surface of bulk nanobubbles. AFM employs a very sharp probe made of silicon or silicon nitride, which is mounted on a highly sensitive cantilever capable of detecting minute force changes. As the probe moves over the liquid surface or the liquid-solid interface, it scans the nanobubbles within the liquid. When the probe approaches a bubble, an interaction force is generated between them, and AFM can record the relationship between this force and the distance. By analyzing these force-distance curves, it is possible to measure the size, shape, and mechanical properties of the nanobubbles.

Dynamic light scattering (DLS) is a method for detecting bulk nanobubbles that works by analyzing changes in scattered light intensity brought on by the Brownian motion of nanobubbles in liquid. Specifically, when employing DLS, the bulk nanobubbles in the solution scatter the incident light. DLS analyzes the rate of Brownian motion of the bubbles by monitoring fluctuations in the scattered light intensity over time. Smaller bubbles, due to their faster Brownian motion, cause more frequent changes in light intensity, while larger bubbles result in slower intensity changes. The DLS technique uses an autocorrelator to analyze the temporal variations in scattered light intensity and generates an autocorrelation function. By evaluating the rate at which this function decays, researchers can determine the size and distribution of the bulk nanobubbles.

Nanoparticle tracking analysis (NTA) is a technique used to observe and assess the concentration of nanobubbles in liquid samples. The fundamental principle of detecting bulk nanobubbles using nanoparticle tracking analysis (NTA) is to track and capture the movement trajectories of nanobubbles in a liquid with the camera of a dark-field microscope. The NTA system analyzes these trajectories to calculate the diffusion coefficient of the nanobubbles and, using the Stokes-Einstein equation, estimates their size. Given the high sensitivity of NTA experiments to camera settings, it is essential to monitor the experiment for extended periods and conduct multiple measurements for both experimental and control groups to reduce errors.

6. THEORIES EXPLAINING THE STABILITY OF BULK NANOBUBBLES

While bulk nanobubbles are commonly regarded as thermodynamically unstable, they display distinctive stability properties in liquid environments, drawing significant interest from researchers. Understanding the stability mechanism of bulk nanobubbles is a prerequisite for realizing their significant application potential in various fields. There are many factors that affect the stability of bulk nanobubbles, such as the chemical and physical properties of the solution, as well as the gas composition in the solution, which may affect the stability of bulk nanobubbles. Although there is no unified and satisfactory explanation for how bulk nanobubbles maintain their ultra-long lifespan, many researchers have proposed various theories to explain the stabilization mechanism of bulk nanobubbles. In this article, we will present some of the currently well-established theories and models in the scientific community that explain the stability of bulk nanobubbles, including the surfactant stabilization theory [65],

the surface charge theory [66], and the dense gas theory [67], which will help people gain a deeper understanding of the stability mechanisms of bulk nanobubbles.

6.1. Surfactant stabilization theory

The adsorption of surfactant molecules on the gas-water interface of bulk nanobubbles can form a hydration layer, which acts as a protective barrier to prevent the diffusion of gas within the bulk nanobubbles, thereby enhancing the stability of the bulk nanobubbles [54]. In 2016, a dynamic equilibrium model for a bulk NB partially coated with hydrophobic materials was provided by Yasui et al [14]. They found that nanobubbles can exist stably when the surface coverage of the hydrophobic material is about 0.5 to 1. The model is shown in Figure 3. After that, Alheshibri and Craig argued that insoluble surfactants forming an armored layer at the bulk nanobubbles interface can reduce surface tension, thereby enhancing the stability of these nanobubbles and preventing their dissolution [68].

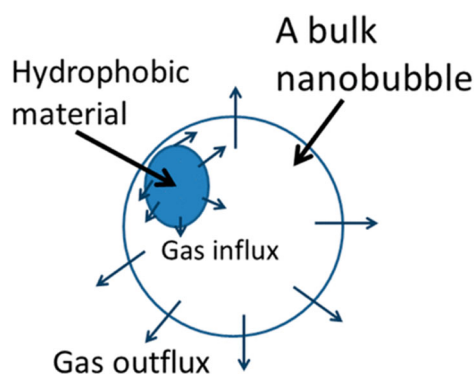


Figure 3. The bulk nanobubbles partially covered by a covering hydrophobic material [14].

6.2. Surface charge theory

The surface charge theory is commonly referred to as the electrostatic model or the diffuse double layer theory. When no additional ions are added into the solution, bulk nanobubbles generally display a negative charge, which has been reported in several studies [69-71]. H^+ and OH^- ions play a major role in the charging mechanism of the bulk nanobubbles [72]. Since the interfaces of the bulk nanobubbles are electrically charged, the diffused double layer hypothesis can be used to explain how the bulk nanobubbles maintain their stability. Figure 4 shows the diffuse electrical double layer formed around the bulk nanobubble.

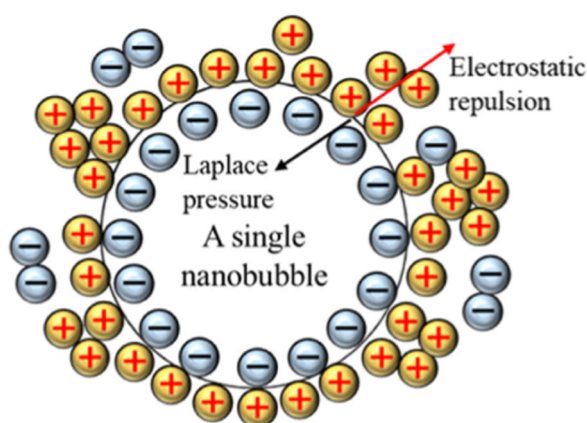


Figure 4. Schematic of the diffused electrical double layer formed around the bulk nanobubble[73].

Dressaire et al. discovered that ions in the solution will accumulate on the surface of bulk nanobubbles, forming a thin film that functions as a barrier to prevent the gas inside the nanobubble from diffusing further; thereby enhancing the stability of the bulk nanobubbles [66]. This phenomenon is called the ion barrier effect. The ion barrier effect provides a good explanation for why bulk nanobubbles can remain stable even in low-concentration NaCl solutions [17]. Furthermore, studies have shown that the external electrostatic pressure produced by the diffused electrical double layer formed around the bulk nanobubble can offset the Laplace pressure inside the bulk nanobubbles [31,74]. Bunkin et al. also discovered that the stability of the bulk nanobubbles is primarily due to the interfacial charge present on their surfaces [75].

6.3. Dense gas theory

In 2008, Zhang et al. compared bulk nanobubbles with high internal gas density and bulk nanobubbles with low internal gas density and found that high internal gas density is one of the reasons why bulk nanobubbles can remain stable [67]. Interestingly, researchers have suggested that a high concentration of dissolved gas in solution may decrease the rate at which gas transfers from nanobubble to the liquid phase, thereby promoting the stability of the bulk nanobubbles [74]. Molecular dynamics simulations and atomic force microscopy have validated the theory that the high-density internal gas inside surface nanobubbles contributes to the stability of the surface nanobubbles [76-78].

In addition, the scholars also found through transmission electron microscopy (TEM) that there is also high-density gas inside the bulk nanobubbles composed of hydrogen [79]. Moreover, molecular dynamics simulations examining the stability of nitrogen nanobubbles suggest that their stability depends on a critical concentration that exceeds typical levels, resulting in an internal nitrogen density much higher than under standard conditions [80]. Meegoda et al. also found through molecular dynamics simulation that oxygen nanobubbles with high initial internal gas density are more stable in both NVT and NPT ensembles and they believe that this stability is due to the conditions of gas supersaturation [81]. It is worth noting that the increased density of the internal gas may lower surface tension, which can improve its ability to restrict gas dissolution. The MacLeod-Sugden relationship, which links surface tension with the densities of liquid and gas, can also be used to account for this phenomenon [82].

7. APPLICATIONS OF BULK NANOBUBBLES

Bulk nanobubbles exhibit extraordinary value and great attractiveness in many application areas due to their unique physical and chemical properties. Figure 5 shows the various application scenarios of bulk nanobubbles in our daily lives. After years of research, the potential applications of bulk nanobubbles have become evident across various fields, including environmental management [83], agriculture [84], biomedicine [85], and industrial processing [86].

7.1. Environmental applications

The environmental applications of bulk nanobubbles primarily include water quality control and wastewater treatment. Water quality generally refers to the chemical, physical, and biological characteristics of water, which is closely related to the animals and plants in the entire ecosystem. Water pollution originates from various sources, including sedimentation of solid materials, pesticides and chemicals from agricultural and industrial activities, nutrients like phosphorus and nitrogen from fertilizers and detergents, harmful algae resulting from eutrophication, and disease-causing microorganisms [88]. In recent decades, various remediation techniques have been developed to address the sources of pollution mentioned earlier, including flotation, flocculation, aeration, and other treatment technologies [89]. To

achieve this, nanobubble (NB) technology is believed to be able to be applied either independently or in support of traditional technologies to improve water quality. Because of their excellent mass transfer efficiency and long-term stability, NBs are employed to solve the hypoxia issue caused by water eutrophication. Kalogerakis et al. reported the outcomes of five large-scale field applications of nanobubble technology for the restoration of major water bodies such as lakes and ponds, conducted at various locations globally [90]. The outcomes showed improved parameters for water quality together with a notable decline in pathogens and chemical oxygen demand (COD).

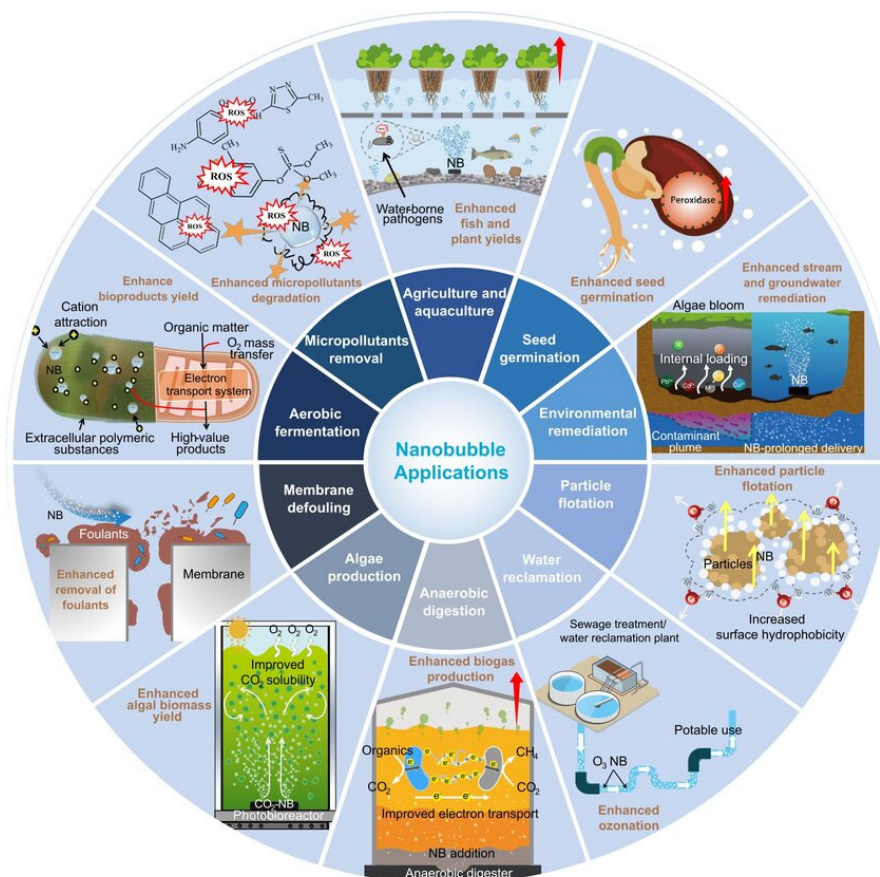


Figure 5. Schematic diagram of the important role played by bulk nanobubbles in various application fields [87].

Industrial, agricultural, and domestic wastewaters are major sources of environmental pollution in contemporary society [88]. It is important to treat and clean wastewater, particularly when dangerous materials (such as heavy metals and poisonous chemicals) are present. Wastewater cleansing is costly because various methods that involve complex chemical processes are used to remove pollutants. The impact of nanobubbles on each stage of wastewater treatment have been explored and wastewater treatment with nanobubbles has been highlighted as a promising alternative to conventional methods of wastewater treatment. In their pioneering study, Kyzas examined the influence of nanobubbles on the adsorption of dissolved heavy metals using activated carbon [91]. The research results show that nanobubbles, as carriers of lead ions, can significantly improve the adsorption rate of heavy metals.

7.2. Agriculture applications

The agricultural applications of bulk nanobubbles mainly include horticulture, hydroponics and aquaculture. Horticulture plays a vital role in agriculture, focusing on the cultivation of fruits, vegetables, flowers, as well as medicinal and aromatic plants [92]. In this field, nanobubble technology has demonstrated impressive outcomes, which are attributed to the improvement of the microbial population, preserving soil moisture, encasing nutrients etc [93,94]. Bulk nanobubbles were used in lab and pilot scale rice farming by Wang et al. [95]. The experimental results indicate that under the influence of nanobubbles, despite a 25% reduction in fertilizer, the height and chlorophyll content of the rice plants remained unchanged.

Hydroponics is another type of gardening in which plants are grown without the use of soil; instead, their roots are submerged in a solution of water and nutrients. Faster growth and less water usage are the primary advantages of hydroponics [96]. In hydroponics, nanobubbles have a two-sided effect on plants. Research has shown that the bulk nanobubbles can effectively manage dissolved oxygen in solutions, enhance the growth of leaves and stems [97], and produce superior morphological and physiological effects compared to traditional aeration methods. However, this benefit is limited to a specific concentration range, beyond which NBs can inhibit plant growth [98].

Aquaculture, as a subset of agriculture, involves a range of processes such as the cultivation, growth, and collection of fish, shellfish, and aquatic vegetation [99,100]. These activities take place in open seas, rivers, lakes, both artificial and natural ponds, as well as indoor facilities [101]. The primary challenges in aquaculture are influenced by factors like water quality and the levels of dissolved oxygen present in the water. Nanobubble technology is an emerging technology that is environmentally friendly and harmless to animals, so it has received widespread attention in the field of aquaculture. Ohnari et al. believed that nanobubbles in aqueous solution are an effective means to accelerate the metabolism of shellfish [102]. Besides, Ebina et al. observed that sweetfish raised in water with added nanobubbles weighed more than those grown in water without nanobubbles, leading them to conclude that nanobubbles can enhance the growth of sweetfish [103].

7.3. Medicine applications

The applications of bulk nanobubbles in the medical field primarily include ultrasound imaging, drug delivery for cancer treatment and the treatment of skin diseases. Biomedical ultrasound imaging, a widely used clinical tool, is employed for diagnosing and treating various diseases. This technique utilizes sound waves above 20 kHz to create images based on how these waves interact with different tissues and structures. By analyzing the timing and intensity of the returning echoes, it is possible to determine the tissue location and scattering characteristics [104]. Nonetheless, the contrast in ultrasound imaging may be reduced because of the similar acoustic impedances of soft tissues [105]. Microbubbles, which feature a stable shell with gas core, are utilized as ultrasonic contrast agents due to their significant impedance mismatch and strong scattering effects on adjacent tissues. Despite their usefulness, microbubbles have restricted clinical applications because their size will keep them in the vasculature [106]. In contrast, nanobubbles are smaller than microbubbles and can more readily pass through biological barriers such the cell membrane [107], tumor vasculature [108], and blood-brain barrier [109]. Therefore, bulk nanobubbles used as contrast agents can generate more detailed ultrasound images and offer more accurate information for diagnosing malignant tumors [110].

Chemotherapy is a major therapeutic option for treating malignant cancerous tumors. However, most chemotherapeutic drugs lack tissue selectivity, leading to adverse side effects on healthy tissues [111]. Targeted nanobubbles can be utilized to enhance drug delivery for the

purpose of cancer treatment. Owing to their small size, targeted nanobubbles can effectively penetrate from blood vessels into adjacent tissues [112]. Additionally, they offer enhanced stability and extended retention time within the systemic circulation. The surface of targeted nanobubbles is functionalized with unique targeting ligands that enable adsorption to particular cancer cells and also pre-packed with genes or chemotherapeutic medications [113]. Furthermore, another area where biomedical nanobubbles are applied is in dermatology. According to reports, nanobubbles can be used for sterilizing [114], antibacterial [115], anti-inflammatory [116], and healing [117] attributes. Consequently, their use in treating different skin conditions appears highly promising.

7.4. Industrial applications

The industrial applications of bulk nanobubbles mainly include surface cleaning, froth flotation, and food processing. One application of nanobubbles in heavy industry is the prevention or remediation of scale formation. Aikawa et al. investigated the effect of nanobubbles on inhibiting corrosion in low-carbon steel [118]. Air nanobubbles reduced corrosion by 50% compared to traditional methods. This study indicates that nanobubbles can be used to coat and clean various metallic surfaces, effectively avoiding corrosion caused by fluids with different chemical compositions. Additionally, Liu et al. used nanobubbles as a cleaning agent to remove bovine serum albumin from the solid-liquid interface and suggested that this process could become an efficient and environmentally friendly cleaning technology [119].

Based on the difference in surface hydrophobicity between goal minerals and gangue, froth flotation is the most often used method of particle cleaning and separation in mineral processing [120,121]. During the flotation process, hydrophobic particles tend to adhere to the bubbles and rise to the froth zone, while hydrophilic particles remain in the slurry as tailings [122]. As high-quality mineral resources become exhausted, the focus has shifted to lower-grade minerals with finely distributed grain sizes, which presents a considerable challenge for traditional flotation methods. In flotation, fine particles often exhibit poor recovery rates due to their low probability of colliding with flotation bubbles [123]. Consequently, it is essential to devise a new method to overcome the size restrictions imposed by conventional flotation techniques. Because bulk nanobubbles are significantly smaller and more numerous, they create more advantageous hydrodynamic conditions for the flotation of fine particles. In the past few years, nanobubble flotation has become a viable method for increasing the flotation effectiveness of ultrafine particles [124].

Nanobubble technology is expected to drive progress in food processing due to its extensive range of potential applications. Bulk nanobubbles can decrease friction and alter the physical characteristics of liquids, leading to increased molecular mobility [125]. Consequently, the presence of nanobubbles may reduce the overall viscosity of liquids, which can improve the processability of foods. Nanobubbles can also serve as an innovative approach for food seasoning. Due to their unique attributes, such as a large specific surface area, enhanced gas solubility in liquids, and high mass transfer efficiency, air nanobubbles with average diameters ranging from several hundred nanometers to less than 10 micrometers can improve the infiltration of liquid seasonings into food [126]. Significantly, it is worth noting that nanobubbles can enhance the freezing and crystallization of food components, thereby achieving better food preservation. Zhang et al. found that the presence of nanobubbles can effectively increase the freezing rate of food during food processing [127].

8. CONCLUSIONS

In conclusion, while extensive research on bulk nanobubbles has yielded numerous remarkable results and advancements over the past twenty years, the field is still in its early

stages, with many challenges yet to be overcome. Firstly, producing bulk nanobubbles with specific small sizes and high concentrations remains a major challenge for their application. Secondly, current detection methods for bulk nanobubbles primarily rely on nanoparticle tracking analysis or dynamic light scattering techniques, which are constrained by their concentration and resolution ranges. Additionally, these methods cannot provide chemical information about the detected particles. Therefore, there is a crucial need to develop new techniques that offer both higher spatial resolution and enhanced chemical sensitivity. Thirdly, while several models have been proposed to explain the stability mechanisms of bulk nanobubbles, a comprehensive explanation for their extraordinarily long lifetime is still lacking. Lastly, the potential of bulk nanobubbles in a wide range of applications is considered to be very promising, which will inspire researchers to continue advancing their research. It is anticipated that, in the near future, nanobubble technology could lead to significant breakthroughs in scientific and engineering fields.

REFERENCES

- [1] Harvey, E.; Barnes, D.; McElroy, W.; Whiteley, A.; Pease, D.; Cooper, K. Bubble formation in animals. I. Physical factors. *Journal of Cellular and Comparative Physiology* 2005, 24, 1-22.
- [2] Epstein, P. S.; Plesset, M. S. On the stability of gas bubbles in liquid-gas solutions. *The Journal of Chemical Physics* 1950, 18 (11), 1505-1509.
- [3] Parker, J. L.; Claesson, P. M.; Attard, P. Bubbles, cavities, and the long-ranged attraction between hydrophobic surfaces. *The Journal of Physical Chemistry* 1994, 98 (34), 8468-8480.
- [4] Lou, S.-T.; Ouyang, Z.-Q.; Zhang, Y.; Li, X.-J.; Hu, J.; Li, M.-Q.; Yang, F.-J. Nanobubbles on solid surface imaged by atomic force microscopy. *Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures Processing, Measurement, and Phenomena* 2000, 18 (5), 2573-2575.
- [5] Ishida, N.; Inoue, T.; Miyahara, M.; Higashitani, K. Nano bubbles on a hydrophobic surface in water observed by tapping-mode atomic force microscopy. *Langmuir* 2000, 16 (16), 6377-6380.
- [6] Borkent, B. M.; Dammer, S. M.; Schonherr, H.; Vancso, G. J.; Lohse, D. Superstability of surface nanobubbles. *Phys Rev Lett* 2007, 98 (20), 204502.
- [7] Zhang, X. H.; Zhang, X. D.; Lou, S. T.; Zhang, Z. X.; Sun, J. L.; Hu, J. Degassing and temperature effects on the formation of nanobubbles at the mica/water interface. *Langmuir* 2004, 20 (9), 3813-3815.
- [8] Zhang, X. H.; Khan, A.; Ducker, W. A. A nanoscale gas state. *Phys Rev Lett* 2007, 98 (13), 136101.
- [9] Alheshibri, M.; Qian, J.; Jehannin, M.; Craig, V. S. J. A history of nanobubbles. *Langmuir* 2016, 32 (43), 11086-11100.
- [10] Lohse, D.; Zhang, X. Surface nanobubbles and nanodroplets. *Reviews of Modern Physics* 2015, 87 (3), 981-1035.
- [11] Liu, Y.; Zhang, X. A review of recent theoretical and computational studies on pinned surface nanobubbles*. *Chinese Physics B* 2018, 27 (1), 014401.
- [12] Zhang, X. H.; Zhang, X.; Sun, J.; Zhang, Z.; Li, G.; Fang, H.; Xiao, X.; Zeng, X.; Hu, J. Detection of novel gaseous states at the highly oriented pyrolytic graphite-water interface. *Langmuir* 2007, 23 (4), 1778-1783.
- [13] Zhang, L.; Zhang, X.; Fan, C.; Zhang, Y.; Hu, J. Nanoscale multiple gaseous layers on a hydrophobic surface. *Langmuir* 2009, 25 (16), 8860-8864.
- [14] Yasui, K.; Tuziuti, T.; Kanematsu, W.; Kato, K. Dynamic equilibrium model for a bulk nanobubble and a microbubble partly covered with hydrophobic material. *Langmuir* 2016, 32 (43), 11101-11110.

- [15] Weijs, J. H.; Seddon, J. R.; Lohse, D. Diffusive shielding stabilizes bulk nanobubble clusters. *Chemphyschem* 2012, 13 (8), 2197-2204.
- [16] Yasui, K.; Tuziuti, T.; Kanematsu, W. Mysteries of bulk nanobubbles (ultrafine bubbles); stability and radical formation. *Ultrasonics Sonochemistry* 2018, 48, 259-266.
- [17] Meegoda, J. N.; Hewage, S. A.; Batagoda, J. H. Application of the diffused double layer theory to nanobubbles. *Langmuir* 2019, 35 (37), 12100-12112.
- [18] Tan, B. H.; An, H.; Ohl, C. D. How bulk nanobubbles might survive. *Phys Rev Lett* 2020, 124 (13), 134503.
- [19] Wang, Y.; Shen, Z.; Guo, Z.; Hu, J.; Zhang, Y. Effects of nanobubbles on peptide self-assembly. *Nanoscale* 2018, 10 (42), 20007-20012.
- [20] Zhang, L.; Zhang, Y.; Zhang, X.; Li, Z.; Shen, G.; Ye, M.; Fan, C.; Fang, H.; Hu, J. Electrochemically controlled formation and growth of hydrogen nanobubbles. *Langmuir* 2006, 22 (19), 8109-8113.
- [21] German, S. R.; Chen, Q.; Edwards, M. A.; White, H. S. Electrochemical measurement of hydrogen and nitrogen nanobubble lifetimes at Pt nanoelectrodes. *Journal of The Electrochemical Society* 2016, 163 (4), H3160-H3166.
- [22] Chen, Q.; Wiedenroth, H. S.; German, S. R.; White, H. S. Electrochemical nucleation of stable n_2 nanobubbles at Pt nanoelectrodes. *Journal of the American Chemical Society* 2015, 137 (37), 12064-12069.
- [23] Wang, Y.; Bhushan, B. Boundary slip and nanobubble study in micro/nanofluidics using atomic force microscopy. *Soft Matter* 2010, 6 (1), 29-66.
- [24] Azevedo, A.; Oliveira, H.; Rubio, J. Bulk nanobubbles in the mineral and environmental areas: Updating research and applications. *Advances in Colloid and Interface Science* 2019, 271, 101992.
- [25] Minamikawa, K.; Makino, T. Oxidation of flooded paddy soil through irrigation with water containing bulk oxygen nanobubbles. *Science of The Total Environment* 2020, 709, 136323.
- [26] Zhou, Y.; Li, Y.; Liu, X.; Wang, K.; Muhammad, T. Synergistic improvement in spring maize yield and quality with micro/nanobubbles water oxygenation. *Scientific Reports* 2019, 9 (1), 5226.
- [27] Endo-Takahashi, Y.; Negishi, Y. Microbubbles and nanobubbles with ultrasound for systemic gene delivery. *Pharmaceutics* 2020, 12, 964.
- [28] Johnson, B. D.; Cooke, R. C. Generation of stabilized microbubbles in seawater. *Science* 1981, 213 (4504), 209-211.
- [29] Glaser, D. A. Some effects of ionizing radiation on the formation of bubbles in liquids. *Physical Review* 1952, 87 (4), 665-665.
- [30] Yount, D. E.; Gillary, E. W.; Hoffman, D. C. A microscopic investigation of bubble formation nuclei. *The Journal of the Acoustical Society of America* 1984, 76 (5), 1511-1521.
- [31] Bunkin, N.; Bunkin, F. V. Bubbles-stable gaseous bubbles in strongly dilute electrolytic solutions. *Sov. Phys. JETP* 1992, 74, 271-276.
- [32] Bunkin, N. F.; Kochergin, A. V.; Lobeyev, A. V.; Ninham, B. W.; Vinogradova, O. I. Existence of charged submicrobubble clusters in polar liquids as revealed by correlation between optical cavitation and electrical conductivity. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 1996, 110 (2), 207-212.
- [33] Cho, S.-H.; Kim, J. W.; Chun, J.-H.; Kim, J.-D. Ultrasonic formation of nanobubbles and their zeta-potentials in aqueous electrolyte and surfactant solutions. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 2005, 269, 28-34.

- [34] Kukizaki, M.; Goto, M. Size control of nanobubbles generated from shirasu-porous-glass (spg) membranes. *Journal of Membrane Science* 2006, 281 (1), 386-396.
- [35] Jin, F.; Li, J.; Ye, X.; Wu, C. Effects of pH and ionic strength on the stability of nanobubbles in aqueous solutions of α -cyclodextrin. *The journal of physical chemistry. B* 2007, 111, 11745-11749.
- [36] Jin, F.; Ye, X.; Wu, C. Observation of kinetic and structural scalings during slow coalescence of nanobubbles in an aqueous solution. *The Journal of Physical Chemistry B* 2007, 111 (46), 13143-13146.
- [37] Ohgaki, K.; Khanh, N.; Joden, Y.; Tsuji, A.; Nakagawa, T. Physicochemical approach to nanobubble solutions. *Chemical Engineering Science - CHEM ENG SCI* 2010, 65, 1296-1300.
- [38] Uchida, T.; Oshita, S.; Ohmori, M.; Tsuno, T.; Soejima, K.; Shinozaki, S.; Take, Y.; Mitsuda, K. Transmission electron microscopic observations of nanobubbles and their capture of impurities in wastewater. *Nanoscale Research Letters* 2011, 6 (1), 295.
- [39] Jia, M.; Farid, M. U.; Kharraz, J. A.; Kumar, N. M.; Chopra, S. S.; Jang, A.; Chew, J.; Khanal, S. K.; Chen, G.; An, A. K. Nanobubbles in water and wastewater treatment systems: Small bubbles making big difference. *Water Research* 2023, 245, 120613.
- [40] Uchida, T.; Oshita, S.; Ohmori, M.; Tsuno, T.; Soejima, K.; Shinozaki, S.; Take, Y.; Mitsuda, K. Transmission electron microscopic observations of nanobubbles and their capture of impurities in wastewater. *Nanoscale research letters* 2011, 6, 295.
- [41] Ushikubo, F. Y.; Enari, M.; Furukawa, T.; Nakagawa, R.; Makino, Y.; Kawagoe, Y.; Oshita, S. Zeta-potential of micro- and/or nano-bubbles in water produced by some kinds of gases. *IFAC Proceedings Volumes* 2010, 43 (26), 283-288.
- [42] Agarwal, A.; Ng, J.; Liu, Y. Principle and applications of microbubble and nanobubble technology for water treatment. *Chemosphere* 2011, 84, 1175-1180.
- [43] Ahmed, A. K. A.; Sun, C.; Hua, L.; Zhang, Z.; Zhang, Y.; Zhang, W.; Marhaba, T. Generation of nanobubbles by ceramic membrane filters: The dependence of bubble size and zeta potential on surface coating, pore size and injected gas pressure. *Chemosphere* 2018, 203, 327-335.
- [44] Demangeat, J.-L. Gas nanobubbles and aqueous nanostructures: The crucial role of dynamization. *Homeopathy* 2015, 104.
- [45] Zhou, C.; Cleland, D.; Snell, J.; Qi, W.; Randolph, T.; Carpenter, J. Formation of stable nanobubbles on reconstituting lyophilized formulations containing trehalose. *Journal of Pharmaceutical Sciences* 2016, 105.
- [46] Liu, S.; Oshita, S.; Makino, Y.; Wang, Q.; Kawagoe, y.; Uchida, T. Oxidative capacity of nanobubbles and its effect on seed germination. *ACS Sustainable Chemistry & Engineering* 2015, 4.
- [47] Fan, M.; Tao, D.; Honaker, R.; Luo, Z. Nanobubble generation and its application in froth flotation (part i): Nanobubble generation and its effects on properties of microbubble and millimeter scale bubble solutions. *Mining Science and Technology (China)* 2010, 20, 1-19.
- [48] Wu, C.; Nasset, K.; Masliyah, J.; Xu, Z. Generation and characterization of submicron size bubbles. *Advances in colloid and interface science* 2012, 179-182, 123-132.
- [49] Ahmadi, R.; Darban, A. K. Modeling and optimization of nano-bubble generation process using response surface methodology. *International Journal of NanoScience and Nanotechnology* 2013, 9, 151-162.
- [50] Ahmadi, R.; Khodadadi, D. A.; Abdollahy, M.; Fan, M. Nano-microbubble flotation of fine and ultrafine chalcopyrite particles. *International Journal of Mining Science and Technology* 2014, 24 (4), 559-566.

- [51] Ang, X.; Truong, T.; Bhandari, B. Effect of carbonation of supersaturated lactose solution on crystallisation behaviour of alpha-lactose monohydrate. *Food Biophysics* 2017, 12.
- [52] Kikuchi, K.; Nagata, S.; Tanaka, Y.; Saihara, Y.; Ogumi, Z. Characteristics of hydrogen nanobubbles in solutions obtained with water electrolysis. *Journal of Electroanalytical Chemistry* 2007, 600 (2), 303-310.
- [53] Takenouchi, T. Behavior of hydrogen nanobubbles in alkaline electrolyzed water and its rinse effect for sulfate ion remained on nickel-plated surface. *Journal of Applied Electrochemistry* 2010, 40 (4), 849-854.
- [54] Wu, C.; Nasset, K.; Masliyah, J.; Xu, Z. Generation and characterization of submicron size bubbles. *Advances in Colloid and Interface Science* 2012, 179-182, 123-132.
- [55] Zhu, J.; An, H.; Alheshibri, M.; Liu, L.; Terpstra, P. M. J.; Liu, G.; Craig, V. S. J. Cleaning with bulk nanobubbles. *Langmuir* 2016, 11203-11211.
- [56] Zhang, L.; Qiu, J.; Shuo, W.; Wang, X.; Lei, W.; Zhao, H.; hu, J.; Zou, Z.; Dong, Y. Formation and stability of bulk nanobubbles generated by ethanol-water exchange. *ChemPhysChem* 2017, 18.
- [57] Millare, J.; Basilia, B. Nanobubbles from ethanol-water mixtures: Generation and solute effects via solvent replacement method. *ChemistrySelect* 2018, 3, 9268-9275.
- [58] Millare, J. C.; Basilia, B. A. Dispersion and electrokinetics of scattered objects in ethanol-water mixtures. *Fluid Phase Equilibria* 2019, 481, 44-54.
- [59] Bunkin, N. F.; Shkirin, A. V.; Ninham, B. W.; Chirikov, S. N.; Chaikov, L. L.; Penkov, N. V.; Kozlov, V. A.; Gudkov, S. V. Shaking-induced aggregation and flotation in immunoglobulin dispersions: Differences between water and water-ethanol mixtures. *ACS Omega* 2020, 5 (24), 14689-14701.
- [60] Chen, M.; Peng, L.; Qiu, J.; Luo, K.; Liu, D.; Han, P. Monitoring of an ethanol-water exchange process to produce bulk nanobubbles based on dynamic light scattering. *Langmuir* 2020, 36 (34), 10069-10073.
- [61] Lou, S.; Ouyang, Z.-Q.; Zhang, y.; Li, X.-J.; hu, J.; Li, M.-Q.; Yang, F.-J. Nanobubbles on solid surface imaged by atomic force microscopy. *Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures* 2000, 18, 2573-2575.
- [62] Walczyk, W.; Schönherr, H. Characterization of the interaction between afm tips and surface nanobubbles. *Langmuir* 2014, 30 (24), 7112-7126.
- [63] Nirmalkar, N.; Pacek, A. W.; Barigou, M. Interpreting the interfacial and colloidal stability of bulk nanobubbles. *Soft Matter* 2018, 14 (47), 9643-9656.
- [64] Ma, X.-t.; Li, M.-b.; Sun, C. Measurement and characterization of bulk nanobubbles by nanoparticle tracking analysis method. *Journal of Hydrodynamics* 2022, 34 (6), 1121-1133.
- [65] Elmahdy, A. M.; Mirnezami, M.; Finch, J. A. Zeta potential of air bubbles in presence of frothers. *International Journal of Mineral Processing* 2008, 89 (1), 40-43.
- [66] Dressaire, E.; Bee, R.; Bell, D. C.; Lips, A.; Stone, H. A. Interfacial polygonal nanopatterning of stable microbubbles. *Science* 2008, 320 (5880), 1198-1201.
- [67] Zhang, L.; Chen, H.; Li, Z.; Fang, H.; Hu, J. Long lifetime of nanobubbles due to high inner density. *Science in China Series G: Physics, Mechanics and Astronomy* 2008, 51 (2), 219-224.
- [68] Alheshibri, M.; Craig, V. S. J. Armoured nanobubbles; ultrasound contrast agents under pressure. *Journal of Colloid and Interface Science* 2019, 537, 123-131.
- [69] Calgaroto, S.; Wilberg, K. Q.; Rubio, J. On the nanobubbles interfacial properties and future applications in flotation. *Minerals Engineering* 2014, 60, 33-40.

- [70] Jia, W.; Ren, S.; Hu, B. Effect of water chemistry on zeta potential of air bubbles. *International Journal of Electrochemical Science* 2013, 8 (4), 5828-5837.
- [71] Yang, C.; Dabros, T.; Li, D.; Czarnecki, J.; Masliyah, J. H. Measurement of the zeta potential of gas bubbles in aqueous solutions by microelectrophoresis method. *Journal of Colloid and Interface Science* 2001, 243 (1), 128-135.
- [72] Takahashi, M. Z potential of microbubbles in aqueous solutions: Electrical properties of the gas-water interface. *The Journal of Physical Chemistry B* 2005, 109 (46), 21858-21864.
- [73] Wang, X.; Li, P.; Ning, R.; Ratul, R.; Zhang, X.; Ma, J. Mechanisms on stability of bulk nanobubble and relevant applications: A review. *Journal of Cleaner Production* 2023, 426, 139153.
- [74] Ushikubo, F. Y.; Furukawa, T.; Nakagawa, R.; Enari, M.; Makino, Y.; Kawagoe, Y.; Shiina, T.; Oshita, S. Evidence of the existence and the stability of nano-bubbles in water. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 2010, 361 (1), 31-37.
- [75] Bunkin, N. F.; Yurchenko, S. O.; Suyazov, N. V.; Shkirin, A. V. Structure of the nanobubble clusters of dissolved air in liquid media. *Journal of Biological Physics* 2012, 38 (1), 121-152.
- [76] Schlesinger, I.; Sivan, U. Three-dimensional characterization of layers of condensed gas molecules forming universally on hydrophobic surfaces. *Journal of the American Chemical Society* 2018, 140 (33), 10473-10481.
- [77] Wang, S.; Zhou, L.; Wang, X.; Wang, C.; Dong, Y.; Zhang, Y.; Gao, Y.; Zhang, L.; Hu, J. Force spectroscopy revealed a high-gas-density state near the graphite substrate inside surface nanobubbles. *Langmuir* 2019, 35 (7), 2498-2505.
- [78] Zhou, L.; Wang, X.; Shin, H.-J.; Wang, J.; Tai, R.; Zhang, X.; Fang, H.; Xiao, W.; Wang, L.; Wang, C.; Gao, X.; Hu, J.; Zhang, L. Ultrahigh density of gas molecules confined in surface nanobubbles in ambient water. *Journal of the American Chemical Society* 2020, 142 (12), 5583-5593.
- [79] Huang, T.-W.; Liu, S.-Y.; Chuang, Y.-J.; Hsieh, H.-Y.; Tsai, C.-Y.; Wu, W.-J.; Tsai, C.-T.; Mirsaidov, U.; Matsudaira, P.; Chang, C.-S.; Tseng, F.-G.; Chen, F.-R. Dynamics of hydrogen nanobubbles in klh protein solution studied with in situ wet-tem. *Soft Matter* 2013, 9 (37), 8856-8861.
- [80] Zhang, M.; Tu, Y.-s.; Fang, H.-p. Concentration of nitrogen molecules needed by nitrogen nanobubbles existing in bulk water. *Applied Mathematics and Mechanics* 2013, 34 (12), 1433-1438.
- [81] Aluthgun Hewage, S.; Meegoda, J. N. Molecular dynamics simulation of bulk nanobubbles. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 2022, 650, 129565.
- [82] Reid, R. C.; Sherwood, T. K.; Street, R. E. The properties of gases and liquids. *Physics Today* 1959, 12 (4), 38-40.
- [83] Lyu, T.; Wu, S.; Mortimer, R. J. G.; Pan, G. Nanobubble technology in environmental engineering: Revolutionization potential and challenges. *Environmental Science & Technology* 2019, 53 (13), 7175-7176.
- [84] Zhao, L.; Teng, M.; Zhou, L.; Li, Y.; Sun, J.; Zhang, Z.; Wu, F. Hydrogen nanobubble water: A good assistant for improving the water environment and agricultural production. *Journal of Agricultural and Food Chemistry* 2023, 71 (33), 12369-12371.
- [85] Hansen, H. H. W. B.; Cha, H.; Ouyang, L.; Zhang, J.; Jin, B.; Stratton, H.; Nguyen, N.-T.; An, H. Nanobubble technologies: Applications in therapy from molecular to cellular level. *Biotechnology Advances* 2023, 63, 108091.
- [86] Tao, D. Recent advances in fundamentals and applications of nanobubble enhanced froth flotation: A review. *Minerals Engineering* 2022, 183, 107554.

- [87] Marcelino, K. R.; Ling, L.; Wongkiew, S.; Nhan, H. T.; Surendra, K. C.; Shitanaka, T.; Lu, H.; Khanal, S. K. Nanobubble technology applications in environmental and agricultural systems: Opportunities and challenges. *Critical Reviews in Environmental Science and Technology* 2023, 53 (14), 1378-1403.
- [88] Manasa, R. L.; Mehta, A. in *Environmental biotechnology vol. 2* (eds K. M. Gothandam, Ranjan, Shivendu, Dasgupta, Nandita, & Lichtfouse, Eric) 197-219 (Springer International Publishing, 2020).
- [89] Qadri, H.; Bhat, R.; Mehmood, M.; Hamid Dar, G. *Fresh water pollution dynamics and remediation*. (2019).
- [90] Kalogerakis, N.; Kalogerakis, G.; Botha, Q. Environmental applications of nanobubble technology: Field testing at industrial scale. *The Canadian Journal of Chemical Engineering* 2021, 99.
- [91] Kyzas, G. Z.; Bomis, G.; Kosheleva, R. I.; Efthimiadou, E. K.; Favvas, E. P.; Kostoglou, M.; Mitropoulos, A. C. Nanobubbles effect on heavy metal ions adsorption by activated carbon. *Chemical Engineering Journal* 2019, 356, 91-97.
- [92] Gaur, R. K.; Verma, R. K.; Khurana, S. M. P. in *Genetic engineering of horticultural crops* (eds Gyana Ranjan Rout & Peter, K. V.) 23-46 (Academic Press, 2018).
- [93] English, N. J. Environmental exploration of ultra-dense nanobubbles: Rethinking sustainability. *Environments* 2022, 9 (3), 33.
- [94] Sha, Z.; Chen, Z.; Feng, Y.; Xue, L.; Yang, L.; Cao, L.; Chu, Q. Minerals loaded with oxygen nanobubbles mitigate arsenic translocation from paddy soils to rice. *Journal of Hazardous Materials* 2020, 398, 122818.
- [95] Wang, S.; Liu, Y.; Li, P.; Wang, Y.; Yang, J.; Zhang, W. Micro-nanobubble aeration promotes senescence of submerged macrophytes with low total antioxidant capacity in urban landscape water. *Environmental Science: Water Research & Technology* 2020, 6 (3), 523-531.
- [96] Sambo, P.; Nicoletto, C.; Giro, A.; Pii, Y.; Valentinuzzi, F.; Mimmo, T.; Lugli, P.; Orzes, G.; Mazzetto, F.; Astolfi, S.; Terzano, R.; Cesco, S. Hydroponic solutions for soilless production systems: Issues and opportunities in a smart agriculture perspective. *Frontiers in Plant Science* 2019, 10.
- [97] Kobayashi, N.; Yamaji, K. Leaf lettuce (*lactuca sativa* l. 'L-121') growth in hydroponics with different nutrient solutions used to generate ultrafine bubbles. *Journal of Plant Nutrition* 2022, 45 (6), 816-827.
- [98] Wang, S.; Liu, Y.; Lyu, T.; Pan, G.; Li, P. Aquatic macrophytes in morphological and physiological responses to the nanobubble technology application for water restoration. *ACS ES&T Water* 2021, 1 (2), 376-387.
- [99] Bostock, J.; McAndrew, B.; Richards, R.; Jauncey, K.; Telfer, T.; Lorenzen, K.; Little, D.; Ross, L.; Handisyde, N.; Gatward, I.; Corner, R. *Aquaculture: Global status and trends*. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences* 2010, 365, 2897-2912.
- [100] Tacon, A. G. Trends in global aquaculture and aquafeed production: 2000–2017. *Reviews in Fisheries Science & Aquaculture* 2020, 28 (1), 43-56.
- [101] Ghobadi, M.; Nasri, M.; Ahmadipari, M. Land suitability assessment (I_{sa}) for aquaculture site selection via an integrated gis-danp multi-criteria method; a case study of lorestan province, iran. *Aquaculture* 2021, 530, 735776.
- [102] Onari, H. Fisheries experiment of cultivated shells using micro-bubbles techniques. *Journal of the Heat Transfer Society of Japan* 2001, 40, 2-7.

- [103] Ebina, K.; Shi, K.; Hirao, M.; Hashimoto, J.; Kawato, Y.; Kaneshiro, S.; Morimoto, T.; Koizumi, K.; Yoshikawa, H. Oxygen and air nanobubble water solution promote the growth of plants, fishes, and mice. *PLoS One* 2013, 8 (6), e65339.
- [104] Averkiou, M. A.; Bruce, M. F.; Powers, J. E.; Sheeran, P. S.; Burns, P. N. Imaging methods for ultrasound contrast agents. *Ultrasound in Medicine & Biology* 2020, 46 (3), 498-517.
- [105] Foley, J.; Eames, M.; Snell, J.; Hananel, A.; Kassell, N.; Aubry, J.-F. Image-guided focused ultrasound: State of the technology and the challenges that lie ahead. *Imaging in medicine* 2013, 5, 1190-1203.
- [106] Krishna, V.; Sammartino, F.; Rezai, A. A review of the current therapies, challenges, and future directions of transcranial focused ultrasound technology: Advances in diagnosis and treatment. *JAMA neurology* 2018, 75 (2), 246-254.
- [107] Jugniot, N.; Massoud, T. F.; Dahl, J. J.; Paulmurugan, R. Biomimetic nanobubbles for triple-negative breast cancer targeted ultrasound molecular imaging. *Journal of Nanobiotechnology* 2022, 20 (1), 267.
- [108] Wu, H.; Abenojar, E. C.; Perera, R.; De Leon, A. C.; An, T.; Exner, A. A. Time-intensity-curve analysis and tumor extravasation of nanobubble ultrasound contrast agents. *Ultrasound in Medicine & Biology* 2019, 45 (9), 2502-2514.
- [109] Deprez, J.; Lajoinie, G.; Engelen, Y.; De Smedt, S. C.; Lentacker, I. Opening doors with ultrasound and microbubbles: Beating biological barriers to promote drug delivery. *Advanced Drug Delivery Reviews* 2021, 172, 9-36.
- [110] Exner, A. A.; Kolios, M. C. Bursting microbubbles: How nanobubble contrast agents can enable the future of medical ultrasound molecular imaging and image-guided therapy. *Current Opinion in Colloid & Interface Science* 2021, 54, 101463.
- [111] Bellotti, E.; Cascone, M.; Barbani, N.; Rossin, D.; Rastaldo, R.; Giachino, C.; Cristallini, C. Targeting cancer cells overexpressing folate receptors with new terpolymer-based nanocapsules: Toward a novel targeted DNA delivery system for cancer therapy. *Biomedicines* 2021, 9, 1275.
- [112] Cooley, M. B.; Abenojar, E. C.; Wegierak, D.; Sen Gupta, A.; Kolios, M. C.; Exner, A. A. Characterization of the interaction of nanobubble ultrasound contrast agents with human blood components. *Bioactive Materials* 2023, 19, 642-652.
- [113] de Leon, A.; Perera, R.; Nittayacharn, P.; Cooley, M.; Jung, O.; Exner, A. A. in *Advances in cancer research Vol. 139* (ed Ann-Marie Broome) 57-84 (Academic Press, 2018).
- [114] Horiuchi, Y. Ozone sterilization: Renewal option in medical care in the fight against bacteria. *American Journal of Therapeutics* 2021, 28 (6), e807-e808.
- [115] Shawli, H.; Iohara, K.; Tarrosh, M.; Huang, G. T.-J.; Nakashima, M.; Azim, A. A. Nanobubble-enhanced antimicrobial agents: A promising approach for regenerative endodontics. *Journal of Endodontics* 2020, 46 (9), 1248-1255.
- [116] Yoshida, K.; Ikegami, Y.; Obara, S.; Sato, K.; Murakawa, M. Investigation of anti-inflammatory effects of oxygen nanobubbles in a rat hydrochloric acid lung injury model. *Nanomedicine* 2020, 15 (27), 2647-2654.
- [117] Gupta, S.; Shende, P. L-proline adsorbed oxygen-loaded nanobubbles in-situ gel for wound healing. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 2022, 647, 129028.
- [118] Aikawa, A.; Kioka, A.; Nakagawa, M.; Anzai, S. Nanobubbles as corrosion inhibitor in acidic geothermal fluid. *Geothermics* 2021, 89, 101962.

- [119] Liu, G.; Wu, Z.; Craig, V. S. J. Cleaning of protein-coated surfaces using nanobubbles: An investigation using a quartz crystal microbalance. *The Journal of Physical Chemistry C* 2008, 112 (43), 16748-16753.
- [120] Yoon, R. H. Microbubble flotation. *Minerals Engineering* 1993, 6 (6), 619-630.
- [121] Nguyen, A.; Schulze, a. *Colloidal science of flotation*. (2004).
- [122] Li, C.; Zhang, H. A review of bulk nanobubbles and their roles in flotation of fine particles. *Powder Technology* 2021, 395.
- [123] Yoon, R. H.; Luttrell, G. H. The effect of bubble size on fine particle flotation. *Mineral Processing and Extractive Metallurgy Review* 1989, 5 (1-4), 101-122.
- [124] Zhang, Z.; Ren, L.; Zhang, Y. Role of nanobubbles in the flotation of fine rutile particles. *Minerals Engineering* 2021, 172, 107140.
- [125] Liu, S.; Kawagoe, Y.; Makino, Y.; Oshita, S. Effects of nanobubbles on the physicochemical properties of water: The basis for peculiar properties of water containing nanobubbles. *Chemical Engineering Science* 2013, 93, 250-256.
- [126] Ogawa, Y.; Iwanaga, M.; Aoki, T. (Google Patents, 2012).
- [127] Tian, Y.; Zhang, Z.; Zhu, Z.; Sun, D.-W. Effects of nano-bubbles and constant/variable-frequency ultrasound-assisted freezing on freezing behaviour of viscous food model systems. *Journal of Food Engineering* 2021, 292, 110284.