ABSTRACT: A variety of approaches have been developed to release contents from capsules, including techniques that use electric or magnetic fields, light, or ultrasound as a stimulus. However, in the majority of the known approaches, capsules are disintegrated in violent way and the liberation of the encapsulated material is carried in a random direction. Thus, the controllable and direction-specific release from microcapsules in a simple and effective way is still a great challenge. This greatly limits the use of microcapsules in applications where targeted and directional release is desirable. Here, we present a convenient ultrasonic method for controllable and unidirectional release of an encapsulated substance. The release is achieved by using MHz-frequency ultrasound that enables the inner liquid stretching, which imposes mechanical stress on the capsule’s shell. This leads to the puncturing of the shell and enables smooth liberation of the liquid payload in one direction. We demonstrate that 1−4.3 MHz acoustic waves with the intensity of a few W/cm² are capable of puncturing of particle capsules with diameters ranging from around 300 μm to 5 mm and the release of the encapsulated liquid in a controlled manner. Various aspects of our route, including the role of the capsule size, ultrasound wavelength, and intensity in the performance of the method, are studied in detail. We also show that the additional control of the release can be achieved by using capsules having patchy shells. The presented method can be used to facilitate chemical reactions in micro- and nanolitre droplets and various small-scale laboratory operations carried in bulk liquids in microenvironment. Our results may also serve as an entry point for testing other uses of the method and formulation of theoretical modeling of the presented ultrasound mechanism.

KEYWORDS: patchy capsules, particle shells, directional release, ultrasound-responsive droplets, acoustic stress

1. INTRODUCTION

Encapsulation, storage, and controlled release of various substances from microcapsules are extensively studied nowadays due to several advantages and numerous applications of such structures. Many applications of microcapsules require the encapsulated content to be liberated on demand. A variety of physical and chemical approaches have been developed to trigger release from different capsule types, and these are reviewed in refs 1−5 In general, the release may be initiated through an internal stimulus, such as the ionic strength of the solution or its pH level, or an external stimulus, for example, electric or magnetic fields, light, or ultrasound. However, in many of the known approaches, including those cited above, capsules are disintegrated in violent way and the liberation of the encapsulated material is in a random direction. This greatly limits the use of microcapsules in applications where the targeted and directional release is desirable. These days, the directional release can be achieved by a limited number of techniques, primarily using magnetic fields that require an encapsulated content to possess a magnetic component. Here, we present a convenient route for controllable and unidirectional release of encapsulated liquid using ultrasound. Our approach is distinctly different from commonly used ultrasonic methods. In most of the ultrasound related studies, capsules are disintegrated by ultrasonic waves generated by devices operating at around 20−50 kHz and high-power output or low-power ultrasound working at MHz frequencies. Cavitation and ultrasonic heating are two mechanisms that usually serve for the shell destruction and the release of the inner substances. There are also other ultrasound approaches that require the usage of specially designed microcapsules. Yet, all of these processes cause rather brisk fragmentation of capsules and/or omnidirectional release of their content. In the proposed method, MHz-
frequency ultrasound waves provide a means for smooth liberation of the inner liquid in one direction.

1.1. Ultrasonic Method. We hypothesize that MHz-frequency ultrasound waves provide a means for the inner liquid stretching that imposes mechanical stress on the capsule’s shell. This, in turn, leads to the puncturing of the shell and enables the inner liquid release along the direction of the ultrasound propagation. Surprisingly, in the context of the content release from capsules, the high-frequency ultrasound mechanism of capsule puncturing and liberation of liquid presented here has not been greatly exploited in research. Other researchers studied the impact of low- and high-frequency ultrasound on a direct rupturing of a capsule’s shell.28 Here, we use the inner liquid to puncture the shell and flow out from the capsule placed in the sample cell, in which a standing wave is generated.

In this work, the high-frequency ultrasound waves propagate through the bulk medium and are reflected back from the wall of a sample cell giving rise to a standing wave. Periodic spatial distribution of acoustic energy density results in a periodic force field. Droplets smaller than around one-half of the ultrasound wavelength located in such a periodic field are acoustophoretically driven toward the pressure nodal (or antinodal) positions of the standing wave, as schematically presented in Figure 1a. Such acoustophoretic motion of droplets (bubbles or solid particles, in general) originates from the acoustic radiation force (ARF),29−32 and it was shown by other researchers to be particularly useful for trapping, sorting, or coalescing droplets.33−35 However, if the droplet size is larger than around one-half of the ultrasound wavelength, it stretches along the wave propagation. Depending on its volume, the droplet may span several ultrasound wavelengths by transferring matter between adjacent nodes in the acoustic field (see Figure 1b) and may eventually break apart. The force that deforms the droplet cannot originate from the ARF, which can only make the droplet to migrate in space as a whole and cannot cause droplet deformation. We assume that this is rather the difference of time-averaged acoustic Lagrangian pressures on both sides of the interface that act on the droplet to deform it. In our research, we use this mechanism for rupturing shells and liberating the inner liquid from capsules, as schematically shown in Figure 1c.

1.2. Homogeneous and Janus Capsules. In our study, we use liquid-containing microcapsules with a shell made of fused microparticles as a model system. The particle capsules are typically produced from particle-covered droplets in Pickering emulsions by interlocking the surface particles through sintering, gel trapping, or covalent cross-linking.35 Their permeability and mechanical properties can be tuned by adequately choosing parameters of the process of the particle shell reinforcement, e.g., sintering time and temperature.36 The capsules with stable shells can be composed of granular37 or colloidal particles.38 The sizes of particle capsules range from hundreds of nanometers to few millimeters.39 In the present study, we use microparticles to form sub-millimeter and millimeter-sized capsules. The main reasons for that are the ease of both the fabrication of capsules and the experimental observation of their mechanical behavior when subjected to ultrasound, as well as the demonstration of the ultrasound mechanism for droplet stretching, breakup, and liberation from a capsule.

The majority of currently fabricated particle capsules (and therefore studied in the context of controllable release) consist of monolayer or multilayer shells, each composed of one type of material.40−43 However, the functionality of microcapsules can be significantly extended if a shell layer is composed of multiple components with different chemical or physical properties. Such patchy capsules, supplemented by functionalities similar to those offered by well-studied patchy particles,44−46 have advantageous properties when compared with their homogenous counterparts. For example, patchy capsules cannot only be propelled, aligned, and oriented in a controlled manner but also may release their cargo in a specific direction.35 Unfortunately, the fabrication of Janus and patchy capsules in bulk quantities remains challenging. Because of this, the literature on their external field-triggered rupturing and release of the encapsulated material practically does not exist. Based on the research results presented here, we aim to contribute to filling the gap in that research area. By communicating the possibilities offered by the patchy capsules,
which we can produce using our recently developed method,47 we will impact not only on the state of art of the encapsulation techniques but also on the improvement of the ultrasound-triggered release methods. As schematically presented in Figure 1c, the additional control of the release can be achieved by using capsules having patchy shells, i.e., an inner liquid is released through the shell with low nominal wall tension.

2. MATERIALS AND METHODS

2.1. Materials. Castor oil (83912, the density of ∼0.96 g/cm3 at 25 °C), the electrical conductivity of ∼50–100 pS/m, the relative permittivity of ∼4.7, and the kinematic viscosity of ∼730 mm²/s at 25 °C) was purchased from Sigma-Aldrich. Silicone oil (6678.1000, Rhodorsil Oils 47, the density of ∼0.96 g/cm³ at 25 °C, the electrical conductivity of ∼5–10 pS/m, the relative permittivity ∼2.8, and the kinematic viscosity of ∼50 mm²/s at 25 °C) was purchased from VWR Chemicals. Polystyrene (PS) particles with a diameter of ∼50 μm (PS50) and ∼100 μm (PS100) were purchased from Cospheer LLC, Santa Barbara. Polyisoprene (PS) particles with a diameter of ∼10 μm (PS10), ∼40 μm (PS40), or ∼140 μm (PS140), each with a density of ∼1 g/cm³, and kinematic viscosities ∼850 mm²/s at 25 °C) was purchased from Formlabs, MA. Polyethylene (PE) particles with a diameter of ∼50 μm (PE50) and ∼100 μm (PE100) were purchased from Cospheric LLC, Santa Barbara. Polystyrene (PS) particles with a diameter of ∼10 μm (PS10), ∼40 μm (PS40), or ∼140 μm (PS140), each with a density of ∼1 g/cm³, were bought from Microbeads, AS, Norway. The surface of PS particles was modified as described in16 to change the three-phase contact angle and increase their affinity toward silicone oil so that the particles attach strongly to the castor oil—silicone oil interface. The used ratio of a acrylic polymer surface modifier (Fluorosil PFC S02AFA, Cytonix, Beltsville) and a methoxy-nonafluorobutane solvent was 1:300. Optically transparent ultrasound gel (carbomer, sodium benzoate, 2-bromo-2-nitropropane-1,3-diol, sodium hydroxide, purified water) was purchased from Ziaja Ltd., Gdańsk, Poland.

2.2. Fabrication of Particle Capsules. 2.2.1. Experimental Setup for Formation of Pickering Droplets. A schematic representation of the experimental setup used to form Pickering emulsion droplets is shown in Figure S1. The setup consisted of a sample cell placed on a mechanical XYZ translation stage, a signal generator (SDG1025, SIGLENT Technologies Co, Ltd., China), a high-voltage bipolar amplifier (UltraVolt SHVA24-BP1, Advanced Energy Industries, Inc.), a digital microscope (AM7115MZTL, DINO-LITTE), a light source (KL 300 LED, Schott AG), and a computer for collecting images and recording videos. The sample cell was made of poly(methyl methacrylate) (PMMA), and its size was 45 mm × 10 mm × 10 mm. Two copper plates constituting electrodes were placed inside the cell. We used an electric field strength of around 230 V/mm in the experiment.

2.2.2. Fabrication of Pickering Droplets with Homogenous Particle Shells. Silicone oil droplets containing PE or PS particles were formed in a cuvette filled with castor oil using a micropipette. Highly ordered jammed Pickering droplets were created using the action of electrohydrodynamic flow and gentle mechanical rotation as described in.17 In short, after the application of a DC electric field, the particles in a bulk liquid are guided toward the droplet’s interface by electrostatic force. As particles reach the surface of a droplet, they are carried toward the electric equator of that droplet by the electric field-induced liquid flow. It takes several minutes for all particles to get onto the interface and eventually form a packed particle monolayer that covers the entire droplet surface. After turning off the electric field, the Pickering droplet remains stable (i.e., neither particle diffusion within the shell nor particle detachment from the interface is observed). A monolayer shell is formed in such a manner that it consists of jammed particles (particle coverage at the surface of around 80%). In the experiment presented in Section 3.5, we used a droplet with a shell composed of multilayered PS particles made by increasing three times the particle concentration that would be otherwise needed for the formation of a monolayer particle shell. To form particle-covered droplets, we used a silicone oil dispersion with particle concentrations presented in Table S1.

2.2.3. Fabrication of Pickering Droplets with Patchy Particle Shells. To form Pickering droplets with patchy particle shells, we used the method that involved the synergetic action of electrohydrodynamic flows and electrocoalescence, as described in ref 47. In short, two particle-covered droplets were made in the same manner as described above, each containing different types of particles. However, this time the concentration of particles was lower than in the case of forming Pickering droplets with homogeneous shells (see Table S1) and chosen such that the particle coverage on the surface of each droplet was around 70%. We then brought together the two droplets coated with particles (mechanically, using a pipette tip) and applied the electric field again to let them coalesce. Given that the coalescence of two droplets of the same size reduces the available surface area by around 20%, the resulting coalesced droplet had higher particle coverage on its surface than the two original droplets before the coalescence. This condition led to the formation of Pickering droplets with heterogeneous shells. Such shells consisted of jammed particles arranged in a nearly hexagonal pattern. After turning off the electric field, the Pickering droplet with patchy shells remained stable (i.e., neither particle diffusion within the shell nor particle detachment from the interface was observed). Particle concentrations in dispersions are listed in Table S1.

2.2.4. Formation of Capsules: Interlocking of the Shell Particles by Microwave Heating. To obtain a capsule with a cohesive particle shell, we interlock particles through heating using a microwave oven (Alaska M8100, nominal power output 800 W). The degree of particle fusing (e.g., porosity and smoothness of the particle capsule) was controlled by heating time. Pickering droplets with homogeneous shells made of PE particles were heated for 15 s, and those coated with the modified PS10 and PS40 were kept in the microwave oven for 30 and 60 s, respectively. These were the optimal conditions for interlocking the surface particles. Microwave oven heating for shorter times resulted in less mechanically stable shells, whereas heating Pickering droplets for a longer time resulted in the disintegration of the PS particle shells or, in case of the PE particle shells, caused phase separation of the melted PE material and the dye used for particle coloring.

The duration of thermal treatment of Pickering droplets with patchy shells was adapted to particles with shorter sintering time. For example, structures with two regions, the first of them made of PE particles and the second of PS40 particles, were heated 15 s, so only the PE part of the shell was sintered. Capsules with two domains composed of PS particles with different sizes, namely, PS10 and PS40, were sintered for 30 s. Therefore, both domains of the patchy capsules obtained different mechanical properties.

2.3. Ultrasound-Induced Bursting and Rupturing of Capsules. The mechanisms of the ultrasound-triggered capsule opening and release of the inner liquid were tested using low- and high-frequency ultrasound. Low-frequency ultrasound impulses (20 kHz, pulsation time 0.1 s, acoustic intensities ∼20, ∼40, or ∼100 W/cm²) were generated by a Sonopuls ultrasonic homogenizer HD 3100 (Bandelin electronic GmbH & Co.). These acoustic intensities I were calculated based on the ultrasound-induced increase in temperature of the medium ΔT, using the equation given in ref 50 and the value of specific heat of castor oil C_p = 1.8 kJ/(kg K).51

\[ I = \frac{m C_p \Delta T}{t S} \]

where \( m \) —the mass of the castor oil, \( t \) —the time interval, and \( S \) —the tip area (0.29 cm²).

The temperature of the medium was measured simultaneously using two methods (a CENTER 309 thermometer with thermocouple and also a Fluke VT02 visual IR thermometer) to reduce uncertainty. The ΔT for the calculation of each acoustic intensity was taken as the average of the results of the 25 repetitions of the experiment.

During the experiments, the end of the working tip was immersed in medium and placed centrally ∼5 mm above the capsule. The experimental setup (see Figure S2a) consisted of an ultrasonic homogenizer, a poly(methyl methacrylate) (PMMA) sample cell (27 mm × 10 mm × 10 mm) placed on a mechanical translation stage, a
The particle ribbon assembled at droplet (see Figure S2b). High-frequency ultrasound waves (2.2, 3.5, and 4.3 MHz, intensity up to 4 W/cm²) were generated by using transducers purchased from Steiner & Martins, Inc., FL. The transducers were driven by a home-made high-voltage generator (DC-5 MHz, voltage up to 150 V). Two ultrasonic transducers with similar resonant frequency were glued to the opposite walls of the PMMA sample cell. We used two separate LC electronic circuits to match impedance between the high-voltage generator and each of the transducer. The LC circuits also enabled tuning the voltage level of each transducer. Most of the experiments were done on capsules immersed in castor oil. Though, we also studied particle capsules embedded in an ultrasonic gel. These capsules were initially made in castor oil and then removed from the oil, placed on a glass slide, rinsed with isopropanol, and finally transferred into the cuvette filled out with the gel.

3. RESULTS AND DISCUSSION

First, we briefly describe and present the fabrication of capsules with homogeneous and patchy shells. Then, we demonstrate the difference between using low-frequency ultrasound to burst the capsule and high-frequency ultrasound used to rupture the capsules. Next, we discuss the viability of the high-frequency ultrasonic method with respect to the capsules size and mechanical properties of their shells. Finally, we show the increased functionality of capsules with patchy shells in comparison to their homogeneous counterparts.

3.1. Fabrication of Particle Capsules. In Figure 2a, we present the formation of a particle-covered droplet (Pickering droplet) with a homogeneous particle shell. A silicone oil droplet (size of ~2 mm) with red PE particles (size of ~50 μm, concentration ~9 wt %) was formed in castor oil. Initially, the majority of the particles were dispersed within the bulk of the droplet. As the droplet was subjected to a DC electric field (230 V/mm), the PE particles were attracted toward the droplet’s interface and strongly bound to it. The induced electrohydrodynamic flows moved particles within the droplet’s surface, made them pack into a ribbon-like structure, which gradually widened and eventually (after around 10 min) covered the entire droplet surface (see also Movie S1). The shell particles were arranged in a jammed, nearly hexagonal structure, as shown in the blow-up. In Figure 2b, we show the formation of a Pickering droplet with a heterogeneous particle shell. We first formed two droplets (size of ~1.6 mm) partially covered with particles, one with PS particles (size of ~40 μm, concentration ~8 wt %) and the other one with red PE particles (size of ~50 μm, concentration ~8 wt %), using the same procedure as described above. Then, the droplets were mechanically brought into close proximity. Subjected to a DC electric field (200 V/mm), the droplets attracted one to another and eventually coalesced forming a Pickering droplet with a heterogeneous shell comprising densely packed particles.
3.2. Response of Droplets with Particle Shells to Low-Frequency Ultrasound (20 kHz). We started ultrasound experiments by investigating the response of droplets with particle shells to the low-frequency (20 kHz) ultrasound. We used pulsed mode to prevent sample heating and to control the energy delivered to the system. 52 By using electric fields, we fabricated three PS40 particle-covered silicone oil droplets, as described in the method section. Two of them were heated up in a microwave oven to interlock the surface particles and create particle capsules with rigid shells, whereas the third one was left unprocessed. We also made a droplet with patchy shells consisting of two different parts. One domain was composed of red PE particles, the second was composed of PS40 particles. The Pickering droplets with a patchy shell were heated up in a microwave oven for 15 s forming a Janus capsule with different mechanical properties (as determined through the test described in the Supporting Information and presented in Movie S3).

First, we tested the behavior of Pickering droplets. Ultrasound pulses with an acoustic intensity of ∼20 W/cm² caused only successive reversible deformations of such droplets (Figure S4a). When stronger ultrasound waves with an intensity of ∼40 W/cm² were used, several pulses were needed to destroy the Pickering droplet. The first few pulses reversibly deformed the droplet pulling it into the area adjacent to the tip of the ultrasonic horn, where the droplet was eventually fragmented by the fourth pulse. The fragmented parts (small droplets and particles) were spread omnidirectionally (see Figure 3a). The application of ultrasound with the intensity of ∼100 W/cm² (the highest available for the experiment) resulted in immediate and complete fragmentation of the droplet by the first pulse (see Figure S4b). The next pulses caused further droplet fragmentation, and the small oil droplets and particles were also spread in all directions.

In contrast to the Pickering droplet, the droplet with the PS particle capsule initially remained rigid and intact in the acoustic field with an intensity of ∼40 W/cm², but after being pulled into area closely adjacent to the working tip, the particle capsule was fragmented by the next ultrasonic pulse. Then, the content of the capsule was spread omnidirectionally by subsequent pulses (see Figure 3b). Again, the use of a stronger acoustic intensity of ∼100 W/cm² resulted in the immediate destruction of the capsule and splashing its contents around.

We also studied the behavior of the droplet with a sintered PS particle capsule and immersed in the gel medium with viscoelastic mechanical properties similar to soft biological materials. The number of ultrasound pulses needed to destroy the PS capsule embedded into the gel medium typically varied between one and three. The proximal half of the spherical

![Figure 3](https://dx.doi.org/10.1021/acsami.9b21484)
capsule was torn off, preceding the fragmentation of the whole structure and spreading the content around by the subsequent pulses (see Figure 3c).

Finally, we carried out an experiment on a droplet with a patchy shell. We hypothesized that the acoustic streaming induced for short time could rupture the mechanically weaker part of the shell (composed of PS particles) and rip off part of the droplet roughly in the direction along the ultrasound wave propagation. In the experiment, the unsintered PS region was situated proximally to the working tip of the homogenizer. We aligned the droplet by gently shearing the liquid around it using a pipet tip. The application of low-intensity ultrasound deformed the PS particle shell. When stronger ultrasound waves with the intensity of $\sim 40$ W/cm$^2$ were used, the PS particle shell fragmented and the content spread around omni-directionally. The remaining PE hemispherical part of the shell initially kept certain integrity but eventually was broken apart (see Figure 3d).

In all mentioned cases after applying the certain number of pulses, the whole shell was completely fragmented. We also carried out experiments using different ultrasound intensities and various pulse lengths and could not achieve the rupturing of particle shells and release of liquid in a controllable way (neither spatial nor temporal). The application of continuous mode ultrasound with the same intensity $\sim 40$ W/cm$^2$ resulted in the localized puncturing of the shell followed by the directional release of the encapsulated content through the perforation. Our experiments showed that only the use of ultrasound with a high frequency of 1 MHz (intensity 2.5 W/cm$^2$) ensures the highest controllability of the release of the capsule’s content.

3.3. Response of Droplets with Particle Shells to High-Frequency Ultrasound (1 MHz). The drastically different behavior of the particle-covered droplet was observed when using the high-frequency ultrasound of 1 MHz. As before, we first studied the behavior of the PS particle Pickering droplet and droplets with homogeneous PS particle capsules subjected to ultrasound. The Pickering droplet (Figure 4a), under the influence of high-frequency ultrasound, stretched along the direction of the ultrasound propagation (see also Movie S5). The droplet returned to its spherical shape after turning off the ultrasound. Application of US waves to droplets with particle capsules immersed either in castor oil (Figure 4b) or viscoelastic gel (Figure 4c) resulted in the localized puncturing of the shell followed by the directional release of the encapsulated content through the perforation. In Figure 4b, we demonstrate that the silicone oil was gradually and directionally liberated from the small fracture in the distal side of the structure. As presented in Figure 4c, liberated oil run down forming a trickle oriented in the direction of the ultrasound wave propagation. Our experiments showed that only the use of ultrasound with a high frequency of 1 MHz (intensity 2.5 W/cm$^2$) ensures the highest controllability of the release of the capsule’s content.

We observed similar behavior when a droplet with a PS particle capsule was embedded in the viscoelastic gel. In such a case, the silicone oil was also directionally released from the small fracture in the distal side of the structure. As presented in Figure 4c, liberated oil run down forming a trickle oriented in...
the direction of ultrasonic wave propagation. Slow outflow was accompanied by the movement of the remaining liquid inside, but the shell as a whole was not disintegrated. Additionally, droplets with capsules deposited in gel did not show any translational movement under the influence of ultrasound as opposed to those immersed in castor oil. Experiments on droplets with PS particle capsules demonstrate that the amount of silicone oil released from the capsules can be controlled by the acoustic intensity, the time of exposure to ultrasound, as well as viscoelastic properties of the medium. Next, we studied a droplet with a patchy capsule prepared similarly to that presented in Figure 3d. The application of ultrasound with an intensity of 2.5 W/cm² resulted in a breakup of the PS particle shell, whereas the PE particle shell remained untouched (see Figure 4d).

3.4. Ultrasound Mechanism and Its Viability. In contrast to 20 kHz ultrasound, waves with a frequency of 1 MHz did not cause the violent fragmentation of Pickering droplets and droplets with particle capsules. We observed only the ultrasound-induced puncture of these structures and the directional release of the content through the perforation. Such gradual outflow of the encapsulated liquid is desirable, especially in the context of various applications. The mechanism responsible for the droplet rupture under the influence of high-frequency ultrasound is elementarily different than acoustically induced cavitation in the host liquid, i.e., the commonly used mechanism emerging at a low-frequency range.

Here, the high-frequency ultrasonic waves provide a means for stretching of the inner liquid, which in turn imposes mechanical stress on the particle shell. The condition for the droplet stretching is that its size is larger than around one-half of a wavelength of the standing wave (here $\lambda/2 \sim 0.75$ mm) formed in a sample cell. Otherwise, a small droplet will be acoustophoretically driven toward the pressure nodal (or antinodal) positions of the standing wave and trapped there, as schematically presented in Figure 1a. If a droplet is large enough it may span several ultrasound wavelengths by transferring mass between adjacent nodes in the acoustic field (see Figure 1b) and eventually split into several small droplets. In Figure 5a and Movie S6, we demonstrate this behavior experimentally. A pure silicone oil droplet (~1 mm) was formed in castor oil and subjected to ultrasound (in the vertical direction). The ultrasound intensity was increased stepwise from 0 to 2 W/cm². Each time the intensity was raised, the magnitude of the droplet deformation also increased. At the ultrasound intensities below 2 W/cm², a steady state was observed. However, at an ultrasound intensity of 2 W/cm², the droplet was in a nonequilibrium state and it stretched spanning almost two ultrasound wavelengths and eventually broke apart. At an intensity of 2 W/cm², we also observed the weak translational motion of the droplet. Typically, we see such motion at high ultrasound intensities resulting from the acoustic streaming, which arises from the nonlinear propagation of a compression wave through an attenuating media. The acoustic streaming can be suppressed by reducing the ultrasound wave path. Such acoustic streaming may exert normal surface stresses on the interface that might contribute to part of the interface deformation. However, the droplet stretching is here predominantly owned to the time-
averaged acoustic force arising from a periodic field force. This force is different from the acoustic radiation force that (if understood in the classical sense) is applied to the center of mass of a droplet enabling its migration in space as a whole.\textsuperscript{[39–35]} It is rather the difference of time-averaged acoustic Lagrangian pressures on both sides of the interface that act on the droplet to deform it. Several experiments and theoretical studies were conducted on flat liquid−liquid interfaces using the radiation pressure of either acoustic or electromagnetic waves that demonstrate qualitatively similar behavior of liquids subjected to external fields, as in our experiments.\textsuperscript{[53,54]} Unfortunately, the calculation of the acoustic radiation stress acting on a droplet larger than \(\lambda/2\) is not a trivial task, and there is a lack of a rigorous theory that would allow us to calculate these two forces. However, we can estimate the order of magnitude of the ultrasound intensity needed to stretch the droplet by balancing the acoustic force with the surface tension force, which tries to minimize the surface area and works against the acoustic stretching force. As the weakly deformed droplet resembles a prolate spheroid, we make simplification regarding the calculations of the surface tension force \(F_s\) approximating the droplet by a prolate spheroid with transverse and conjugate radii \(r_c\) and \(r_c\). The force \(F_s = -3\pi\gamma\Delta r_c\), where \(\gamma\) is the surface tension and \(\Delta r_c\) is the increment of the conjugate radius of a deformed droplet.\textsuperscript{[55]} Thus, \(|F_s| = F_s = 3.5 \times 10^{-3} \text{ N}\), given that \(\gamma \approx 5 \text{ mN/m}\),\textsuperscript{[36]} \(r_c = 0.5 \text{ mm}\), and \(r_c = r + \Delta r_c = 1.5r\). Assuming that the acoustic radiation stress is proportional to the acoustic intensity, its magnitude should be in the range \(\sim 10^{-7} - 10^{-4} \text{ N}\) for the acoustic intensity in the range of 0.5–5 W/cm\(^2\).

For droplets with particle capsules, one needs to consider the contribution from the particle shell elasticity. In our studied system, the particle capsule elasticity dominates over the surface tension. The mechanical strength of a microcapsule depends primarily on the shell composition, structure (defined by, e.g., fusing time or temperature), and its thickness.\textsuperscript{[57–61]}

Typically, the force needed to break microcapsules composed of sintered microparticles is in the order of \(\sim 10^{-4} – 10^{-7} \text{ N}\).\textsuperscript{[61–64]} Indeed, in our experiments, we observed rupturing of shells when acoustic intensities of \(\sim 2 \text{ W/cm}^2\) or higher were used, which roughly corresponds to the acoustic force larger than \(10^{-3} \text{ N}\). In Figure 5b, we show the results of the experiment, in which a droplet (size \(\sim 1.8 \text{ mm}\)) with the PS particle shell was subjected to ultrasound. We increased the ultrasound intensity stepwise from 0 to 2.5 W/cm\(^2\). The acoustic intensities in the range from 0.5 to 2 W/cm\(^2\) did not cause visible deformations of the capsule. The puncturing of this structure and controlled release of the content were exclusively observed for the intensity of 2.5 W/cm\(^2\).

In Figure 5c, we demonstrate that 1 MHz ultrasound operating at rather low acoustic intensities (few W/cm\(^2\)) enabled rupturing of capsules with diameters between 0.6 and 5 mm, which corresponds to volumes of an inner liquid in the range of microliters. Generally, for larger capsules, it was easier to control the relative amount of the released liquid. For the smallest capsule (size \(\sim 0.6 \text{ mm}\)), we were able to release only one quantum of the inner liquid because of the long wavelength of the ultrasound. However, the method can be adapted to capsules with different sizes by increasing the ultrasound frequency. This also allows for better control of the amount of liquids liberated from a capsule.

In Figure 6, we show the results of experiments on pure silicone oil droplets of different sizes (1.7–0.3 mm) formed in castor oil and subjected to ultrasound with frequencies varying from 1 to 4.3 MHz. As the ultrasound frequency increases, the wavelength of the standing wave formed in a sample cell decreases, which affects the magnitude of the cross-sectional area of the stretched droplet (compare panels i–l in Figure 6). For example, the cross-sectional area of the droplet stretched by 1 MHz ultrasound is around 0.44 mm\(^2\), and the droplet stretched by 4.3 MHz is around 0.02 mm\(^2\). Thus, the flux of the liquid is much lower by increasing the ultrasound

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**Figure 6.** Stretching of silicone oil droplets formed in castor oil by ultrasound with different frequencies. (a–d) Droplets of different sizes (1.7–0.3 mm) at rest; (e–h) at the ultrasound intensities around 1.5 W/cm\(^2\); and (i–l) at the ultrasound intensities around 3.5 W/cm\(^2\). The cross-sectional areas of the droplets stretched by 1, 2.2, 3.5, and 4.3 MHz ultrasound are \(\sim 0.44, \sim 0.09, \sim 0.04, \sim 0.02 \text{ mm}^2\), respectively. The calculations were made by approximating a stretched droplet to the cylinder with the diameter equal to the half-wavelength of the ultrasound. In all images, the direction of wave propagation is horizontal.

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**Figure 7.** Liberation of the liquid from capsules using ultrasound with different frequencies. The capsules are roughly the same size, and the shells are made of (a) PE50-PS40 particles, (b) mix of PS40 and PS10 particles, (c) PS40 particles forming a multilayered shell, and (d) PS40 particles forming a monolayer shell. Images captured several seconds after switching on the ultrasound. All capsules were made in castor oil, except the capsule presented in panel (b), which was made in a synthetic photopolymer resin. In all images, the direction of wave propagation is horizontal.
frequency 4.3 times. This is true when assumed that the liquid flow through the punctured shell is the same irrespective of the frequency of the ultrasound. For the moment, we do not know how to control the flow with great precision. Nevertheless, as shown in Figure 7, the release from particle capsules of similar size can be (to a certain degree) controlled by tuning the frequency of the ultrasound.

3.5. Liberation of Liquid at Different Ultrasound Frequencies (1–4.3 MHz). In Figure 7, we present the liberation of liquid from four (roughly the same size) capsules using different ultrasound frequencies (1–4.3 MHz). The application of ultrasound with an intensity around 3 W/cm² resulted in the local puncturing of the shell and the release of an inner liquid. By comparing the images in Figure 7, one can see that the amount of the released liquid from the capsule exposed to 4.3 MHz ultrasound is several times smaller than the amount of liquid released from the capsule subjected to 1 MHz ultrasound. Thus, using higher-frequency ultrasound enables better control of the amount of the released liquid. The experiments shown in Figure 7 confirm that the condition for the successful liquid liberation is that the size of a capsule needs to be larger than the half wavelength of the standing wave. For example, the capsules presented in Figure 7c,d are about 8 times larger than one-half of the ultrasound wavelength. Finally, we note that the acoustic streaming was considerably stronger at higher ultrasound frequencies, which, in turn, caused the capsule to translate along the liquid streamlines, making it more difficult to perform the experiment. The acoustic streaming was not a concern when we studied the liquid liberation from capsules immersed in a gel matrix.

In Figure 8, we present quantitatively the liberation of the liquid from particle capsules immersed in the gel matrix. We prepared 10 samples and subjected half of them to 1 MHz ultrasound and the other half to 3.5 MHz ultrasound. In Figure 8a, we show the results from the experiments performed at 1 MHz ultrasound. The kinetics of liquid liberation is similar in all five tests, though the final amount of the released liquid (at t = 100 s) differs by up to two times (compare the results from Sample 2 and Sample 5). A similar difference between the extreme values was observed for samples subjected to a 3.5 MHz ultrasound. Nevertheless, when averaging the results from the experiments conducted at two different ultrasound frequencies, a significant difference in the release profile emerges, e.g., the average value of the volume of the liquid (at t = 100 s) released at 1 MHz ultrasound is around 4 times larger than that of the liquid released at 3.5 MHz ultrasound (see Figure 8b).

3.6. Taking Advantage of Capsules’ Patchiness. In this section, we present the extended functionality of patchy microcapsules having advantageous properties when compared with their homogeneous counterparts. First, we demonstrate that the control of a directional liquid payload liberation can be enhanced using droplets with Janus shells. In two experiments, presented in Figure 9a,b, the content of the capsule was released either downward or upward. The release in a specific direction was determined by the mechanical properties of shells. The inner liquid was liberated through the more fragile part of the shell, which was in Figure 9a the bottom hemisphere composed of PS particles and in Figure 9b the top hemisphere composed of 140 μm PS particles. The regions with increased mechanical properties maintained their integrity. In both experiments, we used an acoustic intensity of 2.5 W/cm² and the ultrasound wave was emitted from above the capsules.

The droplets presented in Figure 9a,b were aligned by gentle mechanical shearing of the liquid around them using a pipet tip. It was simple and sufficient to illustrate the concept of the shell puncturing and the triggered release. However, the alignment can be more conveniently achieved through a noninvasive manner using external fields. In Figure 9c,d, we show that the addition of a small number of magnetic particles or electrically conductive particles enables the alignment of capsules by a magnetic (Figure 9c) or electric field (Figure 9d). Magnetic or conductive particles are made to form linear structures within capsules. In the presence of an external field, the capsules undergo electro- or magneto-orientation, i.e., they align themselves with the dipolar chains oriented roughly along the electric or magnetic field lines. As the droplets with capsules rotated, the repartition of the particle chains remained.
still, as the particles were jammed within the monolayer shell (see also Movie S7). As shown by the other researchers, external fields can also be used for other purposes, such as capsule assembly or translational motion.\textsuperscript{55–67}

4. CONCLUSIONS

In summary, we have presented a route for stimulating the release of the encapsulated liquid from microcapsules using low-intensity ultrasound. We showed that 1−4.3 MHz acoustic waves with the intensity of a few W/cm\textsuperscript{2} are capable of localized puncturing of the particle capsules with diameters ranging from around 300 \textmu m to 5 mm. The mechanism responsible for this phenomenon is related to the stretching of the inner liquid content, which exerts mechanical stress on the capsule’s shell. The method allows smooth liberation of the liquid in one direction that enables accurate targeting. Such nonviolent and directional release is crucial, for example, for applications where the directional release of an active substance is preferable (especially where cavitation mechanism should be avoided). Currently, the directional release can be achieved by just a few techniques, primarily using magnetic fields that require using an additional magnetic core material.\textsuperscript{12−14} The proposed ultrasound approach works for a large variety of capsule types and particularly well for capsules with a weak or moderate mechanical strength of their shells. In our study, we used microcapsules with a shell made of fused microparticles as a model system. However, we think that the presented concepts and methodology are not limited to the capsules with this type of shells, as long as the mechanical properties of the shell enable their puncturing. Because the method is relatively easy to implement and operate, we expect it to find many applications, including in microfluidic systems. For instance, this technique can be used for various small-scale laboratory operations, such as regulating the release profile of molecules,\textsuperscript{69} supporting microfluidic droplet sorting,\textsuperscript{70} or microcapsule self-reproduction.\textsuperscript{71,72} In this paper, we mostly discussed the response of capsules to ultrasound. Though, our approach can as well be extended to remote manipulation of the droplet and its particle shell, for example, for controllable microcapsule ingestion to facilitate chemical or biological reactions in liquid volumes of microliters.\textsuperscript{32}

We also demonstrated that the additional increase of the method’s performance can be achieved using microcapsules with heterogeneous surfaces with two or three patches (regions with different physicochemical properties). We think that changing the share of the area of an individual domain in the total area of the shell can also lead to better control of the release rate, which is a subject of our next research.

The method has also its limitations. It can be possibly used for smaller capsules than those used in our experiments. Though, we expect it to be very challenging to apply the method for capsules smaller than tens of micrometers, as this would require very high frequencies of ultrasound. Another subtle point is that the method requires the formation of a standing wave, which involves designing a sample cell with certain geometries. Finally, simple single-frequency transducers and their drivers are rather cheap and easily accessible but more advance ultrasonic devices that work in a broad range of frequencies and intensities are expensive.

The major goal of this research was to present conceptually the method and its aspects (rather than focuses on any specific applications) to stimulate further research of local and directional release in microenvironment. We are positive that our experimental results will serve as an entry point for testing other uses of the method and formulation of theoretical modeling of the presented ultrasound mechanism.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsami.9b21484.

Schematic illustration of the experimental setup, consisting of a sample cell placed on a mechanical XYZ translation stage (Figure S1); two setups for studying ultrasound-induced rupturing of capsules (Figure S2); electric field, as a noncontact method, to verify whether particle shells of thermally treated droplets were mechanically stable (Figure S3); particle concentration in silicone oil and droplet sizes (Table S1) (PDF)

Process of formation of a particle-covered droplet using a DC electric field (Movie S1) (MP4)

Fabrication of a Pickering droplet with a heterogeneous shell (Movie S2) (MP4)

Testing the mechanical properties of particle shells by inducing electric stress (Movie S3) (MP4)
Behavior of various droplets subjected to 20 kHz ultrasound (Movie S4) (MP4)
Behavior of various droplets subjected to 1 MHz ultrasound (Movie S5) (MP4)
Pure silicone oil droplet subjected to ultrasound (Movie S6) (MP4)
Alignment of a capsule subjected to an applied E-field (Movie S7) (MP4)

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Author Contributions
Z.R. initiated the project. Z.R., J.B., and T.K. designed all of the experiments. J.B. performed and Z.R. assisted in the experiments with the results presented in Figures 4b,d, 6b, and S3. Z.R. carried out experiments presented in Figures 6 and 7 and most of the experiments, the results of which are shown in Figure 5. T.K. performed experiments with the results presented in Figures 3a–d, 4a,c, 5c, 8, 9a,c, and S4. Z.R., J.B., and T.K. conducted experiments that allowed to prepare Figure 2. T.K. drafted the manuscript. All authors took part in discussions on the finalization of the manuscript. Z.R. administered the submission.

Funding
This work was supported by the Polish National Science Centre [grant number 2015/19/B/ST3/03055]. Z.R. acknowledges financial support from the Polish-U.S. Fulbright Commission through the Fulbright scholarship.

Notes
The authors declare no competing financial interest.

REFERENCES


Direction-specific Release from Capsules with Homogeneous or Janus Shells Using an Ultrasound Approach

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Figure S1. A schematic illustration of the experimental set-up, consisting of a sample cell placed on a mechanical XYZ translation stage, a digital microscope for viewing in the direction perpendicular to the electric field direction, a signal generator and a voltage amplifier for generating high-voltage signals, and a computer for recording videos.

Figure S2. We used two set-ups for studying ultrasound-induced rupturing of capsules. (a) Low frequency (20 kHz) ultrasound impulses were generated by Sonopuls ultrasonic homogenizer HD 3100 from Bandelin electronic GmbH & Co. (b) High frequency (1 MHz) ultrasound waves were generated by Sonaris S from Astar.
Figure S3. We used an electric field, as a non-contact method, to verify whether particle shells of thermally treated droplets were mechanically stable. We applied an electric field to induce electric stress on the capsules. (left) PS-PE Pickering droplet after thermal treatment in microwave oven for ~15 seconds. (middle) Electric stress deformed the left side of the droplet with the shell composed of non-interlocked PS particles, whereas the shell made of interlocked PE particles stayed undeformed owing to its rigidity. (right) After turning off the electric field (t = 0.5 s), the deformed PS shell relaxed and the particle-covered droplet became spherical again. See also the corresponding Movie S3.

We used an electric field, as a non-contact method, to verify whether particle shells of the thermally treated capsules were mechanically stable. We applied an electric field to induce electric stress on the capsules. When a silicone oil droplet or a droplet covered with weakly conductive particles is suspended in castor oil and subjected to a uniform DC electric field, free charges (ionic impurities in oils) accumulate at the droplet’s interface. The electric field exerts force on these charges, resulting in electric stress. For a non-interlocked particle shell the electric stress deforms the drop, whereas shells with interlocked particles stays undeformed owing to the rigidity of such particle shell. In Figure S3 and Movie S3 we demonstrate examples of the performed tests of mechanical properties of shells.

Figure S4. The influence of 20-kHz ultrasound with the intensity of (a) ~20 W/cm² and (b) ~100 W/cm² on a Pickering droplet in castor oil. (a) The Pickering droplet subjected to low intensity ultrasound deformed and relaxed back to the spherical shape without particle detachment from the interface. (b) Application of ultrasound with the highest available intensity resulted in immediate and complete fragmentation of the droplet by the first pulse.

Table S1. Particle concentration in silicone oil and droplet sizes.

<table>
<thead>
<tr>
<th>Figure</th>
<th>Particles</th>
<th>Concentration [wt%]</th>
<th>Droplet size [mm]</th>
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<tr>
<td>2a</td>
<td>PE50(red)</td>
<td>~9</td>
<td>2.0</td>
</tr>
<tr>
<td>2b</td>
<td>PE50(red) / PS40</td>
<td>~8 / ~8</td>
<td>1.6</td>
</tr>
<tr>
<td>3a</td>
<td>PS40</td>
<td>~8</td>
<td>1.9</td>
</tr>
<tr>
<td>3b</td>
<td>PS40</td>
<td>~8</td>
<td>1.9</td>
</tr>
<tr>
<td>3c</td>
<td>PS40</td>
<td>~9</td>
<td>1.8</td>
</tr>
<tr>
<td>3d</td>
<td>PE50(red) / PS40</td>
<td>~6 / ~5</td>
<td>2.7</td>
</tr>
<tr>
<td>4a</td>
<td>PS40</td>
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<td>1.8</td>
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<td>PS40</td>
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<tr>
<td>4d</td>
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<tr>
<td>5a</td>
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5-2
Movie S1. The process of formation of a particle-covered droplet using a DC electric field. Silicone oil droplet containing PE particles is formed in castor oil using a micropipette. After the application of the DC electric field, the particles are guided towards the droplet interface by electrostatic force. On the droplet’s surface they are carried towards the electric equator by the electric-field-induced liquid flows. It takes several minutes for the particles to form a packed particle monolayer that covers the entire droplet surface.

Movie S2. Fabrication of a Pickering droplet with a heterogeneous shell. Two droplets (similar size) partially coated with different particles (red PE and PS) coalesce forming a Janus shell with densely packed particles.

Movie S3. Testing the mechanical properties of particle shells by inducing electric stress. When a droplet with a Janus shell is subjected to a DC electric field for 0.5 s, the part of the shell made of PS particles deforms, whereas the thermally fused PE particle shell remains rigid.

Movie S4. The behaviour of various droplets subjected to 20 kHz ultrasound. Pickering droplet in castor oil deforms reversibly by successive pulses and eventually falls apart. Droplet with PS particle capsule in castor oil initially remains rigid, but finally it is destroyed after being pulled into area near the ultrasonic horn. Droplet with PS particle capsule embedded in gel medium is gradually damaged by few pulses starting from the proximal side. A Pickering droplet with a patchy shell is also fragmented, although the hemispherical part composed of PE particle keeps certain integrity for longer time. In all cases the liquid payload of the capsules is spread omnidirectionally.

Movie S5. The behaviour of various droplets subjected to 1 MHz ultrasound. In acoustic field the Pickering droplet elongates and returns to its spherical shape after the ultrasound is turned off. The liquid payload release from the droplets with PS particle capsules immersed either in castor oil or viscoelastic gel is directional and takes place through the localized shell perforation. Under the influence of ultrasound waves PS particle capsule embedded in gel does not show any translational movement as opposed to that immersed in castor oil. For a droplet with a patchy capsule application of ultrasound results in puncturing of only the PS particle shell region.

Movie S6. A pure silicone oil droplet subjected to ultrasound. The magnitude of the droplet deformation increases when the acoustic intensity is increased from 0.5 to 1.5 W/cm². At the ultrasound intensities smaller than 2 W/cm² a steady state is observed. At an ultrasound intensity of 2 W/cm², the droplet is in a non-equilibrium state, it stretches spanning almost two ultrasound wavelengths and eventually breaks apart.

Movie S7. Alignment of a capsule subjected to an applied E-field. The capsule consists of red PE particles and of silver conductive particles that form short chains. In the presence of an external periodic E-field (100 Hz, in horizontal direction), the capsule undergoes electro-orientation. The size of the capsule is about 1.5 mm. The movie was sped up 3 times.