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Vibration technology-based droplet microfluidic devices for biomedical applications

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Droplet microfluidics has emerged as a versatile and powerful strategy for precise fluid manipulation at the micro- and nano-scales, with widespread applications in biomedical detection, diagnosis, and treatment. Among active control techniques, vibration-based methods are distinguished by their high precision, exceptional biocompatibility, and non-contact nature, which collectively reduce the risk of cross-infection and sample contamination. This review provides a concise summary of the fundamental principles, technological advancements, and representative biomedical applications of vibration-induced droplet manipulation. This work highlights both acoustic methods and other mechanical vibration strategies, including their distinct working mechanisms and potential for integration with other active control methods to enhance flexibility. It explores the extensive range of vibration strategies' applications in biomedicine, including the use as drivers for diverse sample pretreatment processes (cell manipulation, sorting, cultivation, and activity research), biosensors for detecting and diagnosing various biological targets, and post-diagnostic drug treatment studies. Despite their promise, current challenges remain, including equipment complexity, scalability, and the need for robust integration with existing microfluidic systems. Lastly, this review outlines future directions for advancing vibration-based droplet microfluidics, which include the development of new materials, the integration of interdisciplinary technologies, and intelligent control. These initiatives will facilitate the development of integrated devices for rapid disease diagnostics and medical research applications.

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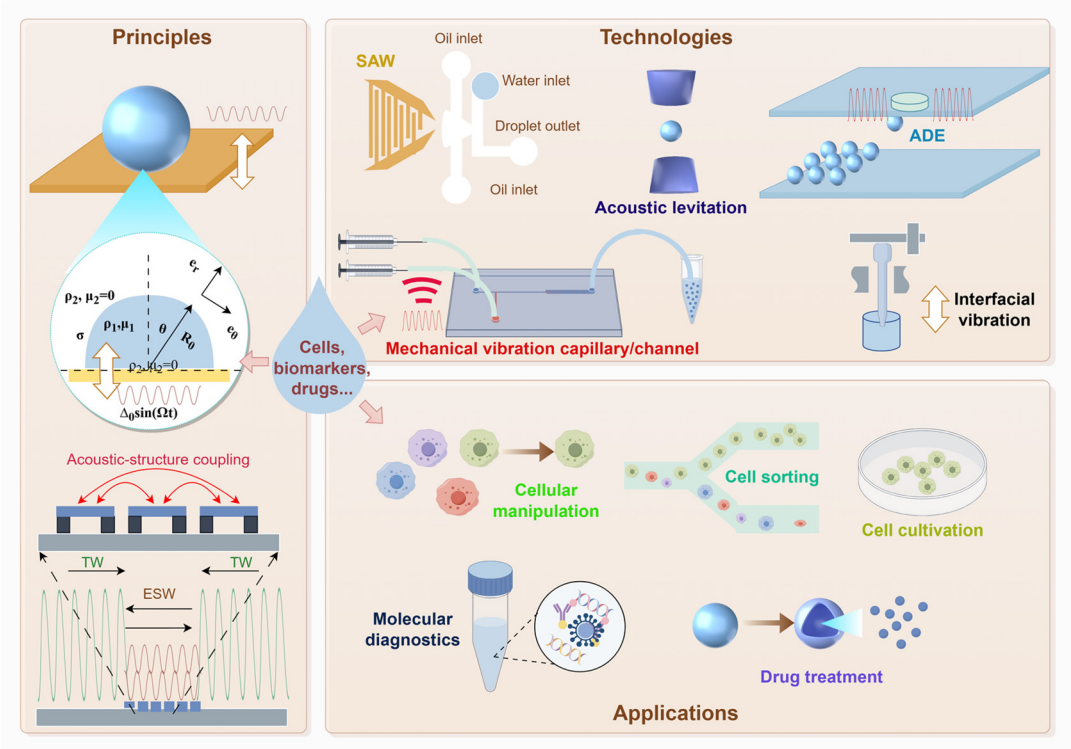
1 Introduction

Droplet microfluidics has emerged as a critical branch of microfluidic technology since the 1990s, offering precise control over fluid management at the micro- and nano-scales. This ability has enabled substantial progress in the fields of materials science, biomedicine, and chemical analysis. The

The team members are from both the Shandong Laboratory of Advanced Biomaterials and Medical Devices in Weihai and the Suzhou Institute of Biomedical Engineering and Technology, Chinese Academy of Sciences. The team focuses on research in the fields of bioenzyme molecular modification, droplet microfluidics, molecular diagnostics and detection, as well as chemical organic material synchronization. In the photograph, the authors are positioned as follows: Peng Yin (fourth from the left in the third row), Yanna Lin (second row, second from right), Maojie Jiang (third row, third from left), Xiangyu Jiang (third row, fifth from left), Xuan Fang (third row, sixth from left), Mengjie Huang (first row, fourth from right), Baihui Zhang (third row, fifth from left), and Fuqiang Ma (second row, fifth from left).



Scheme 1 Vibration technology-based droplet microfluidic devices for biomedical applications (by Figdraw).

construction of highly controllable reaction environments is facilitated by the precise manipulation of microscale droplets, which also significantly reduces the consumption of reagents and samples. Over recent decades, sustained research and technological innovations have expanded the scope of droplet microfluidics, supporting diverse applications in biochemical analysis, drug screening, single-cell encapsulation, molecular diagnostics, and tissue engineering.[1,2]

The developmental trajectory of microdroplet vibration manipulation technology is outlined in Scheme 1 and Fig. 1. Generally, droplet manipulation techniques can be classified into two categories: passive and active. Passive methodologies primarily depend on intrinsic physical forces, including hydrodynamic effects and interfacial tension, which are accomplished through the modulation of microchannel (*via* the capillary effect or biomimetic structural design) or surface wettability design.[3–5] Passive methods frequently lack precision and flexibility, despite their structural simplicity and cost-effectiveness. To address these limitations, active control strategies introduce external fields (including optical, electrical, thermal, magnetic, acoustic, or mechanical stimuli) to enable more precise, programmable manipulation of droplets.[6–11]

Vibration-based manipulation is distinguished by its distinctive advantages among these active strategies. Vibration methods reduce the danger of contamination and cross-infection, a critical factor in aseptic biomedical operations, by facilitating non-contact control of droplets.[12] In addition, vibration-induced manipulation offers a high degree of tunability, allowing for the precise control of droplet generation, transport, coalescence, and splitting through straightforward adjustments to vibration frequency and amplitude. It is essential to note that this method preserves the structural and functional integrity of biological

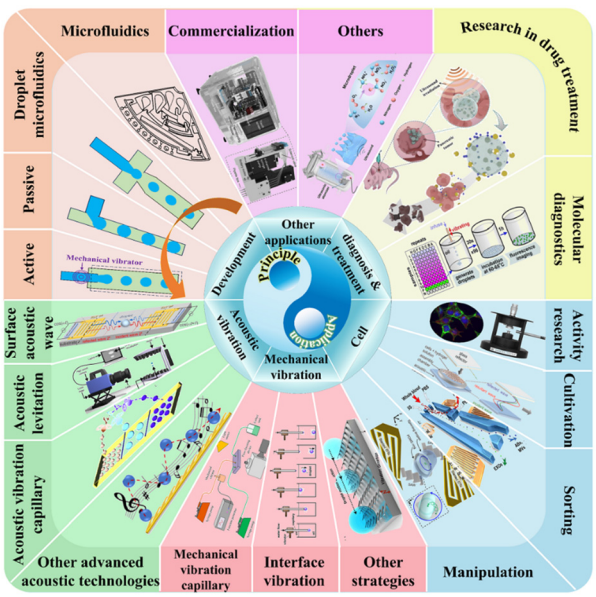


Fig. 1 An overview of advanced vibration manipulation strategies for microdroplets.

samples, thereby ensuring robust biocompatibility. These advantages establish a dependable technical foundation for a variety of applications. Generally, vibration manipulation strategies can be classified into acoustically induced vibration and other mechanical vibration methods; both methods are based on the principle of altering the interfacial tension or internal flow state of a droplet through vibration energy, thereby achieving precise droplet manipulation.[13,14] Furthermore, vibration-based techniques can be integrated with other active manipulation methods, such as electric or magnetic fields, to expand their functional capabilities and enhance system adaptability.[15]

With the rapid development of vibration-based microdroplet manipulation technologies, their integration into biomedical workflows has become increasingly promising. This review summarises recent progress in vibration strategies for microdroplet manipulation, with a focus on the principles, classification, and working mechanisms of acoustic and mechanical approaches. It also highlights representative applications in biomedical research, discusses existing challenges, and outlines prospects for advancing this versatile technology.

2 Bibliometric analysis

2.1 Methodology

All data related to the vibration technology of droplet microfluidic devices reported in the paper were retrieved *via* the advanced search function of the Web of Science Core Collection database. The search criteria were confined to English-language publications, restricted to document types "Article" and "Review", and covered the period from January 2011 to November 4, 2025. The topic search field (TS), which encompasses article titles, keywords, and abstracts, was configured with the following query:

(TS = ("vibration*" OR "acoustic*" OR "control*" OR "acoustic wave*" OR "SAW *" OR "SSAW*" OR "TSAW*" OR "acoustic levitation*" OR "vibration capillary*" OR "vibration channel*" OR "mechanical vibration*" OR "interfacial vibration*") AND TS = ("sensor*" OR "point-of-care testing*" OR "portable device*" OR "diagnosis*" OR "treatment*" OR "biomedical*" OR "techniques*" OR "control*" OR "principle*" OR "manipulation*" OR "method*" OR "strategies*" OR "mechanism*" OR "biomedicine*" OR "pretreatment*" OR "cell*" OR "sorting*" OR "cultivation*" OR "biosensor*" OR "detect*" OR "identification*" OR "biological target*" OR "drug*" OR "molecular diagnostic*") AND TS = ("droplet*" OR "microfluidic*" OR "micro*" OR "nano*" OR "microdroplet*" OR "droplet printing*")).

Eventually, 5549 articles were retrieved for analysis. This search yielded 5549 relevant publications for analysis. Complete information records-including article titles, authors, keywords, journals, and abstracts-were exported as plain text files. The dataset was subsequently analyzed utilizing VOSviewer software (version 1.6.20) to conduct bibliometric analysis and visualization.

2.2 Performance analysis

Statistical data were analyzed through VOSviewer to obtain the research and publication performance. Fig. 2a reveals the growth in publications of vibration technology of droplet microfluidics, depicting both annual and cumulative outputs from 2011 to 2025. The data demonstrate a consistent upward trend in annual publications, commencing with 133 publications in 2011 and surpassing 700 by 2019. By 2025, the annual publication count reached 152, bringing the cumulative total to 5549 papers. This growth pattern reflects expanding research interest and technological development in the field. The cumulative count, represented by the yellow bars, shows an accelerating growth pattern. Particularly noteworthy is the substantial increase in annual publications since 2021, potentially indicating technological breakthroughs or enhanced research investment in this domain.

Fig. 2b presents the top 10 most prolific countries in this research domain. China leads with 2036 publications, followed by the United States (1442) and India (422). The subsequent rankings are occupied by Korea, England, Germany, Canada, Italy, Iran, and Japan, respectively. Although China has a high number of publications, the USA is the most influential, with the highest average citation per paper at 51.86. This indicates a significant impact on research in the USA within this field. In addition, Canada and Korea also have considerable effects, ranking 2nd and 3rd with average citations of 37.44 and 37.23, respectively.

2.3 Co-occurrence analysis of keywords

Keyword co-occurrence analysis reveals the relationships between different concepts through the frequency of simultaneous keyword occurrences in the literature allowing for the identification of major research themes trends and interconnections between various research topics.[16] In Fig. 2c after merging duplicate words the network shows 151 keywords (threshold set to 35) where the size of the nodes reflects the frequency of keyword occurrence. The keywords are primarily divided into four clusters (4 colors green: upper left; yellow: upper right; blue: lower left; red: lower middle) where keywords in the same cluster have similar attributes or are from similar domains. The four clusters in the figure are categorized according to the features of the keyword. The green cluster primarily centers around the design technology which includes technologies such as acoustic waves and vibrations along with their underlying principles mechanisms and performance characteristics. The yellow cluster primarily reflects that its research subjects mainly involve operations such as driving manipulating and separating cells or other biomarkers using the aforementioned technologies. Keywords in the blue cluster primarily indicate its biomedical applications such as biomaterial fabrication particle separation and droplet

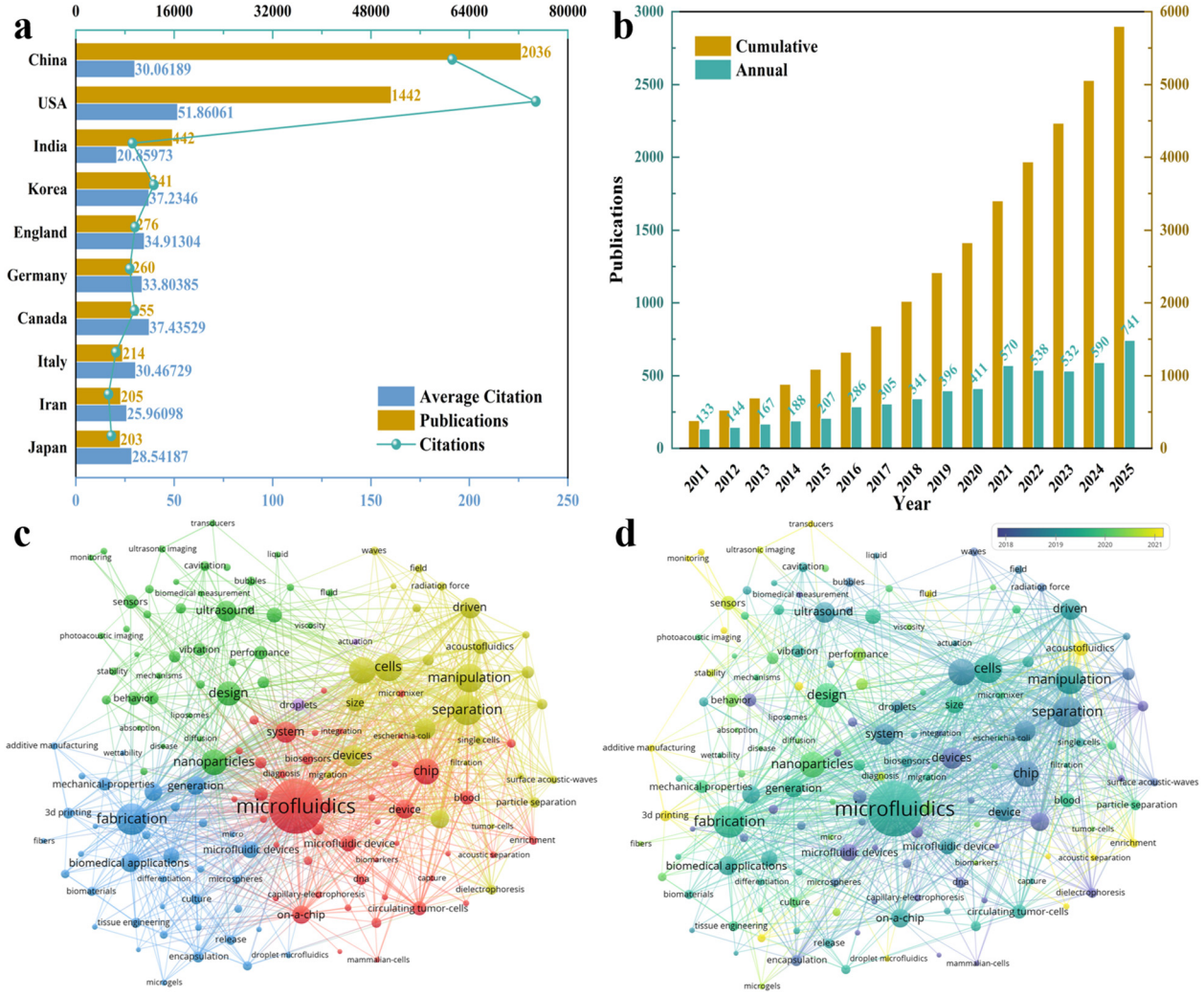


Fig. 2 Bibliometric analysis. (a) The annual and cumulative publications of literature relating to the vibration technology of droplet microfluidic devices between 2011 to 2025. (b) The contribution of the top 10 countries to the vibration technology of droplet microfluidic devices. (c) Co-occurrence network map of author keywords. (d) The overlay visualization for the average emerging time of keywords' co-occurrence network.

generation. The red cluster indicates that the research background of the paper primarily revolves around the microfluidics field encompassing devices systems science and lab-on-a-chip technologies

The overlay visualization in Fig. 2d further provides information on the temporal dimension by indicating the occurrence of keywords over time through different colors, helping researchers to understand the historical trajectory of a concept or technology from its emergence to becoming a research hotspot, as well as the trend of current research focus.[17] The gradient color shifting from purple to blue, then to green, and finally to yellow represents the average occurrence time of keywords from 2018 to 2021. As shown in the figure, research in fields such as microfluidics, biomaterial fabrication, cell manipulation and separation, and ultrasound technology began earlier and has maintained consistent momentum. Meanwhile, studies within these specific subfields—ultrasonic imaging, 3D printing, acoustofluidics, and cell enrichment—are relatively novel, offering valuable reference points for researchers.

3 Strategies for vibrational manipulation of microdroplets

Vibration-based droplet manipulation is a versatile method for managing microscale droplets in microfluidic systems. These methods allow for the precise modulation of droplet generation, transport, fusion, and separation through the application of external vibrations. Depending on the source and nature of the vibrations, they can be broadly classified into acoustically induced vibration and other mechanical vibration strategies. Each technique exploits unique physical principles to induce internal and external forces on droplets, providing flexible control under various experimental conditions. This section discusses the fundamental principles, operating mechanisms, and representative implementations of strategies for vibrational manipulation.

3.1 Acoustic manipulation

In microchannels, increased fluid viscosity markedly influences the Reynolds number and, consequently, the flow regime. Acoustic microfluidics offers an effective strategy to address these challenges by employing piezoelectric materials that generate acoustic waves (mechanical waves) upon electrical excitation.[18–20] These waves generate acoustic radiation forces within the microchannel, which allow the fluid to surmount interfacial tension and achieve controlled directional motion. Acoustic manipulation can be further classified into surface acoustic waves, acoustic levitation, vibrating capillaries, and other emergent acoustic techniques based on the underlying mechanism and intended application.

3.1.1 Surface acoustic wave. Acoustic waves can be broadly classified into two distinct types based on their generation mechanisms and propagation modes: bulk acoustic waves (BAWs) and surface acoustic waves (SAWs). BAWs are ultrasonic longitudinal waves generated by piezoelectric transducers that propagate through the bulk of a material. A common approach involves bonding piezoelectric transducers beneath microchannels to create acoustic resonators, as demonstrated by Leibacher *et al.*, who investigated the use of BAWs for droplet manipulation to achieve operations such as aggregation, sorting, and solution exchange.[21] In the same vein, Lee *et al.* utilized a 30 MHz ultrasonic beam to manipulate and separate droplets of varying sizes within an aqueous phase.[22] While numerous studies have explored BAW-based droplet control, the advent of fork-finger interdigital transducers has highlighted the advantages of SAW technology. SAWs offer greater operational simplicity, higher precision, and enhanced controllability, leading to increasing interest and broader adoption of SAW-based systems over their BAW counterparts.

Surface acoustic waves are elastic waves that travel along the surface of a solid substrate. SAWs can be further classified into surface travelling waves and surface standing waves. Most of the wave energy is confined within a region approximately two wavelengths from the surface and decays rapidly with increasing depth. SAW technology has been extensively utilized in microfluidics for fluid mixing, droplet manipulation, and cell sorting.[23–26]

On the theoretical side, Vandewalle investigated the bouncing behaviour of droplets on a vertically vibrating liquid bath, demonstrating that an array of bouncing droplets can mimic a spin system.[27] This finding has inspired interdisciplinary research at the intersection of

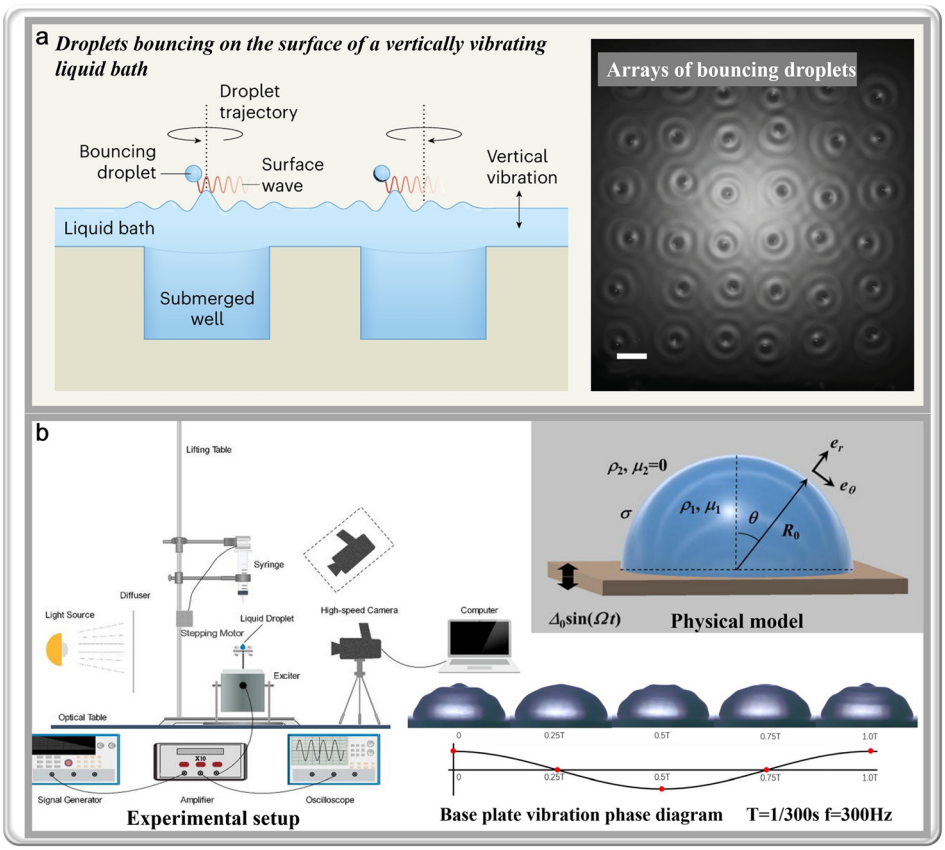


Fig. 3 Theoretical studies on surface acoustic waves. (a) Droplets bouncing on the surface of a vertically vibrating liquid bath. Reprinted from ref. 27, copyright (2021), with permission from Springer Nature. (b) Study on the interfacial instability of vibrating droplets. Reprinted from ref. 28, copyright (2024), with permission from AIP Publishing.

statistical physics, nonlinear dynamics, and fluid mechanics (Fig. 3a). In the case of droplet generation and manipulation, Li *et al.* analyzed the instability of droplet interfaces under vertical vibration.[28] They derived the governing equations and boundary conditions, and applied Floquet analysis to obtain neutral and stable boundaries for harmonic and subharmonic responses under inviscid conditions. Both theoretical predictions and experimental results confirmed that the circumferential waves observed on the spherical liquid surface corresponded to harmonic rather than subharmonic oscillations. These insights establish a solid theoretical foundation for the design and optimization of vibration-induced droplet generation devices (Fig. 3b).

The generation and dispersal of droplets were initially demonstrated by Shiokawa *et al.* in 1989, utilizing a surface acoustic wave (SAW) device that was powered by an alternating current.[29] In the same year, Elrod *et al.* employed a focusing fork-finger transducer with adjustable frequency positioned beneath the liquid surface to generate microdroplets with controllable sizes.[30] Building on these

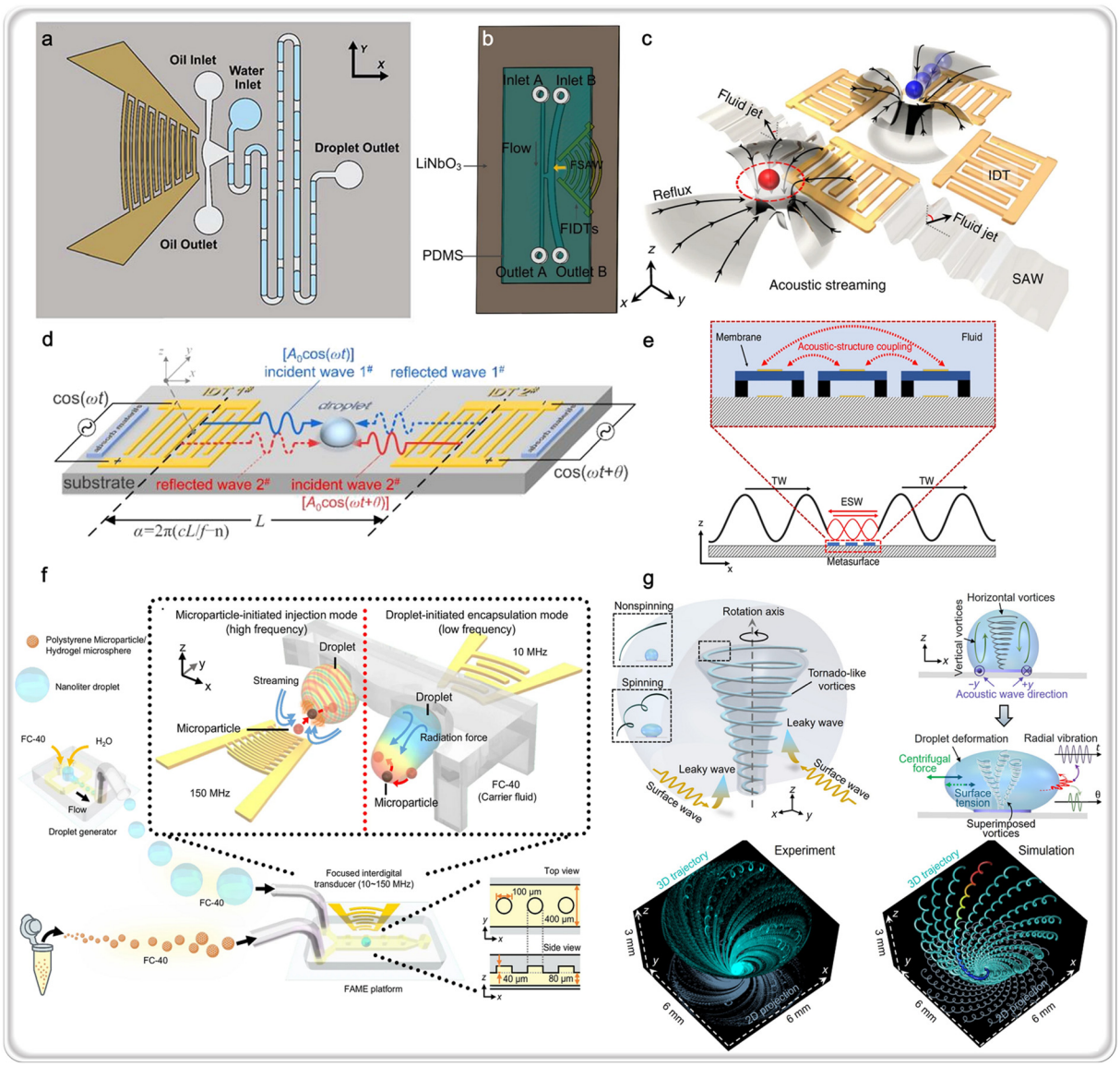


Fig. 4 Research on droplet generation and manipulation using surface acoustic wave (SAW) technology. (a) Application of acoustic radiation force to merge the dispersed phase into the continuous phase, facilitating droplet formation. Reprinted from ref. 34, copyright (2020), with permission from Royal Society of Chemistry. (b) Droplet generation facilitated by focused surface acoustic wave technology. Reprinted from ref. 35, copyright (2019), with permission from Elsevier. (c) Schematic of a digital acoustofluidic technique. Reprinted from ref. 36, copyright (2018), with permission from Springer Nature. (d) Manipulation of droplets through the "excitation–excitation" SAW method. Reprinted from ref. 37, copyright (2022), with permission from Royal Society of Chemistry. (e) Development of a reconfigurable acoustofluidic metasurface platform. Reprinted from ref. 38, copyright (2025), with permission from Springer Nature. (f) Design of a multifunctional microfluidic chip grounded in acoustofluidic principles. Reprinted from ref. 39, copyright (2025), with permission from Springer Nature. (g) Implementation of an acoustofluidic rotational control method using SAW technology. Reprinted from ref. 40, copyright (2025), with permission from American Association for the Advancement of Science.

pioneering studies, numerous researchers have proposed a variety of SAW-based strategies for droplet generation and manipulation.[31,32]

For instance, the working principle of SAW-induced droplet generation is illustrated in Fig. 4. In Fig. 4a, directional acoustic radiation forces generated by surface acoustic waves extrude a dispersed phase into a continuous phase, forming monodisperse droplets through various structural configurations.[33,34] In Fig. 4b, Jin *et al.* utilised focused surface acoustic waves (FSAW) to generate droplets, demonstrating that droplet size can be precisely controlled by adjusting the input voltage and frequency, resulting in uniform and reproducible droplet formation.[35] Zhang *et al.* developed a digital acoustic flow technique (Fig. 4c) that enables non-contact droplet transport and processing using SAW, which was applied to optimize cascade enzyme reactions.[36]

Additionally, Sui *et al.* introduced a novel "excitation–excitation" SAW mode (Fig. 4d) to drive droplets.[37] By adjusting the phase difference between interdigital transducer (IDT) signals, they achieved efficient droplet transport along designated paths, offering improved operational efficiency compared to the traditional "excitation–absorption" mode. Surappa *et al.* designed a reconfigurable acoustofluidic metasurface platform (Fig. 4e) that employs local standing acoustic waves generated by an array of passive membrane resonators to capture and concentrate droplets, holding promise for high-throughput bioanalysis.[38] Zhong *et al.* developed a multifunctional microfluidic chip based on acoustofluidic principles (Fig. 4f) to investigate injection mechanisms across different frequency ranges, enabling rapid, non-contact particle injection from an oil phase into aqueous droplets for multiphase manipulation.[39] Finally, Chen *et al.* proposed an acoustic–hydrodynamic rotational control method (Fig. 4g) that uses SAW to dynamically guide the three-dimensional motion of particles within droplets, facilitating droplet-based biochemical reactions and particle transport within micro-lab systems.[40]

The SAW technique also exhibits significant potential for droplet sorting applications. As illustrated in Fig. 5a, Sesen *et al.* employed a focused fork-finger transducer to generate a

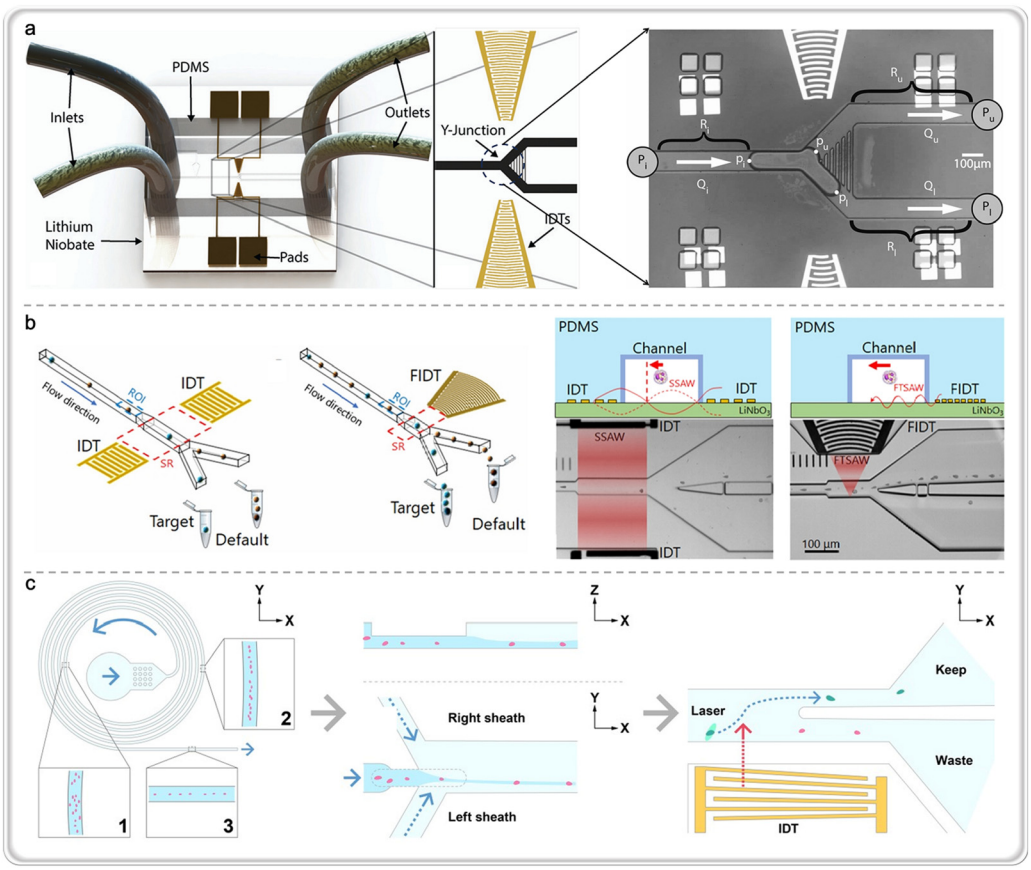


Fig. 5 Research on droplet sorting utilizing surface acoustic wave (SAW) technology. (a) Active manipulation of the liquid plug within the branch channel is facilitated by the establishment of a traveling surface acoustic wave field through a focused interdigital transducer. Reprinted from ref. 41, copyright (2015), with permission from Royal Society of Chemistry. (b) Incorporating a focused fork-finger transducer into a microfluidic platform enables high-throughput single-cell sorting. Reprinted from ref. 43, copyright (2023), with permission from Royal Society of Chemistry. (c) Single-cell sorting is realized through the use of a tilted-finger transducer. Reprinted from ref. 26, copyright (2019), with permission from Royal Society of Chemistry.

traveling surface acoustic wave field within bifurcated microchannels, enabling active control of liquid plugs (large droplets that remain in contact with all channel walls).[41] In a complementary approach, Li *et al.* developed an interdigital transducer with a standing surface acoustic wave field that was generated by a gradually increasing finger spacing.[42] They achieved precise droplet sorting by modulating the distribution of pressure nodes within the channel by tuning the signal frequency. Building on droplet sorting, Nawaz *et al.* incorporated a focused fork-finger transducer within a microfluidic platform (Fig. 5b), enabling high-throughput single-cell sorting.[43] Additionally, Mutafopulos *et al.* developed a slanted-finger transducer configuration (Fig. 5c) that enabled efficient single-cell sorting with an accuracy of up to 90% and a throughput reaching 2000 events per second.[26]

Surface acoustic wave (SAW) technology has demonstrated distinct advantages in droplet microfluidics in recent years due to its high scalability, versatility, and operational simplicity. This method not only promotes fundamental research but also has the potential to be integrated with complementary modules, thereby enabling the development of portable biochemical and medical devices that could enhance rapid diagnostics and personalised medicine. Despite its excellent performance in droplet manipulation, several challenges remain, including energy loss at high frequencies, precise control of droplet size, and maintaining stability under complex microenvironmental conditions. Addressing these limitations will be critical for optimising practical applications. Overall, SAW-based microfluidics presents a wide range of opportunities for the generation and regulation of microdroplets; its further advancement will be facilitated by the integration of other technologies to address the current technical constraints. Through interdisciplinary collaboration and continued innovation, SAW microfluidics is expected to play an increasingly significant role in biomedicine, materials science, and chemical analysis.

3.1.2 Acoustic levitation technology. Acoustic levitation is a technique that employs high-intensity, high-frequency sound waves to produce acoustic radiation forces that counteract the weight of an object, thereby allowing for sustained suspension without direct contact with a supporting surface. This non-contact nature provides significant advantages for studying droplet dynamics and conducting micro-scale biochemical reactions, as it minimises contamination and preserves sample integrity. The technique has undergone significant development since Kundt's groundbreaking demonstration in 1866, which utilized a resonator tube to elevate dust particles. Today, acoustic levitation is widely applied in biochemical analysis, tissue engineering, regenerative medicine, and various droplet manipulation tasks.[44–48]

King conducted a systematic study of acoustic levitation in 1934 and established an expression for the acoustic radiation pressure (eqn (1)).[49] He derived the equation of motion for a particle under the influence of plane waves (eqn (2)) and determined the total acoustic radiation force acting on a sphere by integrating the radiation pressure over its surface. For small particles ($kR_S \leq 1$, k being the acoustic wave number), the acoustic radiation forces in plane travelling and standing wave fields are given by eqn (3) and (4), respectively. In addition, Gor'kov later analyzed the acoustic field from an energy perspective and derived an alternative expression for the acoustic radiation force on a sphere in a plane standing wave field (eqn (5)).[50] When the suspended sphere is approximated as rigid, eqn (5) is equivalent to King's original eqn (4).

A comparison of eqn (3) and (4) indicates that the radiation force acting on a particle is generally greater in a standing wave field than in a travelling wave field. In a travelling wave, the particle is perpetually propelled forward by the net positive radiation force, whereas in a standing wave field, the force varies sinusoidally with position, providing stable equilibrium points for levitation. As a result, standing waves are generally the preferred method for achieving stable acoustic levitation.[51]

$$\langle p - p_0 \rangle = \frac{1}{2\rho c^2}\langle p^2 \rangle - \frac{1}{2}\rho \langle v^2 \rangle \tag{1}$$

$$2\pi {R_S}^2 \int_0^{\pi} (p - p_0)\cos\theta \sin\theta \, \mathrm{d}\theta = -M\frac{\partial^2 \zeta}{\partial t^2} \tag{2}$$

$$F = 2\pi\rho |A|^2 (kR_S)^6 \frac{9 + 2(1-\lambda_\rho)^2}{9(2+\lambda_\rho)^2} \tag{3}$$

$$F = \frac{1}{3}\pi kern.5\rho |A|^2 (kR_S)^3 \sin(2kh)\frac{5 - 2\lambda_\rho}{6 + 3\lambda_\rho} \tag{4}$$

$$F = \frac{1}{3}\pi\rho_0 |A|^2 (\kappa R_S)^3 \sin(2\kappa h)\left(\frac{5 - 2\lambda_\rho}{2 + \lambda_\rho} - \lambda_\rho \frac{c^2}{{c_S}^2}\right) \tag{5}$$

where, $\langle\rangle$ represents time averaging, ρ represents the medium density, v represents the particle velocity, p represents the acoustic pressure, c represents the speed of sound in the medium, R_S represents the sphere radius, M represents the sphere mass, ζ represents the displacement of the sphere in the direction of gravity, θ represents the polar angle relative to the vertical axis, t represents the time, F represents the acoustic radiative force, $\lambda_\rho = \rho_0/\rho_S$, ρ_S represents the sphere density, and c_S represents the speed of sound within the sphere.

King and Gor'kov's derivation of the acoustic radiation force in levitation phenomena laid a robust theoretical foundation for the advancement of acoustic levitation technology. Researchers began to translate the theory into practical engineering applications by building on these principles. Hanson *et al.* made a significant stride toward experimental realization in 1964 by developing the first acoustic levitation device to investigate droplet dynamics.[52] Numerous researchers have since continued to refine and innovate acoustic levitation systems through iterative design and experimental validation.[53]

Typically, these devices mainly consist of a resonant cavity with a source and a reflecting end, forming a standing wave field within the cavity. The sound source is generally a piezoelectric transducer, which excites the piezoelectric material under high-frequency voltage and amplifies the acoustic field intensity using an amplitude horn.

Acoustic levitation devices can generally be categorized into single-axis, multi-axis, and array configurations. For single-axis systems, researchers have primarily focused on optimizing the structures of the emitter and reflector, as well as the inclination angle between their axes, to enhance levitation performance. For instance, Li *et al.* demonstrated that the stability of acoustic levitation can be significantly enhanced by employing an emitter with a large-diameter disc tip.[54] Andrade *et al.* investigated the effect of varying inclination angles and achieved simultaneous levitation and manipulation of two spheres.[55]

Furthermore, Li *et al.* have effectively produced microdroplets at the gas–liquid interface by utilizing ultrasonic levitation in conjunction with acoustic field control.[56] This work facilitated the testing of a variety of chemical reactions and contributed to the resolution of the ongoing debate regarding reaction promotion at "impure" gas–liquid interfaces, where multiple phases, such as solid–liquid or water–oil, may coexist. Zheng *et al.* employed a uniaxial standing wave ultrasonic levitation technique to synthesise size-controlled ZIF-8 materials, which have potential applications in drug encapsulation and release.[57] In addition, they conducted *in situ* measurements of the evaporation kinetics of levitated droplets (Fig. 6a).

Compared with single-axis devices, multi-axis acoustic levitation systems offer superior levitation performance through the non-coaxial arrangement of multiple emitters, with triaxial configurations receiving particular attention. For instance, Stephens *et al.* developed a triaxial device that consisted of three emitters and concave reflectors and examined its levitation properties.[58] Andrade *et al.* demonstrated the levitation of a 50 mm-diameter polystyrene sphere using a tripod-shaped emitter arrangement, overcoming conventional limits on levitation size and acoustic wavelength.[59] Notably, Hong *et al.* successfully levitated a silicone oil droplet using a multi-axis setup (Fig. 6b) and showed that acoustic vortices play a critical role in droplet rotation and morphology control.[60]

Array-type acoustic levitation devices rely on assembling multiple acoustic sources in an array configuration and modifying parameters such as phase difference, amplitude, and frequency to modulate the levitation state.[61] For instance, Marzo *et al.* expanded the emitter count to 60 to achieve stable levitation and three-dimensional manipulation of millimetre-scale particles.[62] Omirou *et al.* utilized a plum-shaped array to levitate multiple spheres

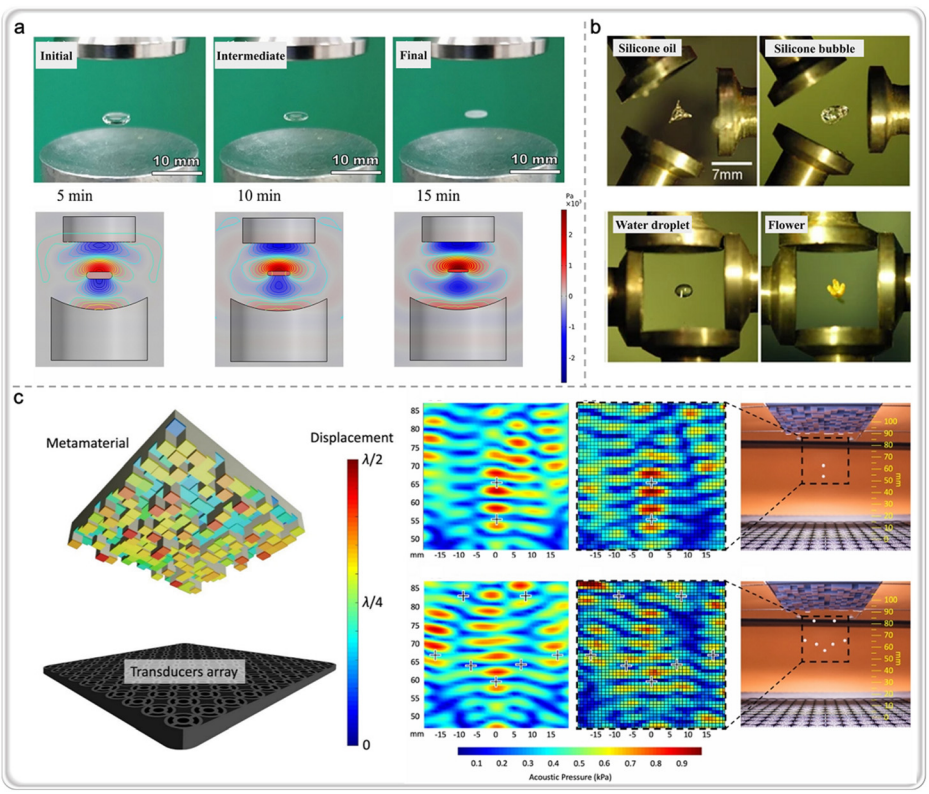


Fig. 6 Acoustic levitation devices. (a) Single-axis acoustic levitation device. Reprinted from ref. 57, copyright (2023), with permission from Royal Society of Chemistry. (b) Multi-axis acoustic levitation device. Reprinted from ref. 60, copyright (2017), with permission from Springer Nature. (c) Array acoustic levitation device. Reprinted from ref. 64, copyright (2020), with permission from Springer Nature.

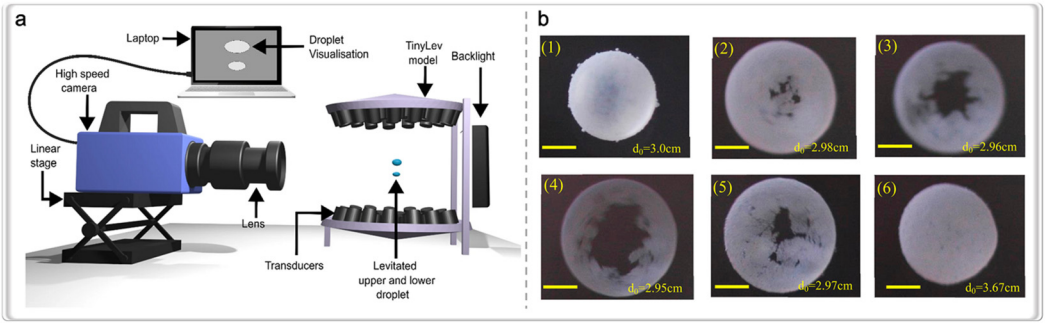


Fig. 7 Study of droplet coalescence and surface layer opening and closing on droplet marbles. (a) Coagulation and mixing of droplets. Reprinted from ref. 69, copyright (2024), with permission from Springer Nature. (b) Image of the opening and closing of the surface particle layer on a droplet of marble. The numbers (1) to (6) in the figure show the sequence diagram of the opening and closing process. Reprinted from ref. 70, copyright (2015), with permission from American Chemical Society.

and adjusted unit amplitudes to coordinate their motion.[63] In another study, Polychronopoulos *et al.* achieved precise levitation of multiple particles at arbitrary positions by combining a transducer array with a reflective acoustic metamaterial featuring variable-height cells (0–λ/2 displacements) (Fig. 6c).[64] These advances offer valuable references for the extension of acoustic manipulation strategies to liquid particles.

Building on advances in droplet manipulation, several studies have explored droplet coalescence and mixing. Under the influence of acoustic radiation forces, liquid bridges can form between adjacent droplets and expand rapidly, ultimately resulting in droplet coalescence.[65] This mechanism has been utilized by researchers to combine mechanical ejection with customized acoustic fields, thereby enabling the mixing and separation of two-phase suspended particles.[66] This approach is frequently implemented in high-sensitivity biochemical reactions. For instance, Nakamura *et al.* adjusted the intensity of the acoustic field to accomplish vertical coalescence of suspended droplets along an annular path, producing larger droplets through multiple cycles and enabling chemical reactions within these larger volumes.[67,68] Vashi *et al.* introduced a versatile acoustic levitation digital microfluidic device (Fig. 7a) that achieves vertical coalescence of droplets suspended in air.[69] They validated the device's feasibility by conducting coalescence experiments using water and glycerol–water mixtures at concentrations of 20% and 40%.

The ultrasonic levitation technique has also been extended to liquid marbles (droplets coated with hydrophobic micro- or nanoparticles). Zang *et al.* demonstrated that enhancing the acoustic field intensity induces droplet deformation and rearrangement of surface particles (Fig. 7b).[70] By increasing the acoustic field strength, the particle layer at the droplet's poles can be opened, while reducing the intensity causes particles near the equator to migrate back, re-closing the granular shell. This approach provides a novel means for dynamic control of the granular layer in droplet marbles encapsulated by non-ferromagnetic particles, offering technical support for advanced droplet-based chemical processes.

3.1.3 Acoustic vibration capillary/channel. In order to enhance the efficiency and portability of particle generation, researchers have integrated capillary microfluidic systems with acoustic vibration. This hybrid strategy simplifies operation, reduces reliance on bulky equipment, and lowers system cost, making it well-suited for resource-limited settings and integrated platforms.

For instance, Foresti *et al.* developed an acoustic printing method that utilizes a subwavelength acoustic resonator (Fig. 8a).[71] This method is capable of precisely ejecting droplets with viscosities varying from 0.5 to 25 000 mPa s and yield stresses exceeding 50 Pa. This significantly broadens the applicable fluid range of acoustic printing. De Lora *et al.* created a droplet generator using a sinusoidal signal amplified and transmitted to a speaker, which induced vibration in a capillary tube and disrupted fluid flow, producing droplets with diameters ranging from 50 to 125 μm (Fig. 8b).[72]

Specifically, He *et al.* utilized a pulsed signal to stimulate a piezoelectric transducer and demonstrated that acoustic vibration near the capillary tip could modulate both droplet size and generation frequency.[73] Their device enabled broad-range droplet formation (6.77–661 μm) with low power consumption and a high degree of integration (Fig. 8c). Ding *et al.* further advanced this concept by developing a portable vibrating capillary droplet platform (Fig. 8d) capable of performing automated bacterial counting and antibiotic susceptibility testing (AST) following droplet incubation and image acquisition.[74] Yin *et al.* designed an acoustic nozzle system that disrupts equilibrium at a water–oil interface through vibrations produced by a PZT transducer.[75] This system enables the generation of high-throughput droplets at rates of up to 2000 droplets per second (Fig. 8e). Fike *et al.* integrated vibrating-tip capillary technology with digital droplet loop-mediated isothermal amplification (ddLAMP), achieving digital nucleic acid detection with a wide dynamic range (2–6000 copies per microlitre) under resource-constrained conditions (Fig. 8f).[76]

In studies of the droplet ejection mechanism, Shenoda *et al.* investigated the mechanism of droplet ejection driven by high-frequency ultrasound.[77] They demonstrated that the

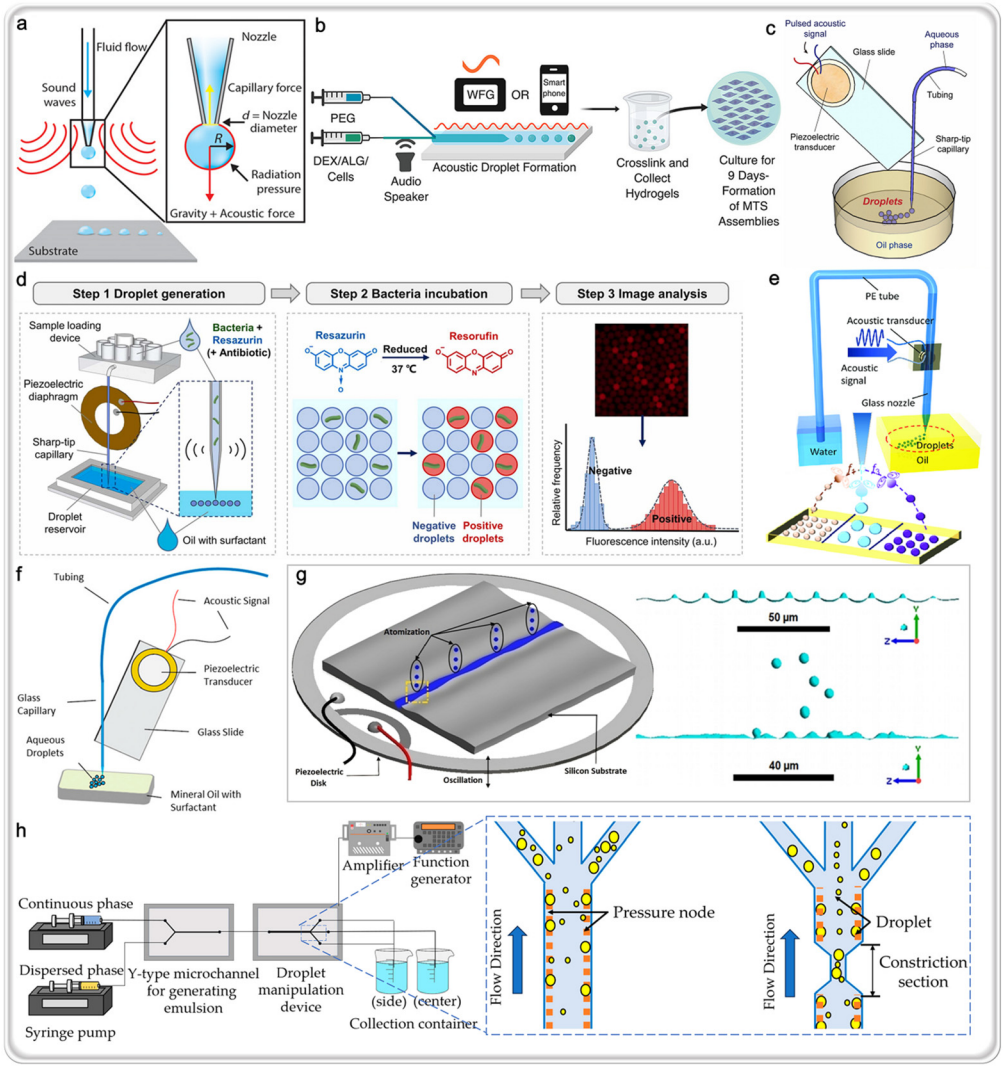


Fig. 8 Investigation of the acoustic vibration capillary/channel method. (a) An acoustic printing technique utilizing subwavelength acoustic resonators. Reprinted from ref. 71, copyright (2018), with permission from American Association for the Advancement of Science. (b) Development of a droplet generation device employing vibration in capillary channels. Reprinted from ref. 72, copyright (2019), with permission from American Chemical Society. (c) Achieving droplet generation across a broad size range by regulating capillary tip vibration through pulsed signals. Reprinted from ref. 73, copyright (2021), with permission from Elsevier. (d) Development of a portable droplet generation platform based on vibrating capillary technology. Reprinted from ref. 74, copyright (2023), with permission from Elsevier. (e) Implementation of an acoustically controlled nozzle. Reprinted from ref. 75, copyright (2023), with permission from American Physical Society. (f) Fusion of vibrating-tip capillary technology with ddLAMP for digital nucleic acid detection. Reprinted from ref. 76, copyright (2024), with permission from MDPI. (g) The mechanism of droplet ejection under high-frequency ultrasound stimulation. Reprinted from ref. 77, copyright (2024), with permission from AIP Publishing. (h) Design of a droplet manipulation device that combines ultrasonic technology with constriction microstructures. Reprinted from ref. 78, copyright (2024), with permission from MDPI.

size of the droplet can be controlled on demand by rationally modulating the interactions among vibration amplitude, frequency, and channel geometry (Fig. 8g). Fujioka *et al.* proposed a droplet manipulation platform that integrates ultrasonic excitation with a shrinkage microstructure approach.[78] They experimentally assessed the dynamics of droplet motion and separation within the device (Fig. 8h).

3.1.4 Other advanced acoustic technologies. In addition to conventional acoustic control strategies, researchers have investigated a variety of advanced acoustic innovations for droplet manipulation. For instance, in 2012, Fang *et al.* introduced a technique for the rapid production of multicellular co-cultures through the use of the acoustic droplet ejection (ADE) method.[79] In this method, the non-contact discharge of droplets with uniform size is facilitated by a focused acoustic radiation pressure generated by a concave acoustic transducer, without the need for supplementary auxiliary equipment. The direct transmission of cell-containing samples is facilitated by this nozzle-less and contamination-free process, which maintains the integrity of the samples.[80]

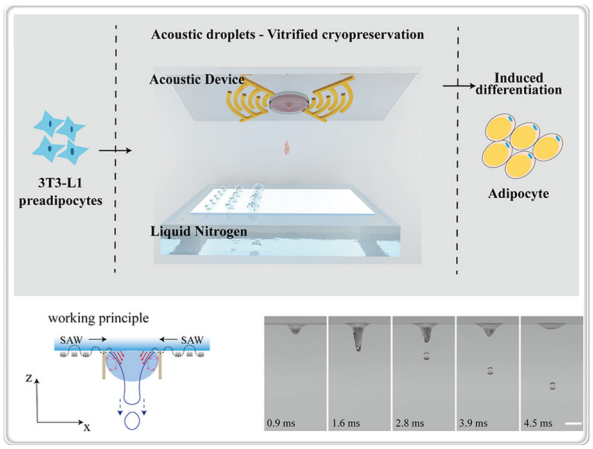


Fig. 9 Development of an acoustic droplet vitrification method by combining ADE technology with vitrification methods. Reprinted from ref. 81, copyright (2021), with permission from American Chemical Society.

Building on this, the acoustic droplet vitrification (ADV) method was developed by combining the ADE technique with solid-surface vitrification to facilitate the efficient processing and cryopreservation of rare cells (Fig. 9).[81] In this workflow, rare cells are first encapsulated and arrayed onto a substrate using the ADE system. The rapid vitrification of hundreds to thousands of cells is facilitated by an incorporated cooling module on the substrate, which employs minimal concentrations of cryoprotectant agents (CPAs) and silk proteins. This method accommodates large cell volumes or cell spheroids, maintaining high post-thaw viability suitable for constructing tissues, organoids, or disease models.[82]

In addition to the ADE technique, researchers have proposed a range of advanced acoustic control strategies for microdroplet manipulation, further expanding the versatility and application scope of acoustofluidic technologies. For instance, He *et al.* devised a high-frequency ultrasonic microdroplet generation technique (Fig. 10a).[83] This technique involves the application of focused ultrasonic waves to the liquid interface, resulting in the formation of stable "liquid spikes" that eject microdroplets onto a target substrate without the necessity of needle tips or nozzles, thus avoiding clogging and tip wear. Zhang *et al.* designed a superhydrophobic scaled surface that facilitates directional droplet transfer through sound-induced transport (Fig. 10b).[84] Yiannacou *et al.* created a programmable microfluidic chip that integrates bulk acoustic wave (BAW) technology with closed-loop machine learning to facilitate the transport and merging of two-dimensional droplets (Fig. 10c).[85] Vachon *et al.* introduced a membrane acoustic wave actuator based on a miniature piezoelectric thin film fabricated through silicon diffusion, which generates bending waves for particle manipulation, with promising applications in biosensing and organoid production (Fig. 10d).[86] Pan *et al.* designed a morphology-variable magnetic micropillar array (Fig. 10e) that captures particles or drives droplet motion *via* local acoustic streaming induced by SAWs.[87]

Notably, in advancing methodological and theoretical understanding, Liu *et al.* collaboratively proposed an acousto-dewetting technique (Fig. 10f) that focuses ultrasonic energy inside droplets to generate strong internal flows, actively altering the three-phase contact line to enable controlled dewetting and shrinkage on superhydrophilic surfaces, without requiring surface modification or additives.[88] Wang *et al.* investigated the direct conversion of sound to gyroscopic vortices on suspended droplets (Fig. 10g).[89] Their findings illustrate how surface curvature oscillations induce high-speed droplet rotation, annular acoustic explosions, and cavitation hotspots, which have the potential to advance applications in acoustic oncology.

In more recent innovative approaches, Li *et al.* developed oscillating microbubble array metamaterials (OMAMs) (Fig. 10h) that use acoustically excited microbubble oscillations to create fluid traps, which facilitate the efficient separation of exosomes and their subpopulations from whole blood.[90] Zhu *et al.* introduced a sound-controlled fluidic processor.[91] This device creates a tunable acoustic swimming force field by spatially coupling acoustic transducers and ultra-smooth surfaces. This enables directional droplet transport, fusion, splitting, and mixing across a wide range of surface tensions (17.9–72.0 mN m^{-1}) and volumes (1–3000 nL). Together, these emerging innovations demonstrate the diverse potential of advanced acoustic manipulation strategies for next-generation microfluidic, biomedical, and materials science applications.

Existing research has extended acoustic manipulation technologies to a variety of microfluidic operations, including pumping, mixing, and particle control.[92–95] However, the interactions between various acoustic modes and microfluidic systems are still not fully comprehended, and acoustic manipulation frequently necessitates an external excitation source that can regulate amplitude, frequency, and other parameters with high precision. These factors may limit the practical application of acoustic manipulation.[14] With the continuous advances in MEMS, micro-laboratory, and microfluidic technologies, the application prospects for acoustic manipulation in droplet-based microfluidics are becoming increasingly promising.

3.2 Mechanical vibration strategies

In addition to utilizing acoustic induction methods, it is also possible to manipulate microdroplets through mechanical actuators (such as pneumatic microvalves, piezoelectric actuators, and mechanical vibrators), which are straightforward to construct, cost-effective, and well-suited for low-cost, high-throughput applications.[96–99]

Numerous researchers have investigated the kinetic behavior of droplet vibration. For instance, Kunz *et al.* simulated the kinematic behaviour and static characteristics of droplets on a horizontally vibrating wall by coupling the

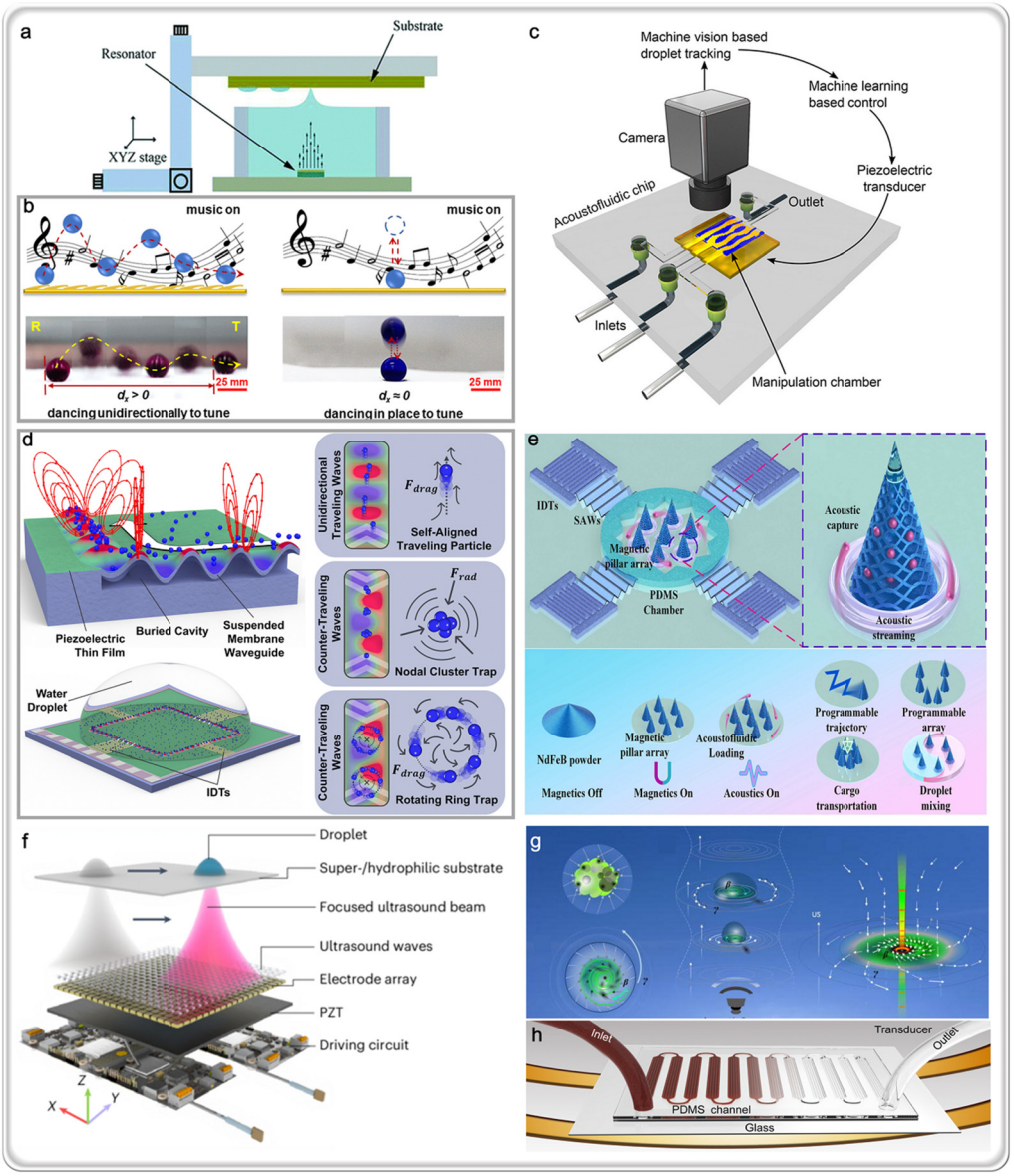


Fig. 10 Various advanced techniques for acoustic manipulation. (a) The study employed high-frequency ultrasound to generate microdroplets. Reprinted from ref. 83, copyright (2018), with permission from Royal Society of Chemistry. (b) The study utilized a superhydrophobic scale-like surface to facilitate sound-induced directional droplet transport. Reprinted from ref. 84, copyright (2022), with permission from American Chemical Society. (c) The study integrated BAW technology with closed-loop machine learning in a programmable microfluidic chip for two-dimensional droplet transport and merging. Reprinted from ref. 85, copyright (2022), with permission from American Chemical Society. (d) A membrane acoustic wave actuator. Reprinted from ref. 86, copyright (2023), with permission from Royal Society of Chemistry. (e) The study designed a morphable magnetic micropillar array for particle capture or droplet actuation. Reprinted from ref. 87, copyright (2024), with permission from Elsevier. (f) The study employed an acoustically induced dewetting method for droplet manipulation. Reprinted from ref. 88, copyright (2025), with permission from Springer Nature. (g) The study explored sound-vortex conversion mechanisms in droplets. Reprinted from ref. 89, copyright (2024), with permission from AIP Publishing. (h) The study developed oscillating microbubble array-based metamaterials (OMAMs). Reprinted from ref. 90, copyright (2025), with permission from American Association for the Advancement of Science.

free energy density of the gas flow phase field with the Navier–Stokes equations incorporating the Korteweg stress tensor (Fig. 11a).[100] Song *et al.* investigated the retraction behaviour of droplets on both fixed and vibrating surfaces, revealing the synergistic effects of inertial forces and vibrational velocity (Fig. 11b).[101] Lei *et al.* conducted experimental and theoretical studies on vibration-driven droplet coalescence on vertical surfaces, established a mass–spring–damper model, and elucidated the droplet phase-shift mechanism, ultimately proposing a strategy to promote coalescence that can be extended to various inclined vibration scenarios driven by different signals (Fig. 11c).[102]

3.2.1 Mechanical vibration capillary/channel. Like acoustic vibration strategies, mechanical vibration of capillaries has been extensively studied for generating droplets by applying mechanical oscillations to a dispersed-phase capillary. This

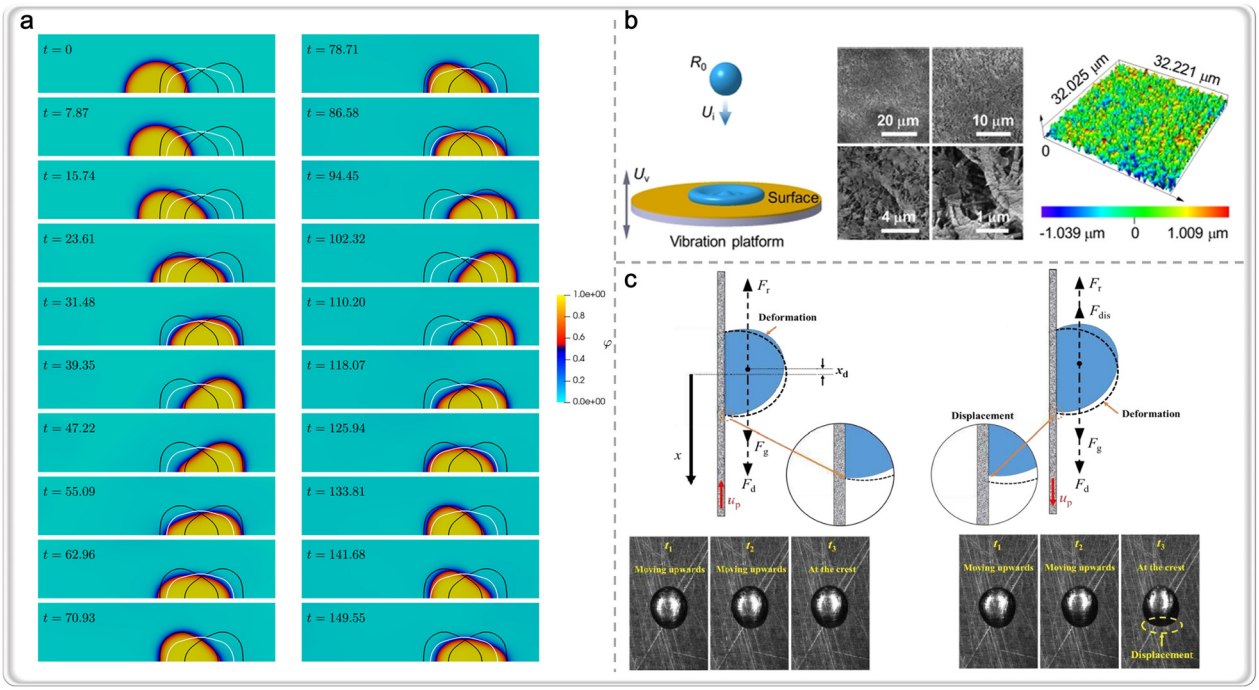


Fig. 11 Investigation of droplet vibration dynamics. (a) The study simulated the motion behavior and static characteristics of droplets on horizontally vibrating walls by integrating the free energy density of the gas flow phase field with the Navier–Stokes equations of the Korteweg stress tensor. Reprinted from ref. 100, copyright (2023), with permission from John Wiley and Sons. (b) The research explored the retraction behavior of droplets on both fixed and vibrating surfaces, uncovering the combined influence of inertial forces and vibration velocity on droplets. Reprinted from ref. 101, copyright (2023), with permission from AIP Publishing. (c) The study examined the dynamics of vibration-induced droplet coalescence on vertical surfaces. Reprinted from ref. 102, copyright (2023), with permission from AIP Publishing.

approach enables the production of highly monodisperse droplets with controllable sizes across a wide range, making it suitable for diverse microfluidic applications.

The working principle is illustrated in Fig. 12a, which demonstrates how a mechanical vibrator induces periodic fluctuations in the dispersed phase within a flow-focusing microfluidic device, resulting in the formation of droplets.[103] Cheung *et al.* developed a glass capillary system (Fig. 12b) that applies transverse and longitudinal perturbations to the inner-phase fluid *via* a mechanical vibrator.[104] This process generates pressure perturbations that break up the jet flow into droplets. The droplet size can be precisely tuned by adjusting the vibration frequency and input voltage.

Researchers have explored the mechanisms of droplet generation in mechanically vibrating capillaries and proposed innovative methods for its optimisation. For example, Zhu *et al.* investigated the effects of mechanical vibration on droplet generation in an isotropic microfluidic channel (Fig. 12c) and found that vibration induces flow rate fluctuations, producing droplets whose frequency synchronizes with the applied mechanical vibration.[98] This enables flexible size tuning across a wide range. Ye *et al.* developed OsciDrop, a non-chip-based multifunctional droplet generation platform (Fig. 12d), which generates stable, uniform droplets in parallel at the tip of a runner tube by oscillating the continuous phase at its distal end.[105] They established a theoretical model incorporating flow rate, amplitude, frequency, and waveform parameters, highlighting that the droplet generation is dominated by inertial forces as characterised by the Weber number. The device's practicality and effectiveness were validated using nucleic acid amplification tests, demonstrating its potential for miniaturisation, standardization, integration, and automation in droplet microfluidic control.

Mechanical vibration strategies have also been widely applied to inkjet printing technologies, which include continuous inkjet (CIJ) and drop-on-demand (DOD) modes. In CIJ printing, capillary instability is exploited to break up the continuous phase into droplets; a piezoelectric actuator generates pressure wave perturbations at the nozzle, causing the jet to fragment into uniform droplets. Compared with CIJ, the DOD method is more straightforward to operate and less costly, and has become the mainstream technology in modern inkjet printing.[106] The working principle of DOD is similar to droplet generation strategies that use acoustic or mechanical vibration of capillaries or channels. Transient pressure pulses produced by piezoelectric devices periodically perturb the continuous jet at the nozzle tip. When the pressure pulse dissipates, the liquid self-segments due to surface tension, enabling controlled jet breakup and continuous droplet formation over short time scales.[107]

3.2.2 Droplet printing using the interfacial vibration method. In 2016, Xu *et al.* introduced a cross-interface emulsification (XiE) technique (Fig. 13a).[108] This method

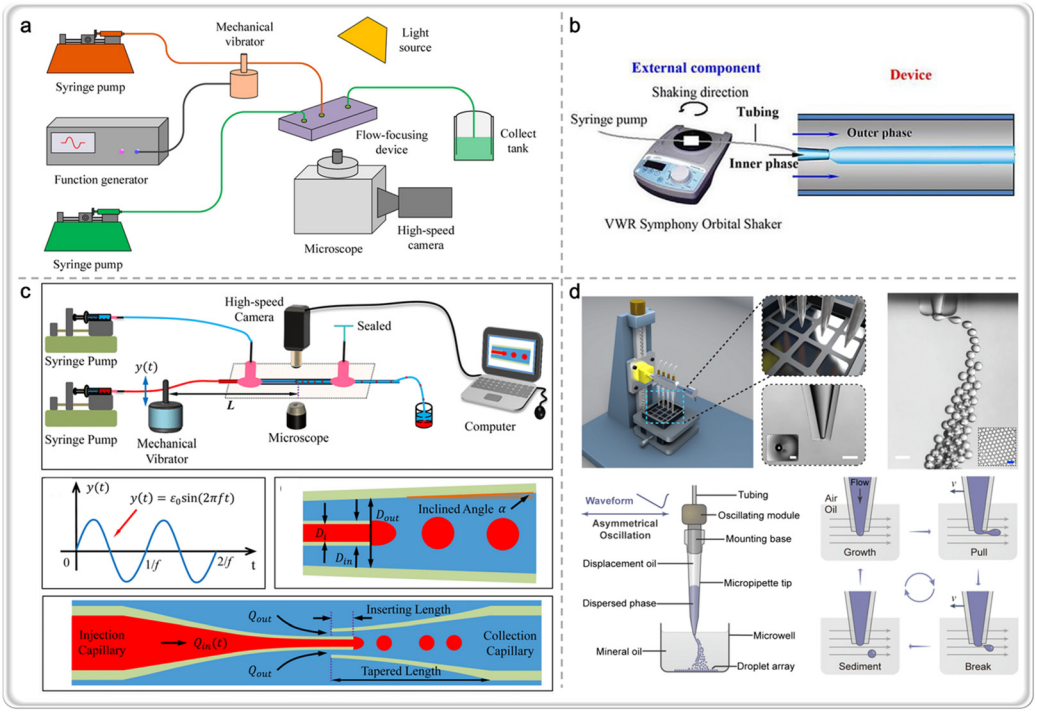


Fig. 12 Research on the mechanical vibration capillary/channel method. (a) Working principle of the mechanical vibration device. Reprinted from ref. 103, copyright (2020), with permission from MDPI. (b) A glass capillary apparatus that induces droplet formation by subjecting the inner phase fluid conduit to transverse and longitudinal perturbations using a mechanical vibrator. Reprinted from ref. 104, copyright (2012), with permission from AIP Publishing. (c) Investigation of the impact of mechanical vibration on droplet generation within co-flow microchannels. Reprinted from ref. 98, copyright (2016), with permission from Springer Nature. (d) A multifunctional microdroplet generation device, OsciDrop. Reprinted from ref. 105, copyright (2022), with permission from American Chemical Society.

utilizes high-frequency capillary vibration at the oil–gas interface to emulsify the continuous phase into monodisperse droplets. These droplets are subsequently deposited onto the bottom of a 96-well plate under the cyclic shear effect of interfacial tension. This method offers a high droplet generation rate, precise volume control (20 pL–10 nL), and reduced fabrication cost, providing a practical solution for complex droplet-based biochemical reactions under simple experimental conditions. Researchers further combined XiE with the dLAMP method to detect H5 subtypes of avian influenza.[109]

Building on this concept, Liao *et al.* used an electric vibrator and function generator to drive a capillary that oscillates vertically at the air–water interface (Fig. 13b).[110] This periodic motion enables the oil phase to enter the aqueous phase from the nozzle tip and be sheared into uniform droplets. Huang *et al.* introduced an inclined shear method (Fig. 13c) in which the capillary vibrates at a controlled inclination angle at the air–water interface.[111] This produces droplets with significant lateral displacement, allowing both droplet generation and directional transport to be tuned by adjusting flow rate, vibration frequency, and tilt angle. Li *et al.* used piezoelectric elements to apply alternating voltage signals to the nozzle, inducing repeated fluid suction and discharge at the orifice.[112] This generates constrained interfacial vibrations, producing uniform microdroplets under the combined effects of viscous and inertial forces (Fig. 13d). Together, these innovations highlight the utility of interfacial vibration techniques for controllable droplet generation in microfluidic applications.

3.2.3 Other advanced manipulation strategies. In addition to the applications discussed in sections 3.2.1 and 3.2.2, which focus on droplet generation, mechanical vibration techniques have also been employed to drive droplets in a variety of complex motions. For example, Lian *et al.* demonstrated four distinct motion modes (including *in situ* deformation, creeping, jumping, and crushing) by combining ratcheting with vertical mechanical vibration (Fig. 14a).[113] However, their study did not fully account for the influences of surface tension, gravity, and adhesion on droplet behaviour. In the same year, Wu *et al.* achieved directional droplet motion on inclined micro-wall arrays using mechanical vibration to generate inertial forces that overcome adhesion resistance (Fig. 14b).[114] Building on this, Zhang *et al.* demonstrated directional droplet manipulation by balancing the inertia driving force and lubrication ratchet-induced adhesion resistance through horizontal or vertical mechanical vibrations (Fig. 14c).[12,115]

Similarly, Hou *et al.* developed a tilted array surface with a shape memory function that enables directional droplet transport through structural deformation and recovery driven by mechanical vibration (Fig. 14d).[116] Additionally, Xue *et al.*

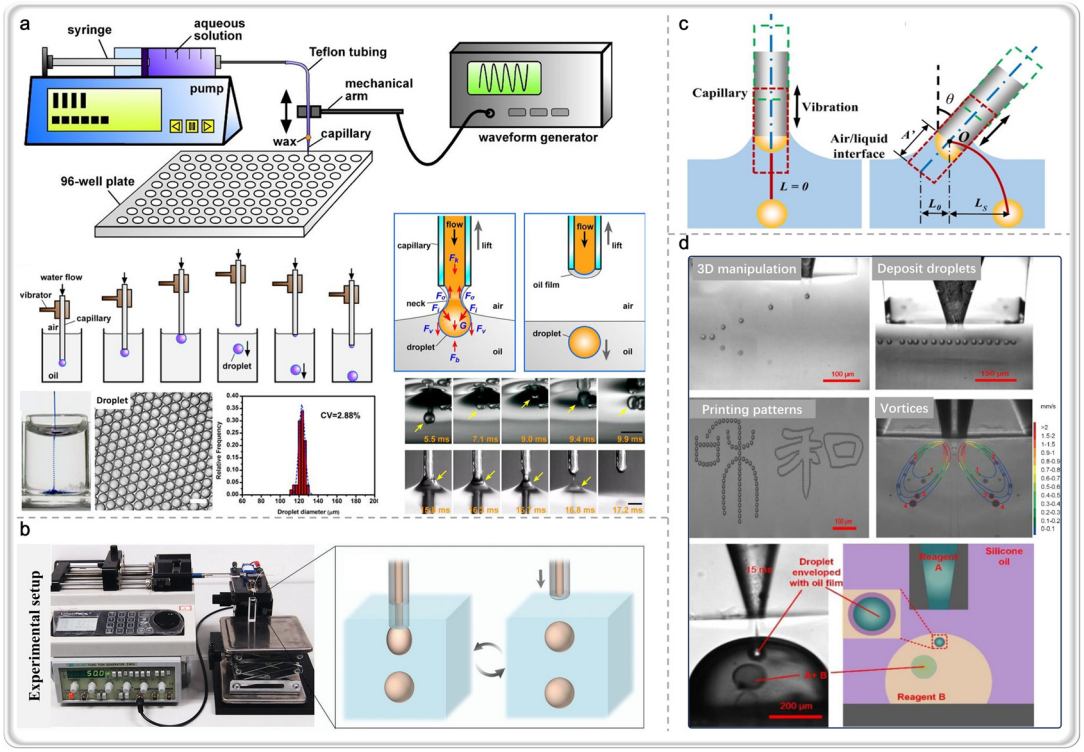


Fig. 13 Interfacial vibration droplet printing technology. (a) Cross-interface emulsification to create droplets. Reprinted from ref. 108, copyright (2016), with permission from American Chemical Society. (b) The use of an electric vibrator and function generator to induce capillary vibration at the air–water interface, leading to droplet formation through shear forces. Reprinted from ref. 110, copyright (2016), with permission from John Wiley and Sons. (c) Inclined plane shear is employed to produce droplets. Reprinted from ref. 111, copyright (2019), with permission from Royal Society of Chemistry. (d) The application of alternating positive and negative voltage signals to the nozzle through piezoelectric elements results in the production of consistently sized microdroplets. Reprinted from ref. 112, copyright (2021), with permission from John Wiley and Sons.

applied vibration techniques to an infiltrated patterned substrate, realizing symmetric/asymmetric vibrational transformations and multimodal responses of liquid droplets (Fig. 14e).[117]

In particular, the functionality of vibration-driven droplet microfluidics can be substantially enhanced through integration with other active manipulation methods, forming sophisticated hybrid systems that leverage complementary physical principles. These systems overcome limitations of individual methods by combining the strengths of different actuation mechanisms, enabling control, flexibility, and functionality in microfluidic operations.

Recent literature demonstrates several innovative hybrid approaches. The combination of acoustic and electric fields creates powerful systems where acoustic methods provide high-throughput particle focusing while dielectrophoresis (DEP) enables highly selective manipulation based on dielectric properties. As demonstrated by Ravula *et al.*, acoustic fields can pre-concentrate particles into defined streams, which are then precisely focused using DEP, achieving throughputs of 10^4–10^5 particles per min with reduced variability in the particles' location.[118] More recent simulations have further explored integrated architectures for simultaneous particle washing, separation, and concentration using coordinated acoustic and DEP forces.[119]

The integration of acoustic and magnetic fields offers another powerful hybrid modality. A notable implementation combines surface acoustic wave (SAW) with reconfigurable magnetic micropillar arrays.[120] In this system, magnetic fields assemble porous NdFeB magnetic micropillars, while SAW-generated acoustic streaming enables efficient particle capture (up to 0.214 MCF) and droplet manipulation (speeds $\leq$3.96 mm s^{-1}). This approach achieves accelerated mixing ($\leq$2.5 s) and enables complex operations like maze navigation, significantly improving the performance over the conventional SAW manipulation technique with acoustic potential wells, as well as greatly enhancing the manipulation efficiency and functionality diversity. Moreover, Lee *et al.* describe a new type of magnetic droplet microfluidic system incorporated with acoustic excitation, which allows not only the enhancement of the droplet mixing performance but also the usability of the selective droplet oscillation technique.[121] Yu *et al.* utilized surface acoustic waves (SAW) in conjunction with Raman spectroscopy to actively enrich 5 μL of 50 nm gold nanoparticles (AuNPs), thereby achieving innovative SERS-active sensing. This SAW-induced AuNP clustering technology offers a rapid, label-free SERS sensing method characterized by exceptional sensitivity and uniformity.[122]

Beyond these combinations, triple-hybrid systems integrating optical, magnetic, and acoustic control

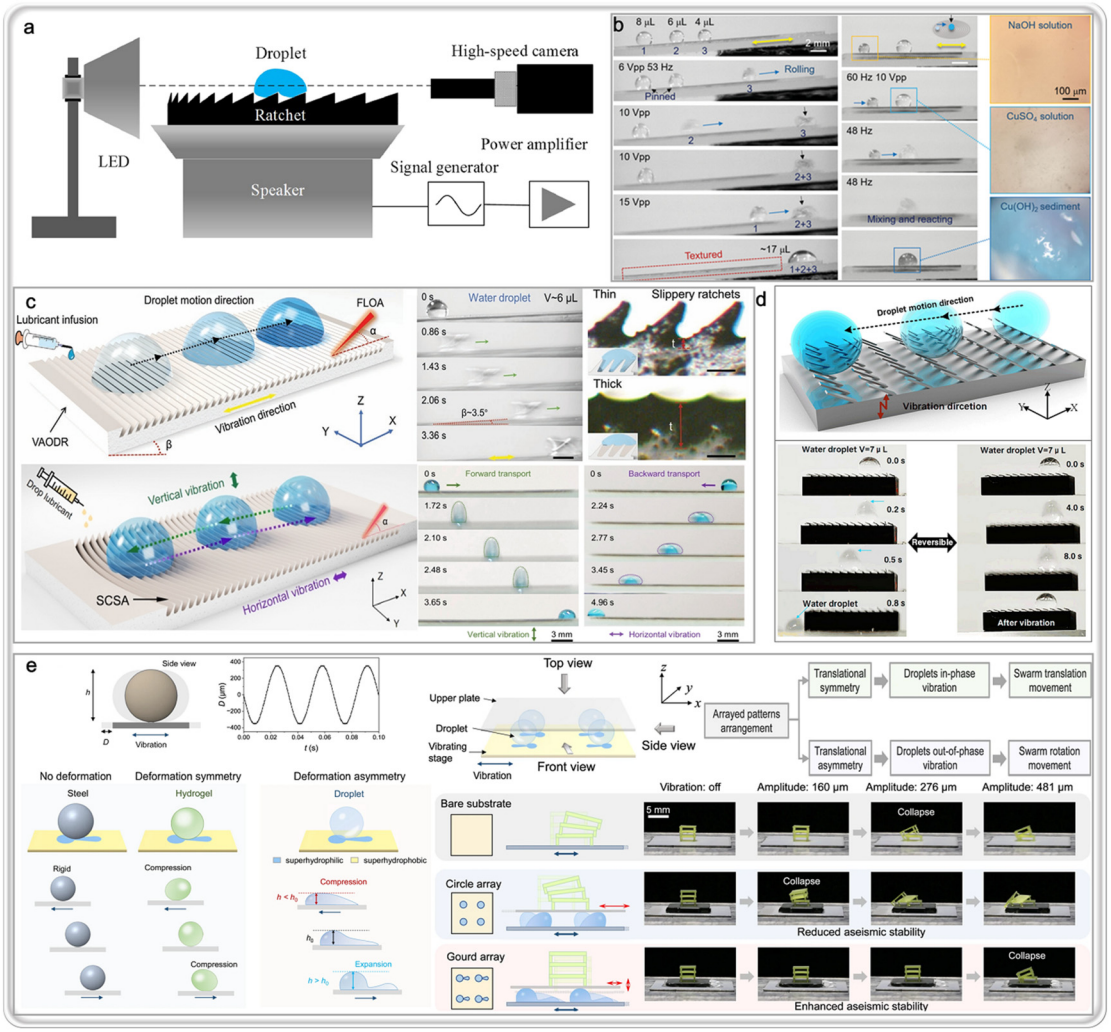


Fig. 14 Other mechanical vibration control methods. (a) By combining a ratchet with vertical mechanical vibration, *in situ* droplet deformation, creeping, jumping, and fragmentation were achieved. Reprinted from ref. 113, copyright (2020), with permission from Elsevier. (b) Directional droplet motion was realized by applying mechanical vibration on an inclined micro-wall array surface. Reprinted from ref. 114, copyright (2020), with permission from John Wiley and Sons. (c) Manipulation of droplet directionality was attained by balancing inertia-driven forces from mechanical vibrations with adhesion resistance from lubricated ratchets. Ref. 12 and 115, copyright (2022 and 2023), with permission from John Wiley and Sons and AIP Publishing. (d) Researchers developed a tilted array surface with shape memory properties, allowing for directional droplet transportation through structural deformation and recovery induced by mechanical vibrations. (Note: due to copyright issues, we are unable to change the content of the original figure, but there may be a spelling error in the figure: "dircetion" should be changed to "direction".) Reprinted from ref. 116, copyright (2024), with permission from Elsevier. (e) Vibration technology was applied to wettability-patterned substrates, achieving symmetric/asymmetric vibration transformation and multimodal responses of droplets. Reprinted from ref. 117, copyright (2024), with permission from Springer Nature.

mechanisms represent the frontier of multi-physical manipulation. Recent work has demonstrated stable optical trapping and controllable rotation of ferrofluid liquid marbles (FLMs) through combined photothermal interactions, magnetic forces, and acoustic control.[123]

The primary synergistic benefits of these hybrid systems include: (1) complementary functionality, where different physical fields address specific limitations of individual methods; (2) enhanced operational flexibility through dynamic reconfiguration capabilities; and (3) performance amplification through sequential or simultaneous field application. However, these advantages come with significant challenges, including increased system complexity requiring sophisticated multi-channel control systems, interfacial issues between different actuation methods, and manufacturing reproducibility concerns, particularly for reconfigurable components like magnetic micropillars.[120,123] Furthermore, the theoretical prediction of multi-physical interactions remains challenging, necessitating further research into the interplay between acoustic streaming forces, magnetic gradients, and viscous drag.[123] Therefore, the design of hybrid systems requires careful optimization to balance performance gains against added complexity and cost.

4 Biomedical research and applications

Vibration-based droplet manipulation is particularly well-suited for a variety of biomedical applications due to its

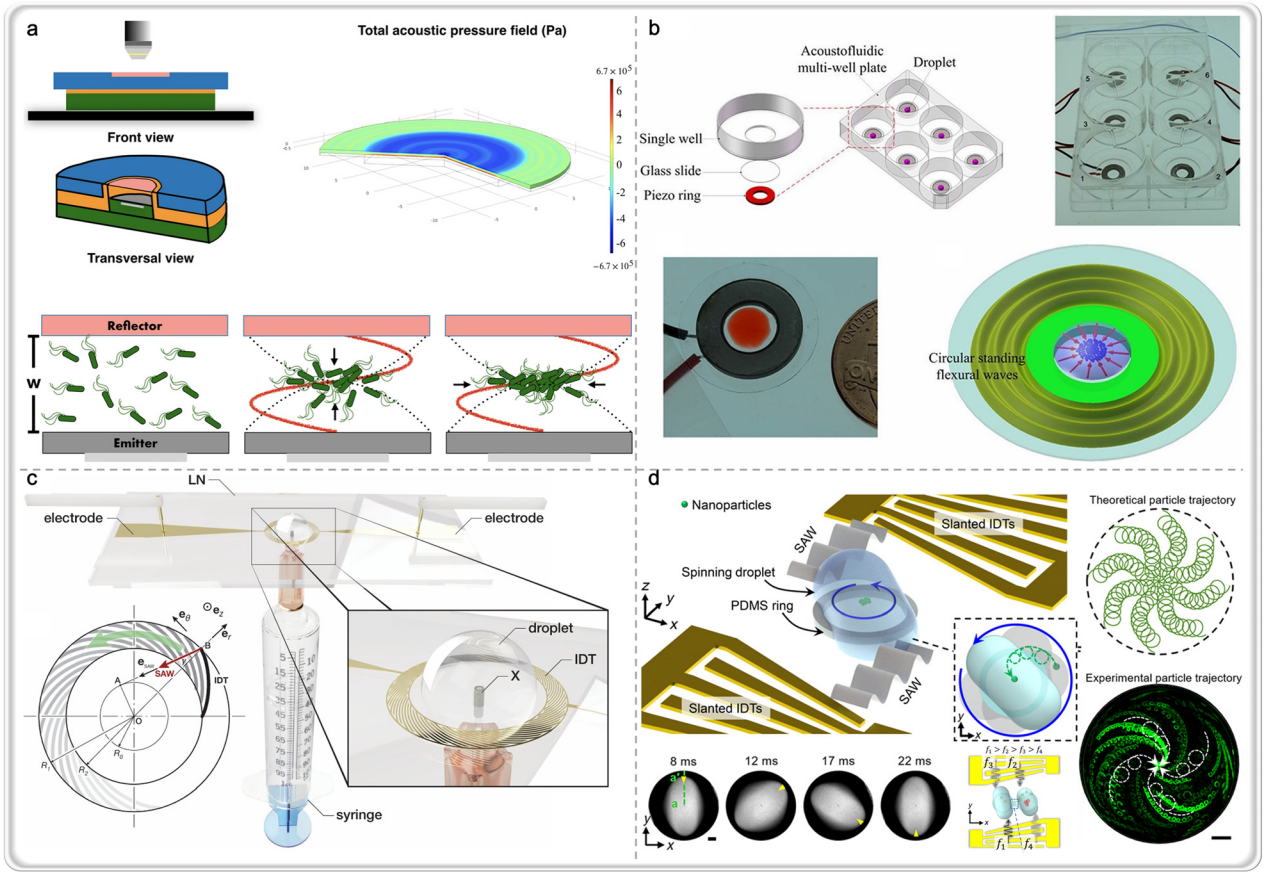


Fig. 15 Applications of vibration technology in cell manipulation. (a) Acoustic levitation devices were utilized to suspend *Escherichia coli*, showcasing enrichment phenomena in microgravity conditions. Reprinted from ref. 135, copyright (2018), with permission from Springer Nature. (b) Cell enrichment was attained through the utilization of acoustofluidic chips. Reprinted from ref. 136, copyright (2020), with permission from Royal Society of Chemistry. (c) A spiral interdigital transducer-based enrichment chip was developed, which utilizes helical flow fields generated within droplets to achieve highly efficient blood cell enrichment. Reprinted from ref. 137, copyright (2021), with permission from Royal Society of Chemistry. (d) Effective enrichment of DNA, exosomes, and proteins was achieved through high-speed droplet rotation induced by acoustic effects from two frequency-modulated interdigital electrodes. Reprinted from ref. 138, copyright (2021), with permission from American Association for the Advancement of Science.

unique advantages, including non-contact operation, high precision, and excellent biocompatibility. These techniques allow for the precise control of droplets containing biological samples, reagents, or living cells, while minimizing the risks of contamination and structural damage. In recent years, vibration-induced manipulation has been successfully applied to sample pretreatment, diagnostics, and treatment.

4.1 Sample pretreatment

4.1.1 Cellular manipulation. In recent years, vibration-based techniques have been increasingly adopted for cell manipulation in experimental research.[124] For example, Saito *et al.* achieved non-contact transport of microorganisms and microbial tissues by adjusting the frequency of acoustic waves in an ultrasonic levitation device.[125] Researchers have also extended acoustic levitation to cell rotation by applying high-frequency vibrations to a cantilever beam, producing ultrasonic beams that are harnessed by microrobots to transport and rotate individual cells.[126–128] This approach holds promise for advancing cell manipulation studies under microgravity conditions.

After achieving precise cell manipulation, researchers have expanded these capabilities towards more advanced applications. For example, Lagerman *et al.* combined ultrasonic vibration with flow focusing to achieve high-throughput and size-tunable single-cell droplet encapsulation.[129] In parallel, several researchers have applied acoustic fluidic control (AFC) to enable real-time, continuous enrichment of particles within dispersed droplets or continuous flow liquids.[130–132] Notably, enrichment strategies based on SAWs have attracted significant attention. For instance, Akther *et al.* designed an acoustic–fluidic chip utilising SAW technology to enrich submicron-sized particles, validating its feasibility through simulations and experiments.[133] Zhao *et al.* investigated particle offset phenomena in SAW microfluidics and demonstrated that surfactants can alter the motion offset of submicron particles, offering a new approach for particle sorting.[134]

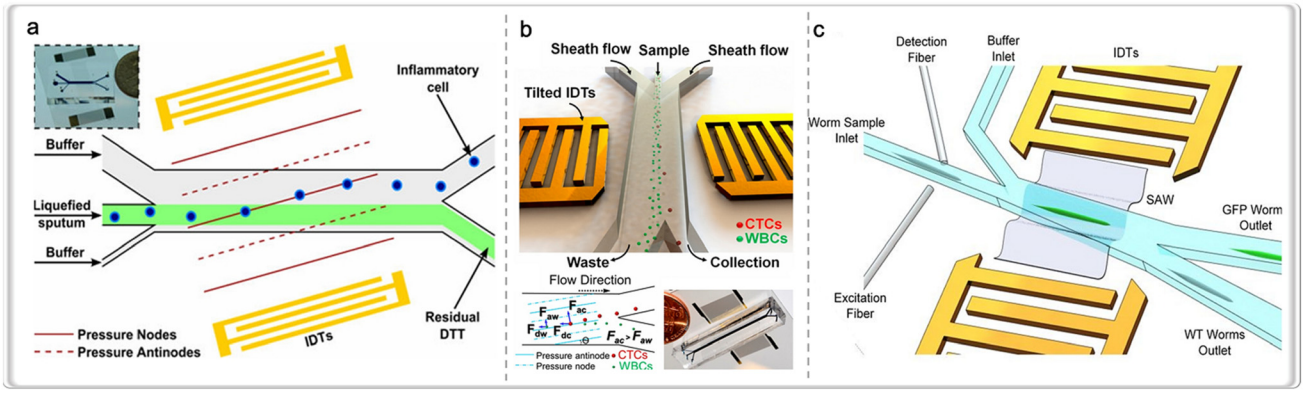


Fig. 16 Application of vibration technology for cell sorting. (a) Sorting of inflammatory cells from sputum samples. Reprinted from ref. 145, copyright (2016), with permission from American Chemical Society. (b) Sorting of tumor cells from clinical samples. Reprinted from ref. 146, copyright (2015), with permission from *PNAS*. (c) Sorting of *Caenorhabditis elegans*. Reprinted from ref. 147, copyright (2020), with permission from Royal Society of Chemistry.

Building on these insights, Gutiérrez-Ramos *et al.* suspended *Escherichia coli* at wave nodes using an acoustic levitation device and observed enrichment under microgravity conditions (Fig. 15a).[135] Liu *et al.* employed a ring-shaped PZT transducer to generate acoustic waves, inducing cellular enrichment within an AFC microfluidic

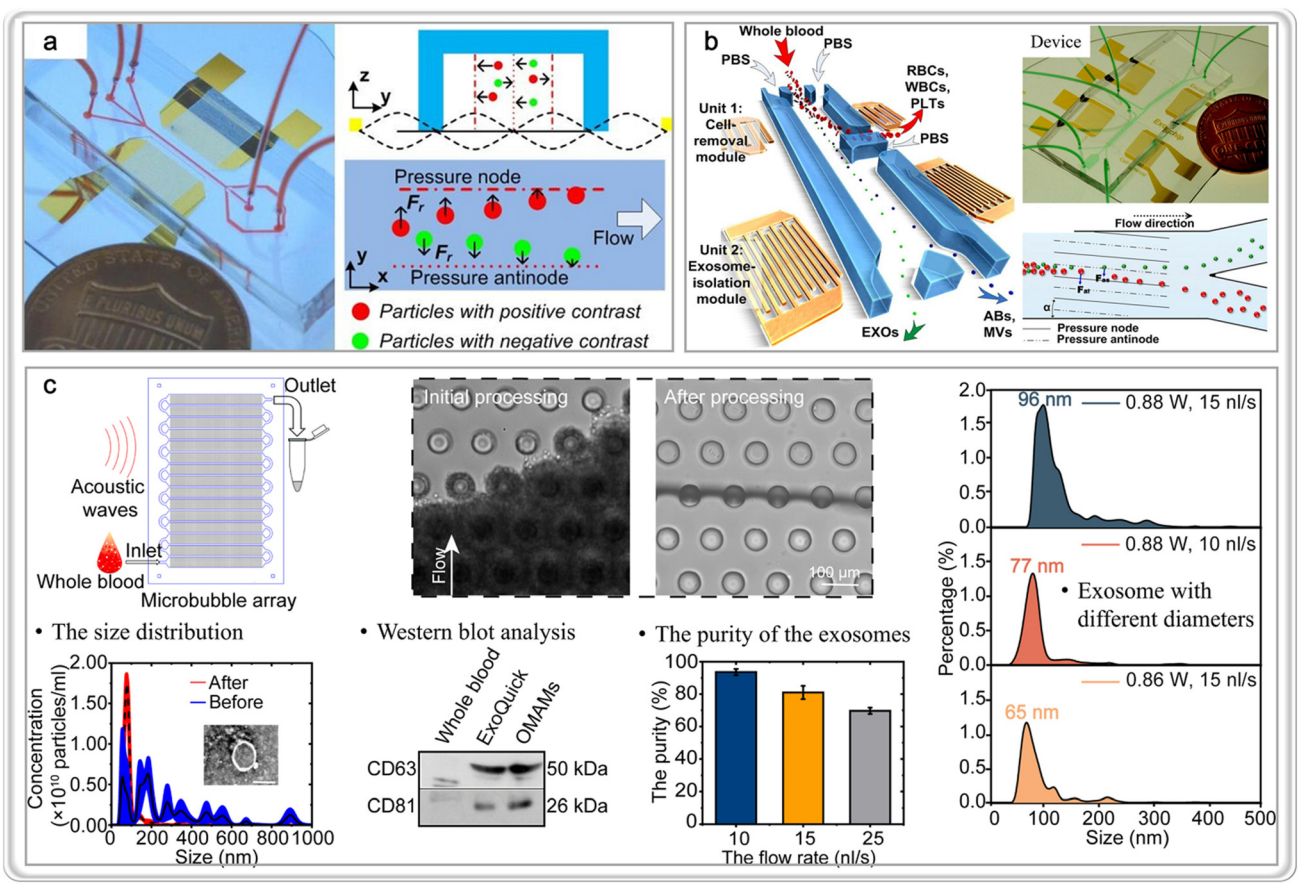


Fig. 17 Application of vibration techniques to sorting of cellular structures or products. (a) Label-free separation of extracellular vesicles and lipoproteins was achieved on surface acoustic wave (SAW) microfluidic chips by exploiting the distinct acoustic properties of these particles. Reprinted from ref. 148, copyright (2019), with permission from Royal Society of Chemistry. (b) A two-stage SAW method, integrating interdigital electrodes with microfluidic chips, was employed to separate exosomes from whole blood. Reprinted from ref. 149, copyright (2017), with permission from *PNAS*. (c) Oscillating microbubble array metamaterials (OMAMs) exhibited the capability to effectively separate exosomes with high purity from whole blood samples. Reprinted from ref. 90, copyright (2025), with permission from American Association for the Advancement of Science.

chip (Fig. 15b).[136] Zhang *et al.* developed an enrichment chip based on a helical fork-finger transducer to achieve efficient blood cell enrichment using the helical flow field generated within droplets (Fig. 15c).[137] Gu *et al.* used acoustic waves produced by two variable-frequency fork-finger electrodes to induce high-speed droplet rotation within a pore, enabling effective enrichment of nanoparticles such as DNA, exosomes, and proteins during the rotation process (Fig. 15d).[138] In addition, researchers have proposed leveraging the limiting effects of phononic crystals on certain SAWs to enhance droplet enrichment.[139,140] Collectively, these technical advances in cell and particle manipulation lay a robust theoretical foundation for developments in cell sorting.

4.1.2 Cell sorting. In disease screening, variations in the concentration of cells and cell secretions can serve as valuable indicators of disease progression, thereby providing valuable indicators for early detection and clinical diagnosis.[141–143] Consequently, separating these targets from complex biological samples holds significant medical value and has driven extensive research into advanced sorting techniques. For example, Mutafopulos *et al.* employed an oblique-finger transducer to sort single cells with an efficiency of up to 90% and a sorting rate reaching 2000 events per second.[26] This approach enabled precise, on-demand encapsulation of single cells in droplets, effectively overcoming the Poisson distribution limitations typically associated with droplet occupancy.[144] Similarly, Nawaz *et al.* integrated a focused interdigital transducer into a microfluidic analytical platform, achieving high-throughput single-cell sorting.[43]

To date, researchers have successfully applied vibrational microfluidics to isolate inflammatory cells from sputum

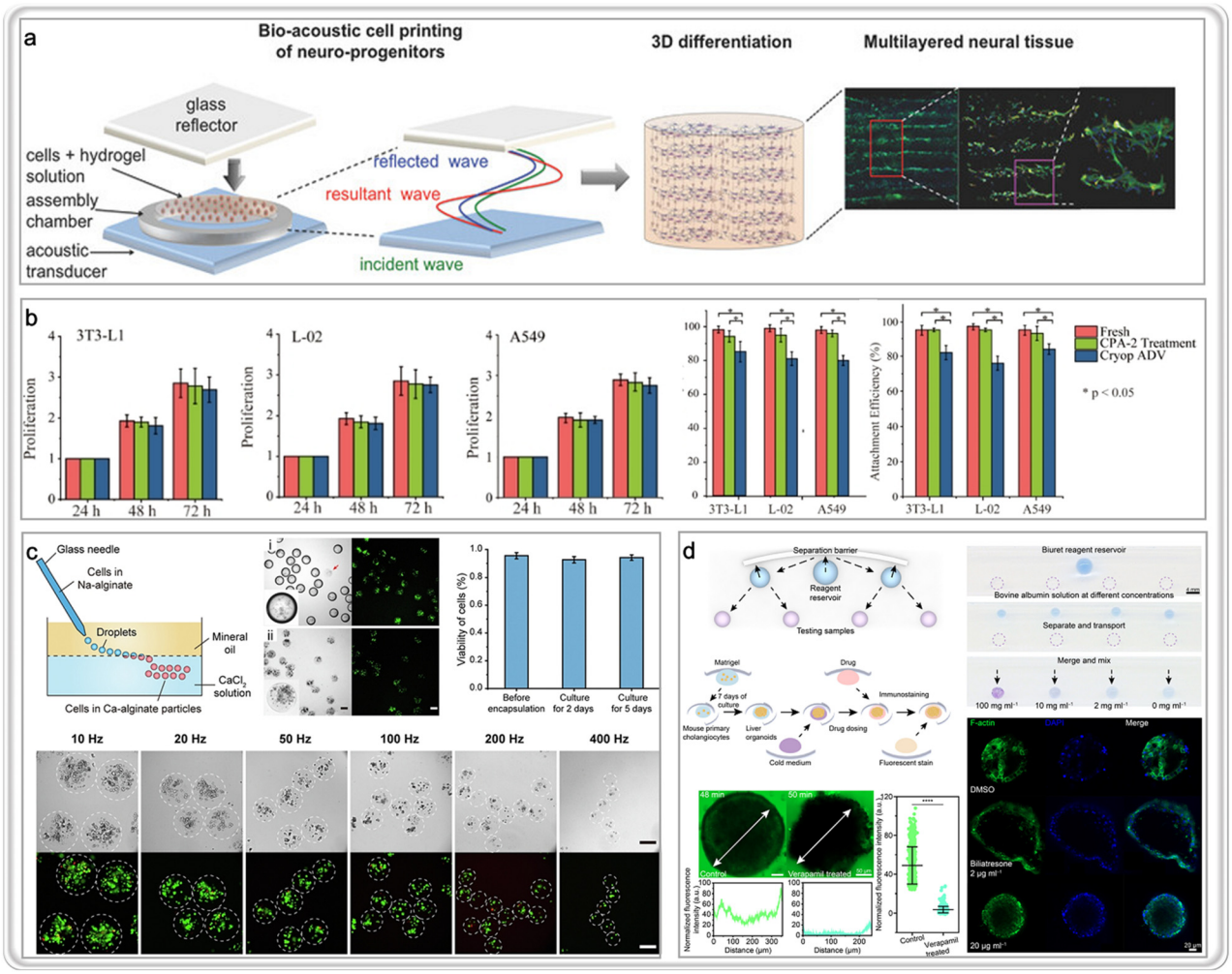


Fig. 18 Vibrating technology is applied in cell culture. (a) A 3D neural network model was created using an acoustic levitation device. Reprinted from ref. 151, copyright (2015), with permission from John Wiley and Sons. (b) Long-term cryopreservation of three different cell lines (a human lung cancer cell line, A549 cells, a human liver cell line, L02 cells, and a mouse embryonic fibroblast cell line, 3T3-L1 cells) was achieved through the acoustic droplet vaporization (ADV) method. Reprinted from ref. 81, copyright (2021), with permission from American Chemical Society. (c) Cell culture was conducted utilizing acoustic vibration capillary technology. The figure shows bright field and fluorescence images of cell-enclosed droplets (i) and cell-laden hydrogel particles (ii). Reprinted from ref. 73, copyright (2021), with permission from Elsevier. (d) An acoustically controlled fluidic processor was utilized for the cultivation of mouse primary liver organoids. Reprinted from ref. 91, copyright (2025), with permission from American Association for the Advancement of Science.

samples (Fig. 16a), tumor cells from clinical samples (Fig. 16b), and the sorting of *Caenorhabditis elegans* (Fig. 16c), demonstrating the considerable promise of vibration-based microfluidics in cell sorting applications.[145–147]

In addition to sorting whole cells, vibrational microfluidic techniques have also been employed to isolate cellular structures and secreted products with significant biomarker relevance. For example, Wu *et al.* exploited the differences in acoustic properties among particles to achieve label-free sorting of extracellular vesicles and lipoproteins on a surface acoustic wave (SAW) microfluidic chip, providing an effective strategy for disease diagnosis based on extracellular vesicle analysis (Fig. 17a).[148] Wu *et al.* combined a fork-finger electrode with a microfluidic chip to isolate exosomes from whole blood using a two-stage SAW approach (Fig. 17b).[149] In this method, erythrocytes, leukocytes, and platelets were first removed, followed by the elimination of microbubbles and apoptotic vesicles, ultimately yielding purified exosomes that can be utilised for early HPV detection based on exosomal genetic material.[150] Li *et al.* proposed oscillating microbubble array-based metamaterials (OMAMs), which leverage acoustically excited microbubble oscillations to filter micron- and nanoscale particles, thereby achieving high-purity exosome isolation directly from whole blood samples (Fig. 17c).[90]

4.1.3 Cell cultivation. Vibration-based manipulation techniques can also be employed to construct three-dimensional cell culture models that mimic the structure and function of natural tissues.[136,138] For example, researchers have used acoustic levitation devices to assemble 3D neural network models (Fig. 18a).[151] Xia *et al.* developed an acoustic droplet vitrification (ADV) method that enables long-term cryopreservation of multiple cell lines (including the human lung cancer cell line A549, the human hepatocyte line L02, and mouse embryonic fibroblast line 3T3-L1) with preserved cell viability and function upon recovery, offering potential for the creation of tissues, organoids, or disease models (Fig. 18b).[81,82] He *et al.* utilised high-frequency acoustic vibration at the capillary tip to generate liquid droplets for 3D cell culture, successfully producing alginate microcapsules of tunable sizes and high cell viability (Fig. 18c).[73] In addition, Zhu *et al.* developed an acoustic fluidic processor that uses a tunable acoustic swimming force

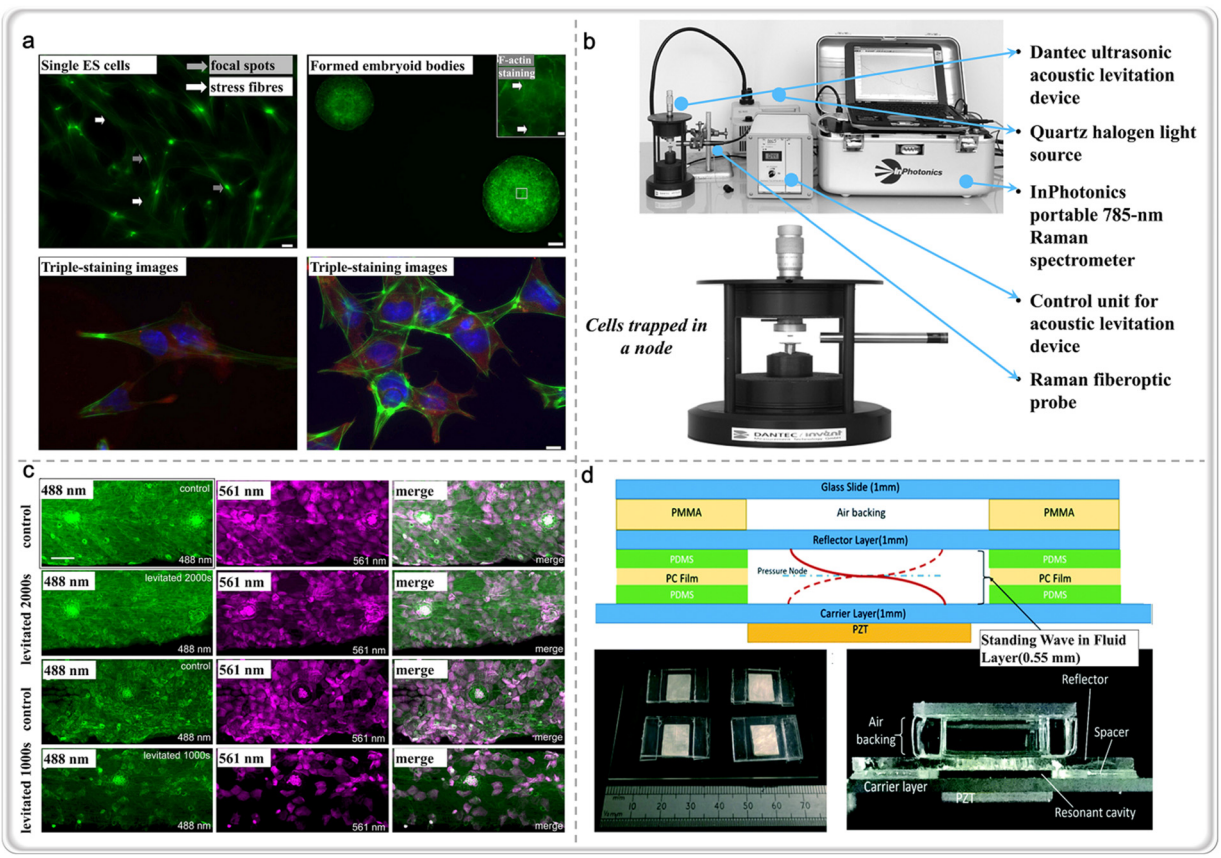


Fig. 19 Investigations of the effects of vibrational techniques on cellular activity. (a) Investigating the effects of ultrasonic levitation on gene expression and pluripotency of embryonic cells. Reprinted from ref. 153, copyright (2011), with permission from Elsevier. (b) Spectral analysis of living cells was performed utilizing acoustic levitation technology. Reprinted from ref. 154, copyright (2005), with permission from American Chemical Society. (c) The impact of acoustic levitation on zebrafish embryo development was studied. Reprinted from ref. 155, copyright (2015), with permission from Springer Nature. (d) The mechanism of acoustically induced stimulation on human cartilage development was examined. Reprinted from ref. 156, copyright (2018), with permission from Royal Society of Chemistry.

field to perform biochemical reactions on various materials and complex substrates.[91] This system has been successfully applied to liver organoid culture in mice and organoid testing of drugs such as verapamil and biliary atresin (Fig. 18d).

4.1.4 Cell activity research. Building on the advantages of acoustic levitation for cell manipulation, researchers have investigated its impact on cellular activity and viability. For example, Bazou *et al.* demonstrated that ultrasound levitation did not affect gene expression or the totipotency of mouse embryonic stem cells for up to one hour, indicating that the potential wells created by prolonged acoustic levitation do not alter cell behaviour (Fig. 19a).[152,153] Wood *et al.* employed acoustic suspension to analyze the spectra of living cells, obtaining the ratio of intracellular carotenoids to chlorophylls (Fig. 19b).[154] Sundvik *et al.* conducted acoustic suspension experiments on zebrafish embryos and found that the process did not significantly affect embryonic development, providing an important approach for manipulating vertebrate embryos (Fig. 19c).[155]

Furthermore, Jonnalagadda *et al.* developed a bioreactor platform to maintain human articular chondrocytes suspended for extended periods and examined the impact of acoustic stimulation on cartilage development by adjusting amplitude, frequency, and related parameters (Fig. 19d).[156]

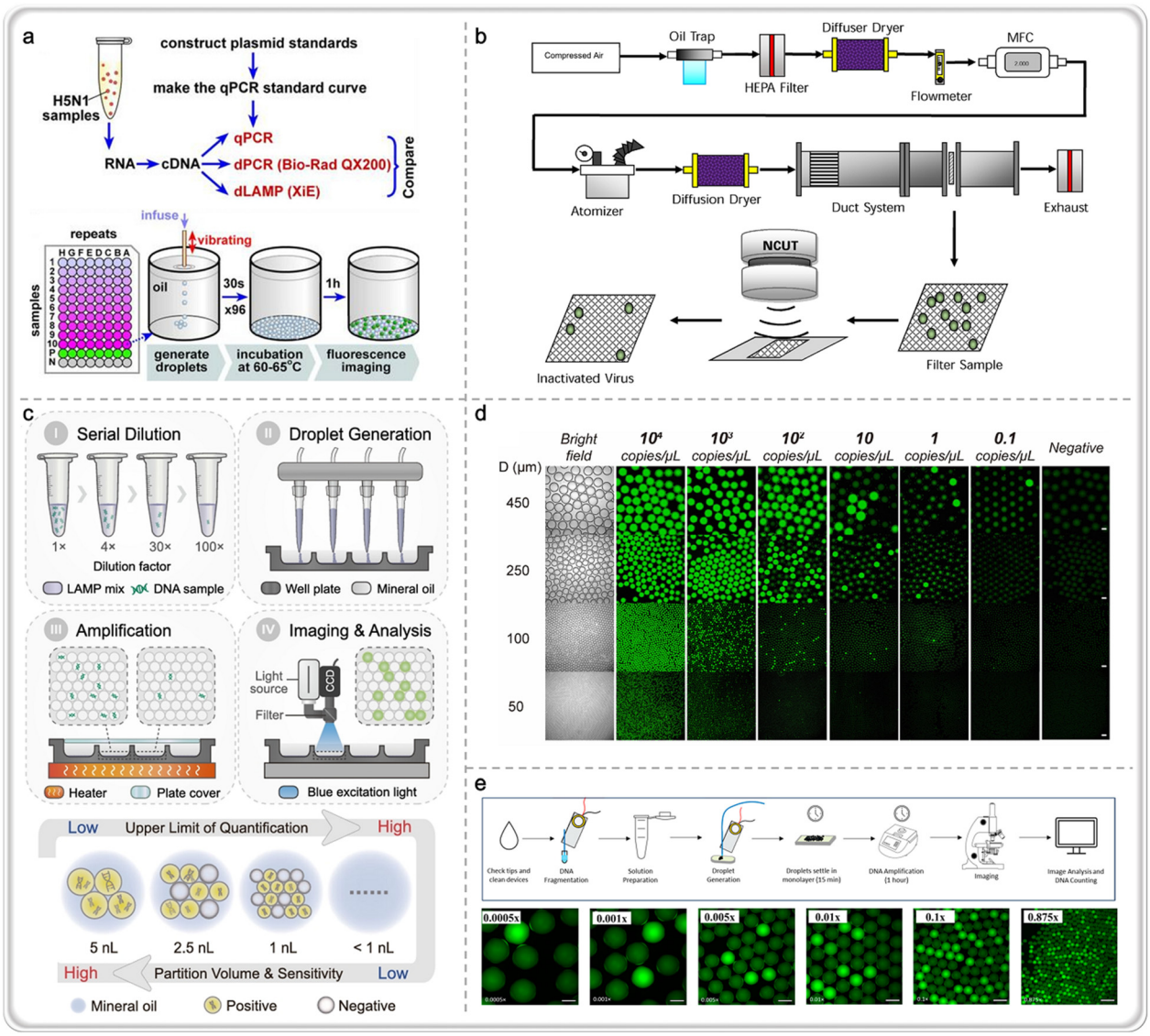


Fig. 20 Applications of vibration technology in molecular diagnostics. (a) Absolute quantification of H5 subtype avian influenza virus through the cross-interface emulsification technology. Reprinted from ref. 157, copyright (2017), with permission from American Chemical Society. (b) Capture of bacteriophage viruses on H14 HEPA filters *via* acoustic levitation. Reprinted from ref. 158, copyright (2018), with permission from Elsevier. (c) Detection of dLAMP and MV-dPCR assays on the OsciDrop device. Reprinted from ref. 105, copyright (2022), with permission from American Chemical Society. (d) Multi-volume digital PCR detection experiments utilizing acoustic vibration capillary technology. Reprinted from ref. 73, copyright (2021), with permission from Elsevier. (e) Integration of vibrating-tip capillary technology with ddLAMP for digital nucleic acid detection with a broad dynamic range (2–6000 copies per μL) under resource-limited conditions. Reprinted from ref. 76, copyright (2024), with permission from MDPI.

4.2 Diagnosis and treatment

4.2.1 Molecular diagnostics. Researchers have increasingly applied vibration-based manipulation techniques for sensitive biomarker detection and point-of-care medical diagnostics, facilitating the development of portable platforms for rapid diagnosis and personalised treatment. For example, Hu *et al.* achieved absolute quantification of H5 subtype avian influenza viruses using the cross-interface emulsification (XiE) technique, demonstrating high sensitivity and specificity (Fig. 20a).[157] Versoza *et al.* captured phage viruses on H14 HEPA (High Efficiency Particulate Air Filter) filters using acoustic levitation, offering a promising approach for downstream viral inactivation (Fig. 20b).[158] Similarly, Ye *et al.* proposed a multifunctional microdroplet generation device, OsciDrop, driven by a Weber number-controlled mechanism.[105] This device facilitates digital loop-mediated isothermal amplification (dLAMP) for the African swine fever virus (ASFV) and multi-volume digital PCR (MV-dPCR) for human genomic DNA, demonstrating its effectiveness for digital nucleic acid detection and molecular diagnostics (Fig. 20c).

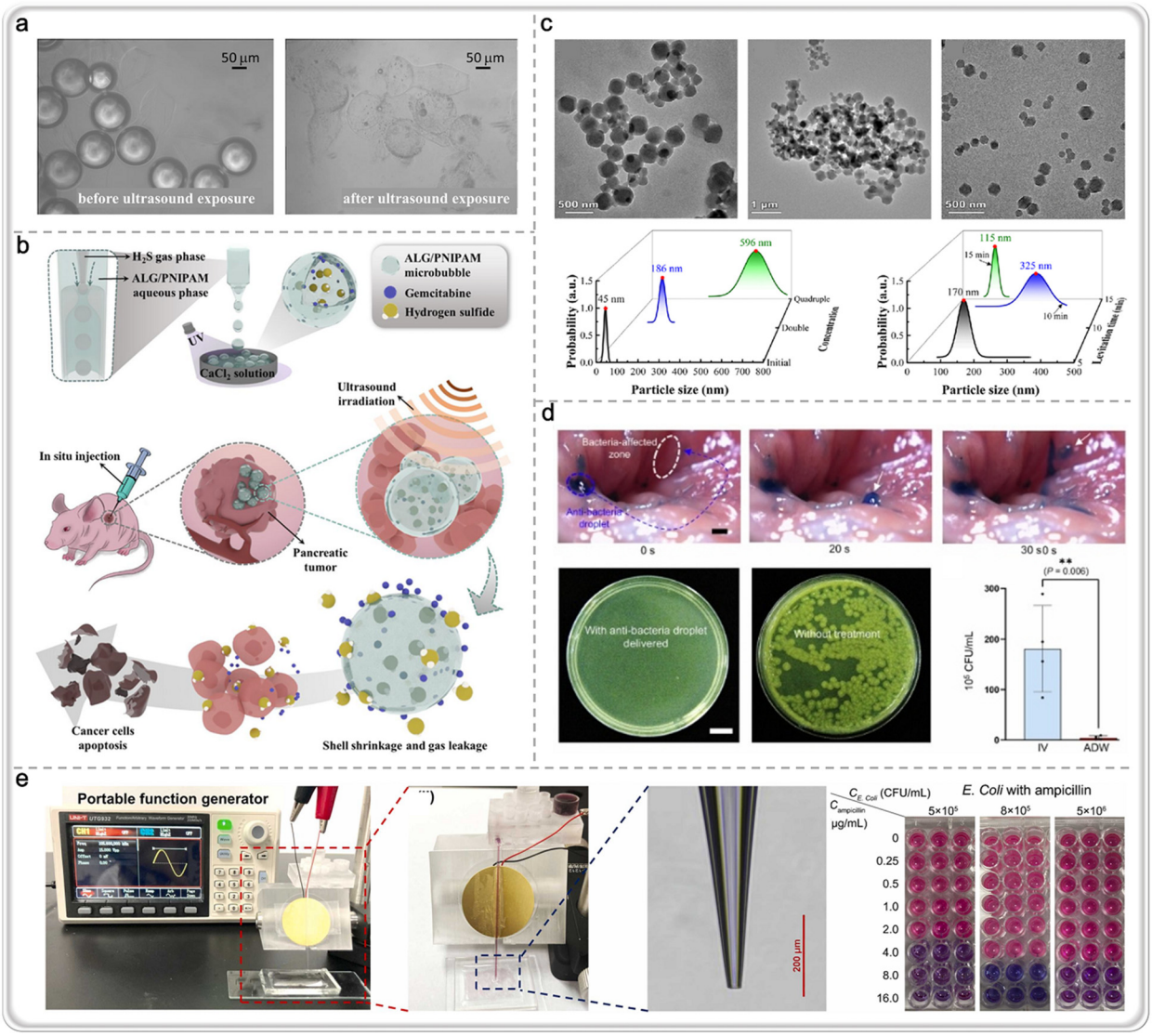


Fig. 21 Applications of vibration technology in pharmaceutical research. (a) The prepared perfluorocarbon-alginate core–oil-shell microcapsules were injected into a polyacrylamide gel for drug release facilitated by ultrasound application. Reprinted from ref. 159, copyright (2014), with permission from American Chemical Society. (b) Ultrasound-responsive hydrogels were fabricated through droplet microfluidics, where acoustic wave-induced gas oscillation led to thermal effects, causing hydrogel shell contraction and subsequent drug release. Reprinted from ref. 160, copyright (2021), with permission from John Wiley and Sons. (c) Monaxial standing-wave ultrasonic levitation was employed to synthesize size-controlled ZIF-8 materials. Reprinted from ref. 57, copyright (2023), with permission from Royal Society of Chemistry. (d) An ultrasonic array system was designed utilizing acoustically induced dewetting for targeted drug delivery. Reprinted from ref. 88, copyright (2025), with permission from Springer Nature. (e) A vibration-capillary-based droplet generation platform was innovated for rapid and precise antimicrobial susceptibility testing. Reprinted from ref. 74, copyright (2023), with permission from Elsevier.

Additionally, He *et al.* used high-frequency acoustic vibration at a capillary tip to generate droplets for absolute nucleic acid quantification *via* MV-dPCR, achieving a dynamic range spanning six orders of magnitude and enabling multiplex detection (Fig. 20d).[73] Fike *et al.* combined vibrating tip capillary technology with ddLAMP, enabling digital nucleic acid detection with a dynamic range of 2–6000 copies per microlitre under resource-limited conditions (Fig. 20e).[76] Collectively, these advancements underscore the potential of vibration-based microfluidic platforms to support rapid, sensitive, and decentralised diagnostic applications.

4.2.2 Research in drug treatment. In drug research, droplet microfluidics is frequently used to regulate the delivery and release of drugs. This technique frequently relies on external stimuli to manipulate particles with stimuli-responsive characteristics. It is important to note that vibration-based manipulation techniques enable precise control over the size and release rate of droplet-based drug carriers, thereby improving the efficiency of delivery and targeted precision.

For instance, Duarte *et al.* injected perfluorocarbon–alginate core–oil-shell microcapsules into polyacrylamide gel (mimicking the tissue matrix environment) and successfully triggered drug release *via* ultrasonication (Fig. 21a).[159] Huang *et al.* utilized droplet microfluidics to create ultrasonically responsive hydrogels.[160] The gel shell contracted and released the encapsulated drug as a result of acoustic-induced gas oscillations, which had promising implications for tumor therapy (Fig. 21b).

Furthermore, Zheng *et al.* synthesised size-tunable ZIF-8 materials (which can be used for the encapsulation and controlled release of drugs) using a uniaxial standing wave ultrasonic levitation technique, and carried out *in situ* droplet evaporation kinetic measurements (Fig. 21c).[57] Liu *et al.* developed an ultrasonic array system based on acoustic de-wetting, whereby they modulated the focused acoustic field and pressure distribution within droplets by adjusting the amplitude and phase of piezoelectric units.[88] This was the first time that precise, residue-free, non-invasive droplet manipulation was achieved on living tissue surfaces, with

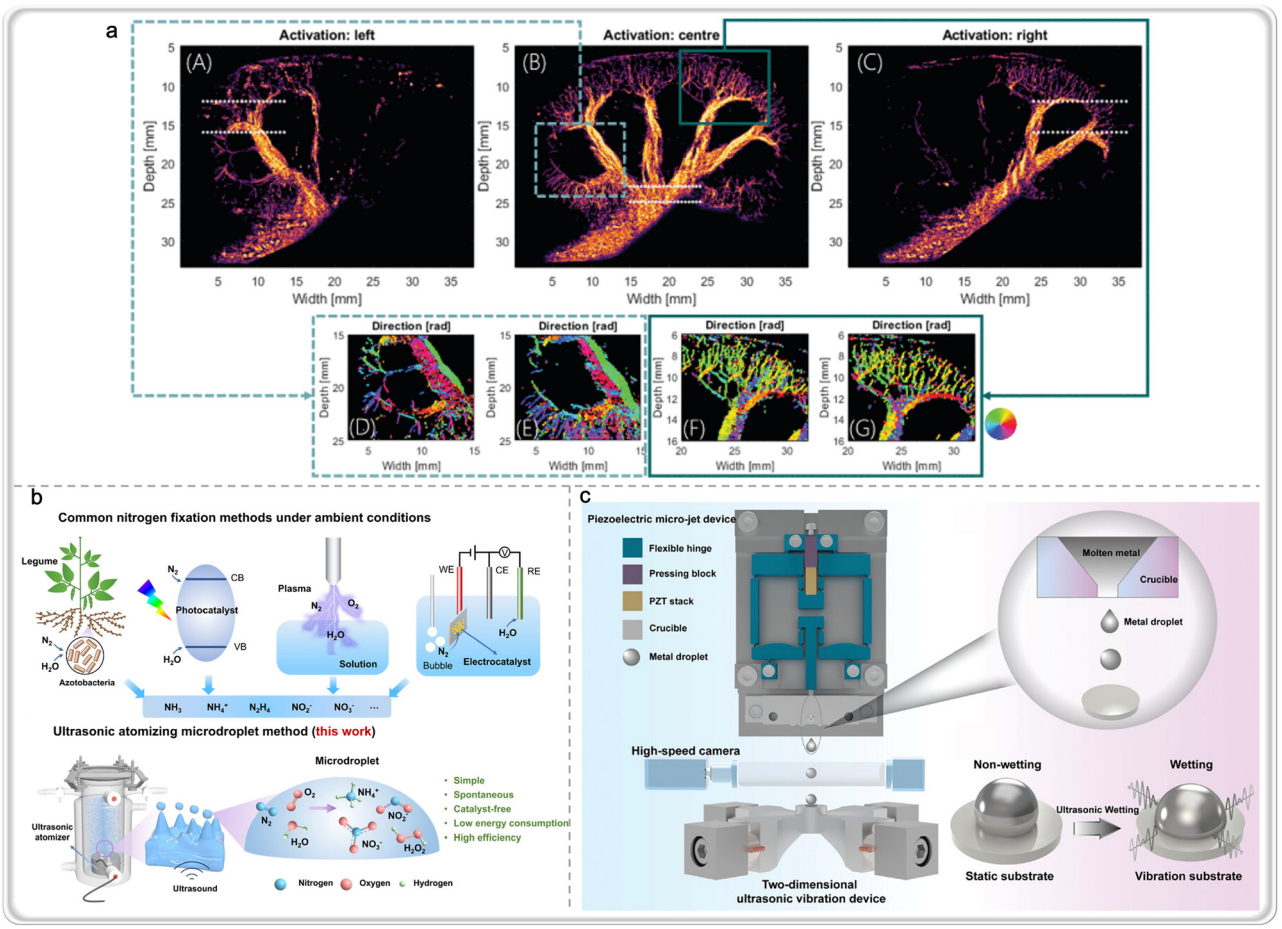


Fig. 22 Other typical applications of vibration technology. (a) Application in ultrasound imaging: the deliberate activation and deactivation of C3F8: C4F10 mixture nanodroplets with AWSALM can highlight different regions of the renal vasculature. (A–C) demonstrate the selective activation of different regions of the microvasculature in the same plane. (D and E) and (F and G) show flow direction in a region of interest for activation regions on the left (D), in the middle (E and F) and on the right (G), respectively. Reprinted from ref. 161, copyright (2023), with permission from IEEE. (b) Application in artificial nitrogen fixation. Reprinted from ref. 162, copyright (2025), with permission from American Chemical Society. (c) Application in medical additive manufacturing. Reprinted from ref. 163, copyright (2025), with permission from John Wiley and Sons.

successful applications in *in vivo* diagnosis and targeted drug delivery (Fig. 21d).

Vibration-controlled droplet microfluidics has been employed for antibiotic susceptibility testing (AST). The global threat posed by multidrug-resistant pathogens underscores the urgent need for rapid and accurate AST. Addressing this, Ding *et al.* developed a vibrating capillary-based droplet generation platform that integrates droplet incubation and automated bacterial counting.[74] This approach is simple, cost-effective, and demonstrates high measurement accuracy with a short response time, showing promise for rapid antimicrobial susceptibility assessment under resource-limited conditions (Fig. 21e).

4.3 Other applications

In addition to the typical applications discussed above, microdroplet vibrational manipulation techniques have also been explored for droplet imaging, biochemical reactions, and medical additive manufacturing. For example, Riemer *et al.* demonstrated for the first time the use of acoustic wave sparsely-activated localization microscopy (AWSALM) and fast AWSALM for *in vivo* super-resolution ultrasound imaging, verifying the feasibility of using ultrasound and acoustically activated nano-droplet contrast agents for rapid and selective imaging of microvascular at sub-wavelength resolution (Fig. 22a).[161] Wang *et al.* employed ultrasonic nebulisation at ambient temperature and pressure to drive a nitrogen fixation reaction under non-catalytic conditions, offering a green alternative for artificial nitrogen fixation (Fig. 22b).[162] Zhao *et al.* utilised a two-dimensional orthogonal ultrasound field to construct a deposition substrate with a radial vibration amplitude gradient, which promoted the wetting and adhesion of metal droplets—generated by a piezoelectric microjet device—on non-wettable surfaces, providing a novel solution for medical metal additive manufacturing (Fig. 22c).[163]

The translation of vibration-based microfluidic technologies from research laboratories to widespread clinical adoption faces several formidable, interconnected barriers. Technical integration complexity poses a primary challenge, encompassing the precision manufacturing of transducers and the synchronization of multi-channel power amplification and control electronics. These requirements elevate system costs and present hurdles for achieving the robustness demanded in clinical settings. Furthermore, novel medical devices, particularly those employing new physical principles, often necessitate navigating complex classifications such as the FDA's De Novo process, which involves comprehensive clinical validation and adherence to Good Manufacturing Practice (GMP) standards, thereby prolonging development timelines and increasing investment. Despite these challenges, we have witnessed significant commercial progress and technological maturation. In the realm of cell research and precision diagnostics, Oblio Biotech Ltd. initiated mass production in 2025 of its Soundpen CB Single-Cell Sorter, a system leveraging an acoustic tweezer chip combined with AI algorithms for non-contact, label-free cell isolation. Concurrently, researchers utilized advanced acoustic droplet ejection (ADE) printing technology to facilitate rapid and stable droplet dispensing. Test results indicate that the generated droplets have a low volume coefficient of variation (CV $<$ 4%), with additional potential for improvement in automation and cost efficiency.[164] The OsciDrop PCR instrument (Fig. 23) was developed using interfacial vibrational droplet array technology, which integrates all aspects of PCR fluorescence analysis to provide a 'sample in, result out' workflow that is fully automated, highly integrated, and capable of high-throughput digital assays with up to 96 samples per run.[165] Similarly, the Snafu DQ24 Digital PCR Instrument employs injection vibration technology to generate

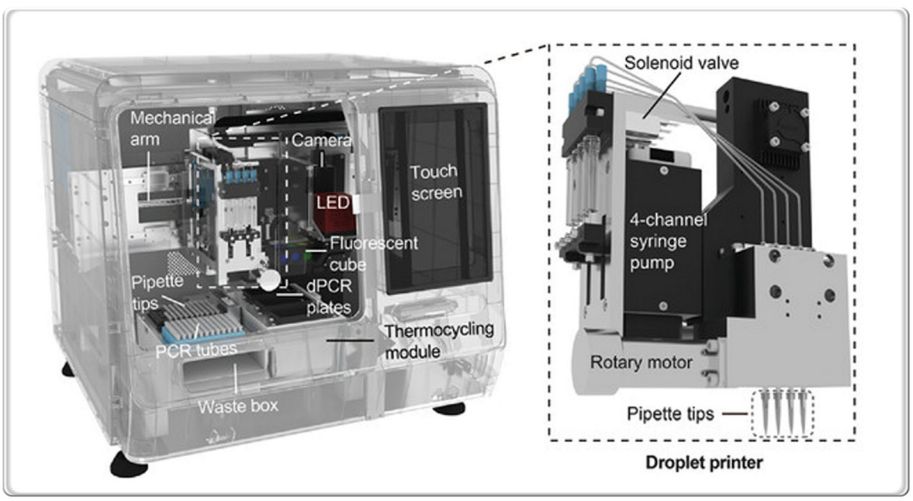


Fig. 23 Commercial application: PCR device. Reprinted from ref. 165, copyright (2024), with permission from John Wiley and Sons.

Table 1 Comparative analysis of key vibration-based technologies for biomedical applications

Application	Technology	Cases & performance	Advantages & limitations	Reference
Cellular manipulation	Acoustic levitation	• Case: 3D rotational control (single bovine oocyte) • Accuracy: 1° • Rotation velocity: 3 rad s^{-1}	• Advantages: achieved cell rotation manipulation, good scalability • Limitations: suitable for individual cells	128
	Combining flow focusing with ultrasonic vibration	• Case: droplet encapsulation • Capture: 25 000 to 50 000 single cells per minute • Droplet volumes: 0.02–0.54 nL • Throughput: up to 140 million droplets per hour	• Advantages: high throughput, systems could be operated in parallel, simple assembly and operation • Limitations: easily affected by device assembly (*e.g.*, nozzle geometry), low scalability	129
	SAW	• Case: sample preparation or purification (enrichment) • It is possible to drive a submicron particle and cell concentration down to 200 nm diameters	• Advantages: only a single IDT set is required to drive, a small footprint, and demonstrate a degree of scalability • Limitations: high cost (eliminating evaporation in the closed setup)	133
Cell sorting	TSAW	• Case: sort cells • Sort purities: in excess of 90% for event rates up to 2000 events per second	• Advantages: sorting speed is comparable to conventional jet-in-air FACS machines, with high purity and viability, high accuracy and screening rate • Limitations: system (*e.g.*, operations) complexity	26
	Acoustofluidics	• Case: isolation of cellular products (exosomes) • Purity: 98.4% (isolate exosomes from an extracellular vesicle mixture)	• Advantages: perform rapid, biocompatible, label-free, contact-free • Limitations: high cost (requires complex microfluidic channels)	149
Cell cultivation	Acoustic droplet vitrification (ADV)	• Case: preservation of rare cells • Viability: >85% for days, >70% for months	• Advantages: high-efficiency handling and preservation of rare cells • Limitations: system (*e.g.*, operations) complexity	81
	Sound-controlled fluidic processor (SFP)	• Case: organoid culturing (mouse primary cholangiocytes) • Viability: higher than 95%	• Advantages: antifouling, lossless, and precise operation capabilities, long-term biocompatibility • Limitations: system (*e.g.*, operations) complexity	91
Molecular diagnostics	Cross-interface emulsification (XiE) technique	• Case: absolute quantification of H5-subtype influenza viruses • Detection limits: less than 10 copies per μL	• Advantages: good scalability, effectively simplifies operation, minimizes droplet loss and coalescence, and speeds up the readout process • Limitations: system (*e.g.*, operations) complexity	109
	Vibrating sharp-tip capillary	• Case: digital nucleic acid tests in a POC setting • Detection range: ~2 to 6000 copies per μL	• Advantages: high dynamic range, simple, and portable • Limitations: it is necessary to reduce the impact of external environmental vibration factors	76
Drug treatment	Ultrasound-responsive delivery microbubbles (UDMs)	• Case: drug release • Initial release percentage: 6.80 ± 0.11% • Overall cumulative release percentage: 63.56 ± 0.39% (after 10 irradiation cycles)	• Advantages: high release percentage • Limitations: system (*e.g.*, operations) complexity	160
	Acoustic dewetting	• Case: drug delivery	• Advantages: precise, residue-free, non-invasive droplet manipulation was achieved on living tissue surfaces • Limitations: system (*e.g.*, operations) complexity	88
	Vibrating capillary	• Case: antibiotic susceptibility testing (AST) • Testing time: ~5 hours	• Advantages: simple, cost-effective, and demonstrates high measurement accuracy with a short response time • Limitations: it is necessary to reduce the impact of external environmental vibration factors	74

droplets by applying reciprocating vibrations to a precision syringe that penetrates the oil surface. This process ensures that the uniformly flowing reaction mixture is split into homogeneous microdroplets by shear forces, enabling automated, integrated, and high-throughput digital detection.

In summary, while the commercialization of vibration technology in biomedicine faces certain challenges, recent advancements underscore its tangible progress and potential to address unmet clinical needs. The path toward broader adoption hinges on concerted interdisciplinary efforts aimed at simplifying core components through advanced materials and integrated electronics, fostering modular and standardized system architectures to enhance reliability and reduce costs, and proactively engaging with regulatory bodies to streamline clinical validation. Continued innovation along these trajectories is essential for these sophisticated physical technologies to transition into viable, competitive, and ultimately mainstream clinical solutions.

Based on the above description of the application scenarios for vibration technology, we know that while both acoustic wave and mechanical vibration methods utilize vibrational energy for microfluidic manipulation, they present distinct trade-offs that make them suitable for different application scenarios. As listed in Table 1, we systematically compare multiple critical operational parameters of key vibration technologies. Acoustic technologies excel in applications demanding high precision and minimal biological perturbation. They achieve remarkable performance in single-cell manipulation, with acoustic levitation enabling precise rotational control of individual cells while maintaining viability exceeding 95%, and traveling surface acoustic wave systems accomplishing high-purity cell sorting (>90%) at rates of 2000 events per second. Furthermore, acoustofluidic platforms demonstrate exceptional capability in nanoscale particle isolation, achieving 98.4% purity in exosome separation from complex biological mixtures.

In contrast, mechanical vibration technologies offer distinct advantages in operational simplicity and practical implementation. These systems prove particularly valuable in point-of-care diagnostics and resource-limited settings, with cross-interface emulsification achieving detection sensitivity below 10 copies per μL for viral pathogens and vibrating capillary platforms reducing antibiotic susceptibility testing time to approximately 5 hours. The technological divergence between these approaches represents a trade-off between precision and practicality: acoustic systems provide superior manipulation capabilities for delicate biological procedures, while mechanical vibration platforms deliver robust, cost-effective solutions for clinical diagnostics and high-throughput processing.

The comparative analysis reveals that acoustic vibration technologies generally involve more complex instrumentation and higher implementation costs but offer unparalleled precision in single-cell analysis, nanoparticle separation, and sophisticated tissue engineering applications. Mechanical vibration methodologies, while potentially limited in ultimate precision and susceptible to environmental interference, provide accessible, scalable solutions for biomedical applications requiring operational efficiency and practical deployment. Researchers and relevant enterprises may select different technical solutions based on their actual needs.

5 Conclusions and outlook

As a micro- and nanoscale fluid manipulation strategy with broad application prospects, vibration-based methods offer non-contact operation, high precision, and excellent biocompatibility. These advantages help minimise contamination and structural damage to biological samples, thereby significantly improving experimental reliability. Current research has expanded the use of vibration technologies to diverse microfluidic operations, such as pumping, mixing, and particle manipulation.

Vibration manipulation strategies can be broadly categorised into acoustic manipulation and other mechanical vibration techniques. Acoustic manipulation method typically necessitates external excitation sources and precise tuning of parameters such as amplitude and frequency, while other mechanical vibration techniques are more suitable for laboratory or specialized settings due to the more complex system design and larger equipment footprints. These practical limitations underscore the necessity for further technological optimization to broaden the scope of real-world applications.

The pathway towards the commercialization of advanced vibration technologies is obstructed by three principal, and deeply interconnected, challenges: inherent equipment complexity, formidable scale-up barriers, and critical integration bottlenecks. The equipment complexity predominantly arises from the precision manufacturing of transducers and actuators, the requirement for high-power, multi-channel driving electronics with precise phase and amplitude control, and the computational overhead for real-time field modulation. This intrinsic complexity is severely compounded by system integration challenges, which pertain to the absence of standardized, robust interfaces for seamlessly coupling the vibrational core with peripheral modules—including fluidic handling, optical sensing, and digital control systems—thereby obstructing the development of reliable platforms. These limitations collectively undermine practical scale-up, where the principal obstacles manifest as an inability to meet industrial benchmarks for throughput, robustness, and cost-efficiency. To bridge this translation gap, future research must prioritize the co-design of simplified and robust transducers, the development of integrated and modular electronic drivers, the establishment of plug-and-play system architectures, and the implementation of model-based control strategies. Only through such a holistic and interdisciplinary approach can these sophisticated vibration-based systems evolve into industrially viable and competitive solutions. Moreover, practical applications often demand multiple complex target functions, necessitating the integration of vibration-based manipulation with other microfluidic technologies to develop more comprehensive and versatile microfluidic systems.

Addressing these challenges will require continuous technological innovation and close interdisciplinary collaboration to fully realise the potential of vibration-assisted droplet microfluidics in the biomedical field. Future developments may focus on the following aspects: (1) intelligent control: current active droplet manipulation largely relies on external equipment and skilled operators. Integrating artificial intelligence, such as using machine learning algorithms to identify droplet motion states and correlate them with vibration parameters, will enable autonomous, adaptive control strategies. (2) Miniaturisation and portability: to support rapid point-of-care diagnostics and personalized treatments, the miniaturisation and lightweight design of existing devices should be further enhanced. (3) Novel materials and fabrication: continued exploration of new piezoelectric materials and vibration–generation mechanisms will support the development of highly biocompatible devices with improved manipulation performance. (4) Advanced control strategies for digital detection: integrating microdroplet vibration control with cutting-edge nucleic acid amplification techniques (such as CRISPR-based or isothermal amplification assays) will have far-reaching implications for digital nucleic acid detection and promote the widespread adoption of digital diagnostics. Together, these advances will help realise the full potential of vibration-based droplet microfluidics in supporting next-generation biomedical research and precision medicine.

Author contributions

Conceptualization: Peng Yin, Fuqiang Ma; data curation: Xuan Fang, Mengjie Huang; formal analysis: Yanna Lin, Baihui Zhang; funding acquisition: Fuqiang Ma; investigation: Maojie Jiang, Xiangyu Jiang; methodology: Peng Yin; project administration: Fuqiang Ma; resources: Yanna Lin, Maojie Jiang; supervision: Fuqiang Ma; visualization: Peng Yin, Baihui Zhang; writing – original draft: Peng Yin; writing – review & editing: Peng Yin, Fuqiang Ma.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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