

Two Forces Are Better than One: Combining Chemical and Acoustic Propulsion for Enhanced Micromotor Functionality

Published as part of the *Accounts of Chemical Research* special issue “*Fundamental Aspects of Self-Powered Nano- and Micromotors*”.

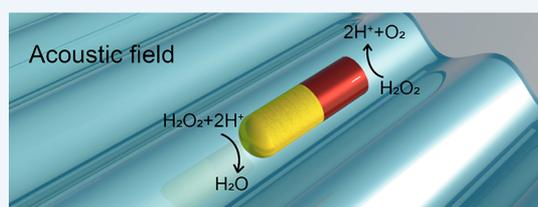
Liqiang Ren,[†] Wei Wang,^{*,‡} and Thomas E. Mallouk^{*,†} 

[†]Department of Chemistry, Biochemistry and Molecular Biology, Physics, and Engineering Science and Mechanics, The Pennsylvania State University, University Park, Pennsylvania 16802, United States

[‡]School of Materials Science and Engineering, Harbin Institute of Technology (Shenzhen), Shenzhen, Guangdong 518055, China

CONSPECTUS: Engines and motors are everywhere in the modern world, but it is a challenge to make them work if they are very small. On the micron length scale, inertial forces are weak and conventional motor designs involving, e.g., pistons, jets, or flywheels cease to function. Biological motors work by a different principle, using catalysis to convert chemical to mechanical energy on the nanometer length scale. To do this, they must apply force continuously against their viscous surroundings, and because of their small size, their movement is “jittery” because of the random shoves and turns they experience from molecules in their surroundings.

The first synthetic catalytic motors, discovered about 15 years ago, were bimetallic Pt–Au microrods that swim in fluids through self-electrophoresis, a mechanism that is apparently not used by biological catalytic nanomotors. Despite the difference in propulsion mechanisms, catalytic microswimmers are subject to the same external forces as natural swimmers such as bacteria. Therefore, they follow similar scaling laws, are subject to Brownian forces, and exhibit a rich array of biomimetic emergent behavior (e.g., chemotaxis, rheotaxis, schooling, and predator–prey behavior). It was later discovered, quite by accident, that the same metallic microrods undergo rapid autonomous movement in acoustic fields, converting excitation energy in the frequency (MHz) and power range (up to several W/cm²) that is commonly used for ultrasonic imaging into axial movement. Because the acoustic propulsion mechanism is fuel-free, it can operate in media that have been inaccessible to chemically powered motors, such as the interior of living cells. The power levels used are intermediate between those of ultrasonic diagnostic imaging and therapy, so the translation of basic research on microswimmers into biomedical applications, including *in vivo* diagnostics and drug delivery, is possible. Acoustic and chemical propulsion are applied independently to microswimmers, so by modulating the acoustic power one can achieve microswimmer functionalities that are not accessible with the individual propulsion mechanisms. These include motion of particles forward and backward with switching between chemical and acoustic propulsion, the assembly/disassembly equilibrium of particle swarms and colloidal molecules, and controllable upstream or downstream propulsion in a flowing fluid. This Account relates our current understanding of the chemical and acoustic propulsion mechanisms, and describes how their combination can be particularly powerful for imparting enhanced functionality to micromotors.



1. INTRODUCTION

Synthetic micromotors (or microswimmers) convert energy from their surroundings into motion in fluids. They can translate, spin, or rotate, and they combat the low Reynolds number constraints on their swimming strategies as do living microorganisms. The rapid development of micromotors over the past two decades not only provides deeper insight into the microscopic and biological world, but also extends into far-reaching research fields such as nonequilibrium physics and artificial intelligence. Furthermore, the prospect of using micromotors to perform complex tasks such as drug delivery, diagnosis and environmental remediation has received significant and mounting interest.^{1–4}

The autonomous swimming of bimetallic microrods was first observed in solutions of H₂O₂,^{5,6} and later studies demon-

strated fuel-free propulsion of Janus particles by electric and magnetic fields, light, and ultrasound.^{7–12} These research efforts have greatly expanded the capabilities of Janus particle swimmers, enabling them to work in complex environments and to carry out tasks that would be difficult or impossible with chemical power alone.

This Account focuses on the behavior of metallic micromotors powered by chemical fuels, ultrasound, and especially by their synergistic combination. When powered by the catalytic reactions of chemical fuels, particles can communicate with each other or respond to external stimuli. Interesting collective behaviors emerge, such as self-assembly, oscillation,

Received: May 31, 2018

Published: August 6, 2018

and chemotaxis.^{13,14} As a primitive form of intelligence, sensing and response to the environment have both fundamental implications and practical applications as active matter. On the other hand, acoustic propulsion is safer for biological samples, tolerant of high ionic strength and viscous fluids, and is able to drive microswimmers at much faster speeds, making it attractive for developing biomedical microrobotics. Many proof-of-concept applications such as biodegradation of blood and intracellular sensing have already been demonstrated, although serious scientific and technological issues remain. Importantly, chemical fuels and ultrasound operate in largely compatible ways with the same bimetallic particles. Combining the two propulsion mechanisms thus provides new dimensions for researchers to develop microswimmers with novel functions, and to understand their motion and assembly at the microscale.

2. BIMETALLIC MICROSWIMMERS POWERED BY CHEMICAL FUELS

Bimetallic, rodlike Janus particles are typically fabricated by template-assisted electrodeposition (Figure 1), producing in

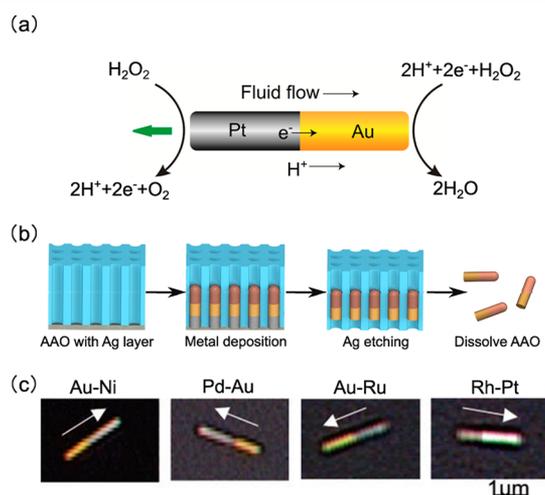


Figure 1. (a) Schematic of the self-electrophoretic propulsion of a Au–Pt bimetallic rod.¹ (b) Fabrication of metallic microrods by template-assisted electrodeposition.⁹ (c) Examples of bimetallic rods of different combinations.¹⁵ The direction of self-electrophoretic movement in H_2O_2 is indicated by the arrow. Reproduced with permission from refs 1 and 15, Copyright 2012 and 2006 American Chemical Society; ref 9, Copyright 2013 Elsevier.

each batch $\sim 10^8$ nearly identical particles that are a few micrometers long and hundreds of nanometers in diameter. While these particles were originally designed to function as bubble rockets by decomposition of H_2O_2 to water and oxygen, on the micrometer length scale, the dominant propulsion mechanism is self-electrophoresis.¹⁵ For Pt–Au rods, the oxidation and reduction of H_2O_2 occur preferentially at the Pt end (anode) and the Au end (cathode), respectively, resulting in a gradient of proton concentration along the length of the rod. The proton gradient creates a local electric field that drives the negatively charged particle toward its anode (Pt). Geometric modifications such as core–shell structures¹⁶ can increase the swimmer speed by restricting proton diffusion. In addition, incorporation of a Ni segment enables magnetic steering that has proven important for both fundamental studies and applications.¹⁷

These self-propelled microswimmers can communicate with each other, self-assemble or interact with a charged boundary. In H_2O_2 solution, Pt–Au rods attract each other and form staggered doublets and triplets,¹⁴ and similar assembly has been found for trisegmented metallic microrods (Figure 2a).^{18,19} The active particles can also collect charged tracer

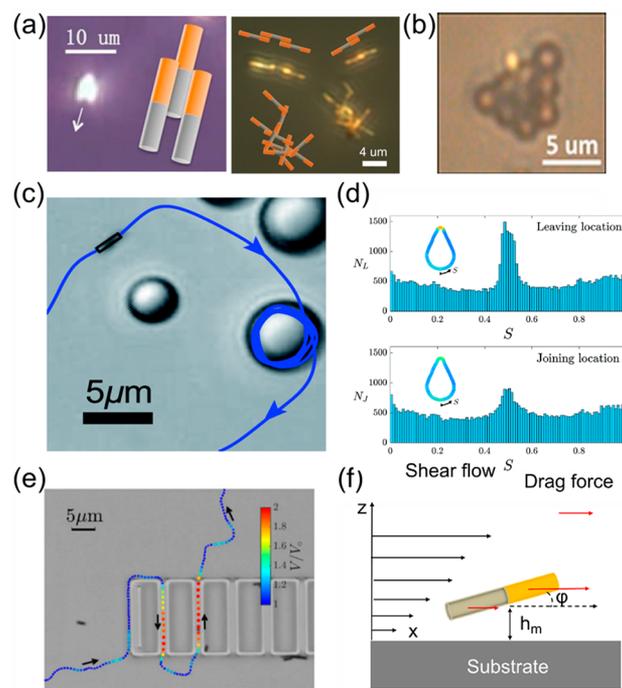


Figure 2. (a) Self-assembly of bimetallic and trisegmented metallic microrods.^{14,18} (b) 2D trapping of passive particles at one end of a bimetallic rod.¹⁴ (c) Microrods are trapped by a large passive particle and orbit around it.²⁰ (d) Teardrop-shaped posts capture microswimmers and guide them to depart at the tip.²¹ (e) Microswimmers move faster in confining channels than in open environments.²⁶ (f) Microrod (Au–Rh) tilting as a result of electrokinetic interaction between the rod and the substrate. The tilted microswimmers sense shear flow and exhibit rheotaxis.²⁷ Reproduced with permission from ref 14, Copyright 2013 National Academy of Sciences; refs 18, 20, and 21, Copyright 2016, 2014, and 2017 Royal Society of Chemistry; ref 26, Copyright 2016 American Physical Society; ref 27, Copyright 2017 American Chemical Society.

particles by electric dipolar effects to form highly ordered 2D structures (Figure 2b). If the tracer is larger than the swimmer, the latter can be temporarily trapped by the larger particle through a swimmer–boundary interaction (Figure 2c,d).^{20,21} Related experiments have shown that the orientation, speed, and trajectories of swimmers can all be significantly affected by the presence of boundaries and their charges, shapes, sizes and 3D structures.^{22–25} For example, Au–Rh particles moved 5 times faster in a narrow channel ($W = 1.2 \mu\text{m}$ and $H = 2 \mu\text{m}$) than outside the channel (Figure 2e).²⁶ The strong confinement alters the electric field distribution around the swimmer and induces an electroosmotic flow at the channel wall, both of which increase the speed. The electrokinetics near a charged surface also affect the orientation of a moving rod, and when coupled with an external flow can lead to surprising results. For example, Ren et al. reported that the swimmer–boundary interaction enables bimetallic rods to sense shear flow and move up- or downstream (rheotaxis). This is because the electro-osmotic flow on the negatively charged channel floor

exerts forces that tilt the two ends of a bimetallic rod in opposite directions (Figure 2f). The tilted particle experiences a shear force that aligns it with the flow direction.²⁷

3. ACOUSTIC PROPULSION OF MICROPARTICLES

3.1. Metallic Microparticles in a Standing Acoustic Field

Switching from chemical power to a field-driven, external power source often sacrifices the autonomous character of microparticle propulsion. For example, when a ferromagnetic segment or layer is incorporated into the particle, it can be propelled by a rotating magnetic field, but all swimmers move in the same lock-step fashion. In contrast, bimetallic microrods exhibit high-speed autonomous motion when driven by MHz frequency ultrasound.²⁸ This effect was discovered accidentally in experiments designed to levitate metallic particles so that their catalytically driven movement could be studied far from the solid floor of the sample cell. Bimetallic (Au–Ru) or monometallic (Au) microrods not only levitated to the center of the acoustic chamber, but also put on a wild show that included random axial motion at speeds of 200 $\mu\text{m/s}$ (~ 70 body lengths/s), local orbital motion, in-plane axial spinning, and dynamic assembly into polar spinning chains (Figure 3a).

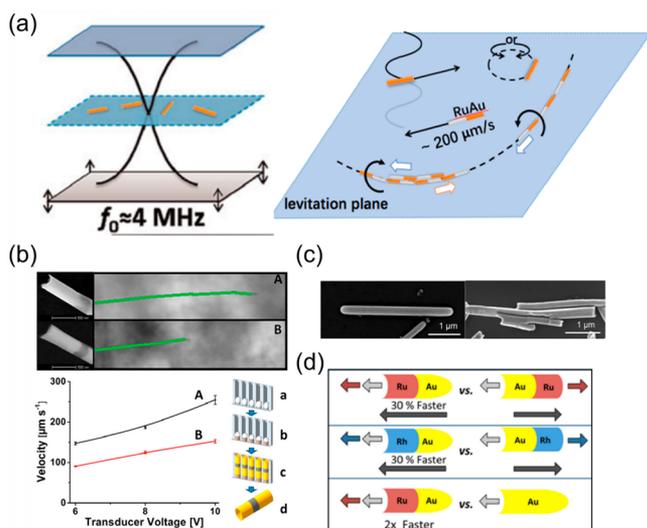


Figure 3. Acoustic propulsion of metallic microrods in a cylindrical cell. (a) Particles are levitated to the levitation plane and exhibit various motions, including axial propulsion, orbital motion, axial spinning, and assembly into chains.²⁸ (b) Metallic microrods fabricated in a nanoparticles-modified template have a higher degree of asymmetry (more concave) and show faster speed in acoustic fields.³⁰ (c) Ag rods with no axial asymmetry are not propelled by ultrasound, whereas Au rods of a similar size with a concave end show orbital motion.³¹ (d) Both density and shape asymmetry have an impact on the directionality of microswimmers, but the density is the dominant effect.³² Reproduced with permission from refs 28 and 30–32. Copyright 2012, 2013, 2017, and 2016 American Chemical Society.

Very soon our hard drives were filled with fascinating videos, but understanding these observations took much longer. Recent experimental and theoretical efforts provide a preliminary but unified picture of how ultrasound induces these kinds of motion with metallic microrods.

The manipulation of microparticles by acoustic waves in liquids has been well studied, and pressure nodes of various

shapes, such as planes, lines, rings, and spheres, can be created by manipulating the acoustic wavelength, phase, or propagation direction. Micro- and nanoparticles, cells or even microorganisms are trapped by these nodes to form static or dynamic patterns.²⁹ Vertically propagating acoustic waves in a cylindrical cell (Figure 3a) set up a standing wave at the resonant frequency, creating a pressure node at the midpoint of the cell. Particles are therefore trapped in the levitation plane by the primary acoustic radiation force.

However, what happened with metallic rods in this levitation plane was quite unexpected. It was obvious that their autonomous, axial motion in random directions was not driven by the acoustic radiation force or fluidic convection (e.g., bulk acoustic streaming), since in both cases the rods would move collectively in one direction. The direction and the speed of axial motion were found to be critically affected by swimmer shape.²⁸ In particular, microrods fabricated by electroplating consistently had one concave and one convex end. They preferentially moved toward their concave ends, and the greater the asymmetry (i.e., more concave) the faster the motion, as evidenced by an increase in speed up to 67% for rods fabricated against nanospheres inside the template pores (Figure 3b).³⁰ Zhou et al. discovered that silver microrods free of concavity and convexity (Figure 3c), but of similar sizes and shapes, did not self-propel, whereas nearby asymmetric gold rods moved rapidly, lending strong support to the shape asymmetry argument.³¹ A second critical factor affecting directional motion is the density; for bimetallic or multimetallic rods, the less dense segment always leads the axial motion regardless of the shape asymmetry (Figure 3d).³² For example, Au–Ru bimetallic rods move toward their lighter Ru end and are 30% faster if the Ru end is also the concave end. In contrast, polymer rods of similar shapes and sizes are levitated but not propelled by ultrasound, suggesting that a critical density (or acoustic contrast) is needed for acoustic propulsion.

Initially a mechanism based on asymmetric scattering of ultrasound on the rod surface was proposed, referred to as “self-acoustophoresis” (Figure 4a). However, this mechanism is implausible considering that the wavelength of sound was roughly 100 times larger than the particle. Nadal and Lauga developed a theory that models the metallic rod as an axisymmetric near-sphere in a standing acoustic wave. In this model, the particle acts as a rigid body moving in a uniformly oscillating velocity field (Figure 4b).³³ The oscillation induces a so-called steady streaming on the particle surface. By integrating the streaming stress over the surface, a propulsion force is generated due to the asymmetric shape. This model explained semiquantitatively the faster motion of more concave rods and the requirement for a large density contrast between the rods and the fluid; the latter effect explains why metallic rods undergo fast axial propulsion but polymer rods do not. While this early model did not consider bimetallic rods, Collis et al. later proposed a more general framework that applies to solid particles of arbitrary shape and density distribution (Figure 4c).³⁴ Interestingly, their study predicted that bimetallic rods would move with the concave end and lighter end leading at low acoustic Reynolds number ($Re \ll 1$), but in the opposite direction at high Re . Au–Ru rods have been found to move exclusively toward their Ru ends in our experiments, suggesting that the theory of acoustic propulsion is promising yet possibly incomplete.

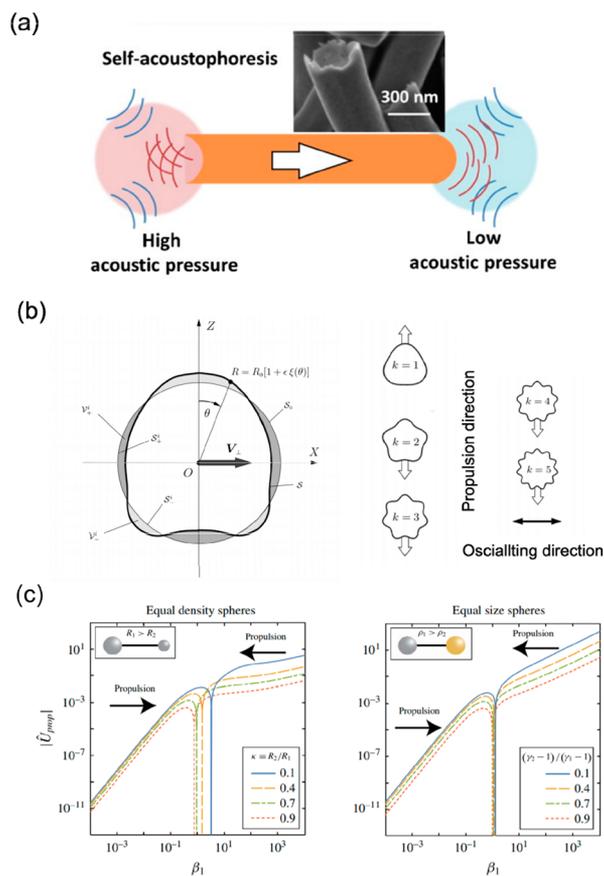


Figure 4. Theoretical models for the autonomous propulsion of axisymmetric particles by ultrasound. (a) Acoustic scattering model initially proposed.⁹ (b) Asymmetric surface acoustic streaming model based on near-sphere geometry.³³ (c) General surface acoustic streaming framework that considers both shape and density effects, and predicts reversal of direction at high Reynolds number.³⁴ Reproduced with permission from ref 9, Copyright 2013 Elsevier; ref 33, Copyright 2014 AIP Publishing; ref 34, Copyright 2017 Cambridge University Press.

Acoustically driven movement beyond axial propulsion has received relatively little attention until recently, when experimental studies have revealed that the local orbiting of acoustic motors can also be explained by the asymmetric streaming theory.³¹ One key observation was that Au microrods with obvious shape asymmetry (i.e., banana-shaped

rods) orbited with different radii that were insensitive to the driving power, and the direction of rotation was equally distributed between clockwise and counterclockwise (Figure 5a). In another recent study, control of rotary motion was achieved by manipulating the shape asymmetry of metallic microplates. A twisted star-shape microplate with 3 fins always spun toward the fin tip in standing acoustic waves, whereas a microplate with 4 fins spun oppositely (Figure 5b). A numerical simulation based on the Nadal–Lauga model suggested that the spinning direction and speeds of a microplate are related to a dimensionless frequency parameter, and there is a point at which the microplate reverses its direction as the parameter increased.³⁵ The close correspondence between the model and experiments in these studies confirms the dominant role of local acoustic streaming in propulsion.

Surface acoustic streaming is also likely to explain the spinning chains of metallic microrods that form with acoustic propulsion.³¹ Because of the imperfect plane wavefront from the transducer as well as the reflection from the chamber's side walls, acoustic waves not only propagate vertically, but also in the levitation plane. This forms lateral pressure nodes that collect the rods into chains, as supported by the observation of ring or line patterns formed by tracer particles. In addition, metallic microrods aligned on lateral nodes simultaneously oscillate perpendicularly and parallel to the levitation plane, because of the simultaneous propagation of sound waves in both directions. A phase delay between the two oscillation modes was proposed by Zhou et al. to induce rotating surface acoustic streaming, thus causing the rods to spin.³¹ Although controlled rotation of microspheres with MHz acoustic waves has been demonstrated using two orthogonal standing waves,³⁶ direct proof of this mechanism for the kilohertz spinning of nanorods³⁷ has yet to be found.

Although theory and experiment have yet to achieve a perfect match, these preliminary results have laid a solid foundation for understanding the activity of metallic microswimmers in acoustic standing waves, and have pointed out promising directions for designing novel and more versatile micromachines that are acoustically powered and controlled. It is also important to note that bulk acoustic waves are not required for autonomous propulsion. Oscillating pressure waves can be realized in other experimental configurations, such as surface acoustic waves and nodal lines near substrates. An example was reported recently and will be discussed in more detail below in the context of *rhettaxis*.²⁷

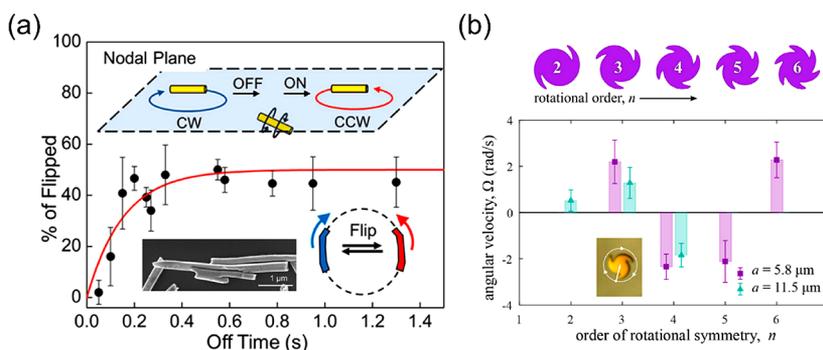


Figure 5. Shape asymmetry determines the directional motion of acoustic microswimmers. (a) Bent microrods orbit in the levitation plane.³¹ (b) Twisted star-shaped microplates spin in clockwise or counterclockwise directions, depending on their chirality and number of arms.³⁵ Reproduced with permission from refs 31 and 35. Copyright 2017 and 2018 American Chemical Society.

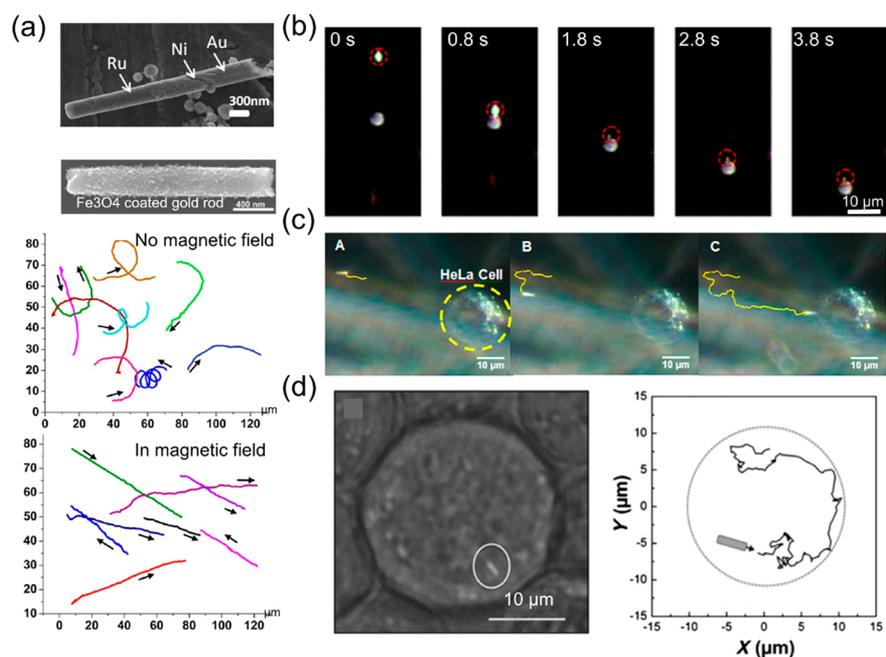


Figure 6. Controlling the autonomous motion of acoustically propelled swimmers for bioanalytical applications. (a) Steering with an external magnetic field by integrating ferromagnetic (Ni or Fe_3O_4) segments into microrods.^{30,39} (b) Pick up and transport of passive particles with an acoustically propelled and steered micromotor.²⁷ (c) Steering acoustic propelled rods with a magnetic field toward living mammalian cells in phosphate buffer solution.³⁸ (d) Propulsion of Au microrods in living HeLa cells with an acoustic field.⁴⁰ Reproduced with permission from refs 30, 27, and 38, Copyright 2013, 2017, 2013 American Chemical Society; refs 39 and 40, Copyright 2017 and 2014 John Wiley and Sons.

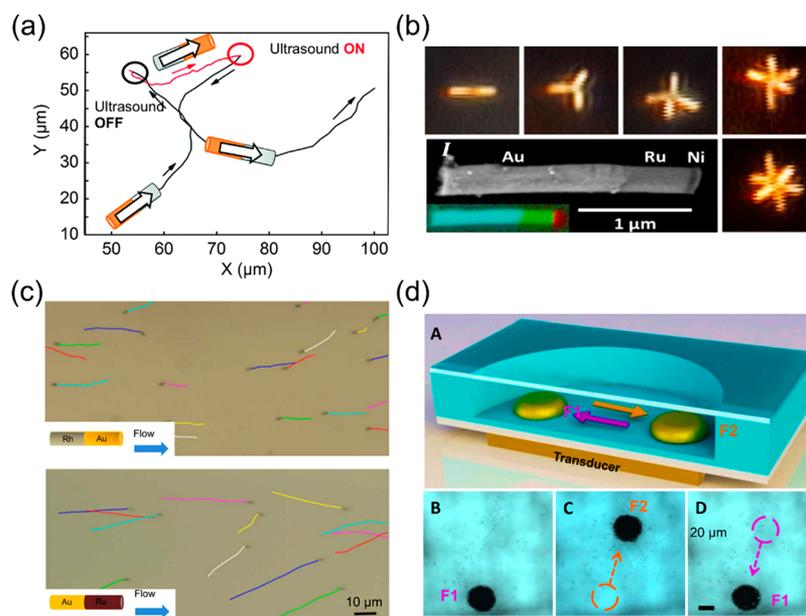


Figure 7. (a) Reversible axial motion of Au–Ru microswimmers in a chemical-acoustic field.⁴³ (b) Microrods with a Ni tip self-assemble into multimers and the process is dynamically controlled by acoustic power.⁴⁷ (c) Enhancement or reversal of the rheotaxis of chemically propelled bimetallic particles with acoustic fields.²⁷ (d) Formation of swarms and rapid deployment of microswimmers with a tunable acoustic field.⁴⁸ Reproduced with permission from ref 43, Copyright 2015 Royal Society of Chemistry; refs 47, 27, and 48, Copyright 2014, 2017, and 2015 American Chemical Society.

3.2. Acoustic Microswimmers in Biological Applications

Due to their small size, biocompatibility, and ability to move autonomously even in viscous media, acoustic microswimmers are interesting for drug delivery, sensing, and probing the local structure and viscosity of intercellular and intracellular environments. Microrods containing short ferromagnetic segments can be guided by a magnetic field to target

mammalian cells or bacteria (Figure 6a,c).^{30,38,39} The acoustic radiation force can also be used to confine particles along a pressure line for efficient cargo pickup and release (Figure 6b),²⁷ which can be made chemically specific by functionalizing the microrods.²⁸

An interesting property of acoustic micromotors is that they can be efficiently internalized by living cells. Powered Au

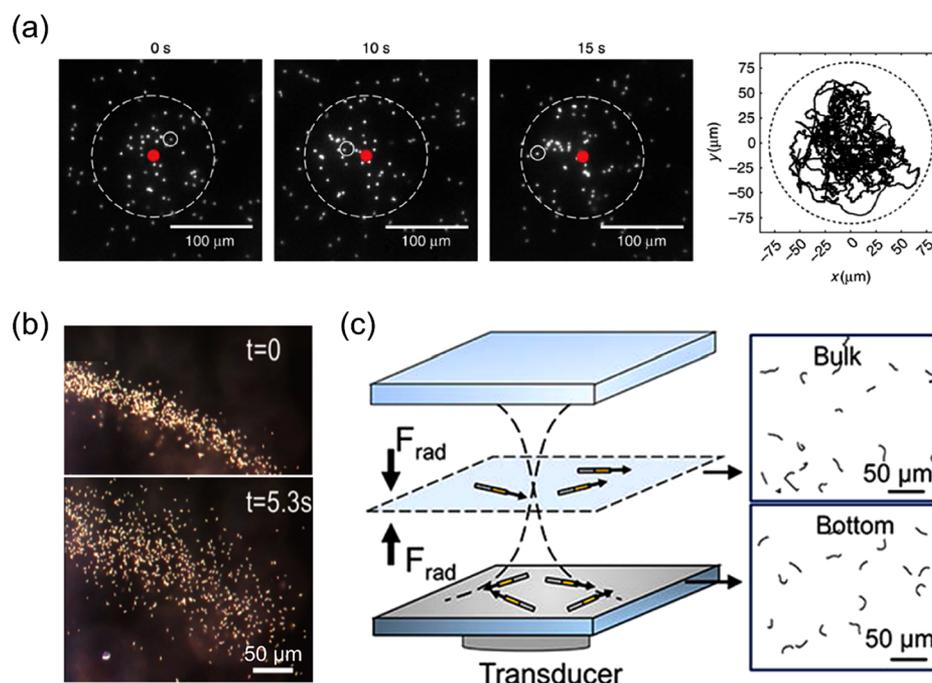


Figure 8. (a) Using the acoustic radiation force as a virtual boundary to confine Pt-polystyrene Janus swimmers.⁵⁰ (b) Transition of chemical microrod motors from an acoustic trapping field to an acoustic force-free environment.⁴³ (c) Acoustic levitation is a powerful technique for studies of boundary effects. Chemically powered swimmers are levitated to the boundary-free environment and compared to motors moving near a boundary.⁵¹ Reproduced with permission from ref 50, Copyright 2016 Nature Publishing Group; ref 43, Copyright 2015 Royal Society of Chemistry; ref 51, Copyright 2018 American Chemical Society.

microrods inside HeLa cells were observed to collide with intracellular structures, providing a new probe of their mechanical properties (Figure 6d).⁴⁰ The detection and delivery of biochemically active molecules such as siRNAs and the Cas9/sgRNA complex is efficient with acoustically powered motors, which overcome mass transport limitations in the viscous intracellular medium.^{41,42}

4. SYNERGY BETWEEN CHEMICAL AND ACOUSTIC PROPULSION

4.1. Orthogonal Propulsion in a Chemical-Acoustic Hybrid Field

By now it should be obvious that bimetallic microparticles can be propelled by two orthogonal processes: a chemical mechanism that relies on asymmetric surface catalysis and an acoustic mechanism that involves particle shape and density asymmetry. Wang and co-workers showed that these two forces can propel Au–Ru microrods in opposite directions, and therefore their motion can be reversed by switching the ultrasound on and off (Figure 7a).^{28,43} A few other systems have exhibited similar external control, notable examples being flexible magnetic nanorods and magnetic nanohelices.^{44–46} Particle trajectories with chemical and acoustic propulsion were significantly different, indicating that particle shape asymmetry plays different roles for these two processes. Microrods with Ni tips formed multimers due to magnetic forces. In an acoustic field, these microswimmers dynamically assembled and disassembled, and the equilibrium distribution of multimers was affected by the acoustic power as an effective temperature (Figure 7b).⁴⁷

A more recent study combined chemical and acoustic propulsion in a completely different configuration to study particle rheotaxis.²⁷ The device was designed to form a

pressure nodal line near the bottom substrate, running parallel to the chamber side walls, so that microrods could be propelled by acoustic waves near the bottom surface. When H₂O₂ was introduced into the channel and the acoustic transducer was off, both Au–Ru and Au–Rh microswimmers exhibited positive rheotaxis, moving upstream with their Au ends and Rh ends against the flow, respectively. When the acoustic field was applied, on the other hand, Au–Rh microswimmers moved faster against the flow (enhanced positive rheotaxis), while Au–Ru microswimmers reversed their direction and moved downstream (negative rheotaxis). Therefore, both positive and negative rheotaxis could be achieved with the same bimetallic rod by switching the ultrasound on and off (Figure 7c).

4.2. Understanding Chemical Propulsion with an Assist from Acoustics

Besides serving as an attractive power source, ultrasound also enables research on active matter as a trapping force. This is useful for studying boundary effects on microswimmer motion, and for the controlled aggregation of powered particles, where collective behavior and interparticle interactions can be studied conveniently and dynamically. This application relies on acoustic nodes (points, lines, or planes) that are formed by standing acoustic waves, which generate trapping forces that are commonly much stronger than the propulsion force of a chemically powered microswimmer. In the presence of the acoustic field, particles are collected into polar chains in a ring-shaped pressure node, or into a swarm in a point pressure node. The position and shapes of the pressure nodes can be rapidly switched by changing the frequency, resulting in a rapid displacement of the entire trapped swarm of microswimmers (Figure 7d).^{43,48} Similarly, the motion of chemical bubble-propelled microrockets can be instantaneously turned off by

trapping the swimmer in a pressure node and disrupting its bubble evolution.⁴⁹

While a strong acoustic node collects microswimmers into clusters, a relatively weak one behaves as a virtual boundary that is useful for studying active matter in confined environments.⁵⁰ For example, Brady et al. used a 2D near-harmonic acoustic trap whose radius is larger than the microswimmers' run length to confine Janus platinum-polystyrene motors (Figure 8a). By balancing the trapping force with a propulsion force, a unique swim pressure could be calculated. Wang et al. showed that an acoustically aggregated band of microswimmers underwent rapid and spontaneous disintegration when the acoustic field was switched off, as individual particles broke free from the acoustic confinement (Figure 8b).⁴³ The dispersion dynamics showed an interesting transition and a characteristic time scale that could be related to other types of active matter, such as bacteria. These studies demonstrated that replacing physical boundaries with virtual acoustic boundaries can simplify the experiment to provide insights into a number of biophysical processes.

In addition, acoustic levitation is a powerful technique for elucidating boundary effects on chemically powered swimmers.^{22–25} In a typical experiment (Figure 3a), particles are levitated away from any boundaries, and their behavior is observed immediately after the acoustic fields is turned off. For example, Wang et al. noted that H₂O₂ propelled Au–Ru microswimmers moved faster in the levitation plane (~33 μm/s) than at the bottom surface (~20 μm/s).⁴¹ In an experiment intended to examine surface charge effects,⁵¹ Au–Ru particles moved more slowly on surfaces functionalized with positively and negatively charged polyelectrolyte films (Figure 8c). Again, acoustic levitation proved critical in determining that ions released from the polyelectrolytes, rather than static surface charges, caused the decrease in speed. They also showed that silica boundaries had negligible effects on either the speed or the directionality of PMMA-AgCl Janus particles that were propelled by light-induced self-diffusiophoresis.⁵² Although acoustic levitation offers the advantage of studying particle motion in a bulk fluid, it is limited by the short sedimentation time of dense microswimmers.

5. CHALLENGES AND PROSPECTS

The single particle dynamics and collective behavior of micromotors can be dynamically modulated by combining chemical and acoustic propulsion. This feature is enabling in the study of active matter, and is already leading to interesting new functionality such as particle rheotaxis and intracellular sensing. Moving forward, we see interesting prospects and challenges alike. First, it is crucial to fabricate at the nano- and microscales particles of well-defined and precisely controlled shapes, sizes, and material composition. This is required for mechanistic studies, in which the dynamics of particles in ultrasound can be systematically examined and compared to theory/simulation. It is also essential for almost any application where the speeds, directionality, chirality and power need to be precisely controlled. Traditionally, samples for acoustic propulsion have been synthesized by chemical methods (electrodeposition in alumina templates, for example), resulting in heterogeneity and polydispersity. A recent study by Sabrina et al. used lithography to produce samples of different shapes and sizes.³⁵ However, this technique is still limited by material selection, low particle yield, and nearly planar shapes accessible to lithography. Progress in the

synthesis of unusual colloids is expected to contribute significantly in this respect.

New designs for acoustic propulsion systems are also urgently needed. Cylindrical acoustic chambers are used by a number of research groups, adapted from the original design of our 2012 study,²⁸ where a soft material (Kapton tape layers or a silicone spacer) separates two hard surfaces, the substrate is a stainless steel plate or a piece of silicon wafer, and the top is typically a microscope coverslip. The piezoelectric transducer is glued to the silicon wafer approximately below the center of the chamber. This design, while intended to produce a uniform vertical pressure node, generates a complicated pattern of lateral nodes because of bowing of the substrate and reflection of acoustic waves. Better control of the acoustic field must be achieved in order to distinguish the effects of the radiation force, asymmetric streaming and rotational streaming, and to provide important quantitative analysis that will aid in the comparison of theory and experiment. As noted above, acoustically propelled particles are tolerant of the high ionic strength and high viscosity of biological media. However, in vivo applications of acoustically propelled microswimmers will require the projection of acoustic energy far (mm to cm) away from the transducer, which is not achieved with current megahertz frequency standing wave designs. Toward this end, surface acoustic wave coupled microfluidic devices²⁷ and holographic control of acoustic energy patterns⁵³ are relatively new and enabling ideas.

Once we are equipped with a better understanding of their operating mechanism and a set of refined tools and samples, there are exciting prospects of acoustic microswimmers and their applications in connection with chemical power. For example, one might combine acoustic tweezing with autonomous propulsion, to separate and even dice passive objects trapped inside the pressure node. Since the microswimmers are much smaller than the acoustic wavelength, the combination of acoustic propulsion and acoustic trapping forces could increase the resolution and add additional dimensionality to current acoustic tweezing techniques. Another interesting application might be in engineering macroscopic self-organized materials. The long-range acoustic radiation force can periodically pattern microparticles on the length scale of hundreds of microns,⁵⁴ but with no control of individual particle polarity. On the other hand, local chemical gradients can orient microswimmers relative to each other, and they can also be manipulated by external light or magnetic fields. The combination of acoustic patterning and local chemical reactions could thus lead to soft materials with novel mechanical or optical properties.

With new tools on both the experimental and theoretical fronts, our understanding of active microparticles powered by chemistry and ultrasound will continue to progress. We have already seen fascinating individual dynamics and collective behavior of particles powered by these separate mechanisms. When operating together, the combination of chemistry and ultrasound adds a synergistic level of control and functionality that should enable applications of microswimmers in materials science, biomedicine, and other fields.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: wwang.hitsz@gmail.com.

*E-mail: tem5@psu.edu.

ORCID 

Thomas E. Mallouk: 0000-0003-4599-4208

Funding

The authors' work described above has been supported by the Penn State MRSEC under NSF Grant DMR-1420620. W.W. also acknowledges funding by the National Natural Science Foundation of China (11774075 and 11402069), Natural Science Foundation of Guangdong Province (No. 2017B030306005), and the Science Technology and Innovation Program of Shenzhen (JCYJ20170307150031119).

Notes

The authors declare no competing financial interest.

Biographies

Liqiang Ren received his BS degree from Harbin Institute of Technology (2010), and his MS degree in optics from Fudan University (2013). He is currently a PhD student at Penn State. His research focuses on the development and applications of acousto-fluidic systems and micromotors.

Wei Wang received his BS from Harbin Institute of Technology (2008), and his PhD in Chemistry from Penn State (2013) under the supervision of Thomas Mallouk. He is currently a full professor in the School of Materials Science and Engineering at Harbin Institute of Technology (Shenzhen). Dr. Wang's research interests include active and biomimetic materials, micro/nanomachines, and dynamic assembly and patterns.

Thomas E. Mallouk received his ScB degree from Brown University (1977), and his PhD from the University of California, Berkeley (1983). He is currently Evan Pugh University Professor at Penn State, where his research is focused on several problems in the area of nanoscience.

REFERENCES

(1) Wang, J.; Gao, W. Nano/Microscale Motors: Biomedical Opportunities and Challenges. *ACS Nano* **2012**, *6*, 5745–5751.

(2) Kim, K.; Guo, J.; Liang, Z.; Fan, D. Artificial Micro/Nanomachines for Bioapplications: Biochemical Delivery and Diagnostic Sensing. *Adv. Funct. Mater.* **2018**, *28*, 1705867.

(3) Katuri, J.; Ma, X.; Stanton, M. M.; Sánchez, S. Designing Micro- and Nanoswimmers for Specific Applications. *Acc. Chem. Res.* **2017**, *50*, 2–11.

(4) *Nanomachines*; Wang, J., Ed.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2013.

(5) Paxton, W. F.; Kistler, K. C.; Olmeda, C. C.; Sen, A.; St. Angelo, S. K.; Cao, Y.; Mallouk, T. E.; Lammert, P. E.; Crespi, V. H. Catalytic Nanomotors: Autonomous Movement of Striped Nanorods. *J. Am. Chem. Soc.* **2004**, *126*, 13424–13431.

(6) Fournier-Bidoz, S.; Arsénault, A. C.; Manners, I.; Ozin, G. A. Synthetic Self-Propelled Nanorotors. *Chem. Commun.* **2005**, *0*, 441.

(7) Fan, D.; Yin, Z.; Cheong, R.; Zhu, F. Q.; Cammarata, R. C.; Chien, C. L.; Levchenko, A. Subcellular-Resolution Delivery of a Cytokine through Precisely Manipulated Nanowires. *Nat. Nanotechnol.* **2010**, *5*, 545–551.

(8) Moran, J. L.; Posner, J. D. Phoretic Self-Propulsion. *Annu. Rev. Fluid Mech.* **2017**, *49*, 511–540.

(9) Wang, W.; Duan, W.; Ahmed, S.; Mallouk, T. E.; Sen, A. Small Power: Autonomous Nano- and Micromotors Propelled by Self-Generated Gradients. *Nano Today* **2013**, *8*, 531–534.

(10) Xu, T.; Gao, W.; Xu, L. P.; Zhang, X.; Wang, S. Fuel-Free Synthetic Micro-/Nanomachines. *Adv. Mater.* **2017**, *29*, 1603250.

(11) Rao, K. J.; Li, F.; Meng, L.; Zheng, H.; Cai, F.; Wang, W. A Force to Be Reckoned With: A Review of Synthetic Microswimmers Powered by Ultrasound. *Small* **2015**, *11*, 2836–2846.

(12) Li, J.; Li, T.; Xu, T.; Kiristi, M.; Liu, W.; Wu, Z.; Wang, J. Magneto-Acoustic Hybrid Nanomotor. *Nano Lett.* **2015**, *15*, 4814–4821.

(13) Hong, Y.; Blackman, N. M. K.; Kopp, N. D.; Sen, A.; Velegol, D. Chemotaxis of Nonbiological Colloidal Rods. *Phys. Rev. Lett.* **2007**, *99*, 178103.

(14) Wang, W.; Duan, W.; Sen, A.; Mallouk, T. E. Catalytically Powered Dynamic Assembly of Rod-Shaped Nanomotors and Passive Tracer Particles. *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110*, 17744–17749.

(15) Wang, Y.; Hernandez, R. M.; Bartlett, D. J.; Bingham, J. M.; Kline, T. R.; Sen, A.; Mallouk, T. E. Bipolar Electrochemical Mechanism for the Propulsion of Catalytic Nanomotors in Hydrogen Peroxide Solutions. *Langmuir* **2006**, *22*, 10451–10456.

(16) Jang, B.; Wang, W.; Wiget, S.; Petruska, A. J.; Chen, X.; Hu, C.; Hong, A.; Folio, D.; Ferreira, A.; Pané, S.; Nelson, B. J. Catalytic Locomotion of Core-Shell Nanowire Motors. *ACS Nano* **2016**, *10*, 9983–9991.

(17) Wang, J. Cargo-Towing Synthetic Nanomachines: Towards Active Transport in Microchip Devices. *Lab Chip* **2012**, *12*, 1944.

(18) Jewell, E. L.; Wang, W.; Mallouk, T. E. Catalytically Driven Assembly of Trisegmented Metallic Nanorods and Polystyrene Tracer Particles. *Soft Matter* **2016**, *12*, 2501–2504.

(19) Davies Wykes, M. S.; Palacci, J.; Adachi, T.; Ristroph, L.; Zhong, X.; Ward, M. D.; Zhang, J.; Shelley, M. J. Dynamic Self-Assembly of Microscale Rotors and Swimmers. *Soft Matter* **2016**, *12*, 4584–4589.

(20) Takagi, D.; Palacci, J.; Braunschweig, A. B.; Shelley, M. J.; Zhang, J. Hydrodynamic Capture of Microswimmers into Sphere-Bound Orbits. *Soft Matter* **2014**, *10*, 1784.

(21) Davies Wykes, M. S.; Zhong, X.; Tong, J.; Adachi, T.; Liu, Y.; Ristroph, L.; Ward, M. D.; Shelley, M. J.; Zhang, J. Guiding Microscale Swimmers Using Teardrop-Shaped Posts. *Soft Matter* **2017**, *13*, 4681–4688.

(22) Chiang, T. Y.; Velegol, D. Localized Electroosmosis (LEO) Induced by Spherical Colloidal Motors. *Langmuir* **2014**, *30*, 2600–2607.

(23) Katuri, J.; Uspal, W. E.; Simmchen, J.; Miguel-López, A.; Sánchez, S. Cross-Stream Migration of Active Particles. *Sci. Adv.* **2018**, *4*, eaao1755.

(24) Simmchen, J.; Katuri, J.; Uspal, W. E.; Popescu, M. N.; Tasinkevych, M.; Sánchez, S. Topographical Pathways Guide Chemical Microswimmers. *Nat. Commun.* **2016**, *7*, 10598.

(25) Das, S.; Garg, A.; Campbell, A. I.; Howse, J.; Sen, A.; Velegol, D.; Golestanian, R.; Ebbens, S. J. Boundaries Can Steer Active Janus Spheres. *Nat. Commun.* **2015**, *6*, 8999.

(26) Liu, C.; Zhou, C.; Wang, W.; Zhang, H. P. Bimetallic Microswimmers Speed Up in Confining Channels. *Phys. Rev. Lett.* **2016**, *117*, 198001.

(27) Ren, L.; Zhou, D.; Mao, Z.; Xu, P.; Huang, T. J.; Mallouk, T. E. Rheotaxis of Bimetallic Micromotors Driven by Chemical-Acoustic Hybrid Power. *ACS Nano* **2017**, *11*, 10591–10598.

(28) Wang, W.; Castro, L. A.; Hoyos, M.; Mallouk, T. E. Autonomous Motion of Metallic Microrods Propelled by Ultrasound. *ACS Nano* **2012**, *6*, 6122–6132.

(29) Mulvana, H.; Cochran, S.; Hill, M. Ultrasound Assisted Particle and Cell Manipulation On-Chip. *Adv. Drug Delivery Rev.* **2013**, *65*, 1600–1610.

(30) Garcia-Gradilla, V.; Orozco, J.; Sattayasamitsathit, S.; Soto, F.; Kuralay, F.; Pourazary, A.; Katzenberg, A.; Gao, W.; Shen, Y.; Wang, J. Functionalized Ultrasound-Propelled Magnetically Guided Nanomotors: Toward Practical Biomedical Applications. *ACS Nano* **2013**, *7*, 9232–9240.

(31) Zhou, C.; Zhao, L.; Wei, M.; Wang, W. Twists and Turns of Orbiting and Spinning Metallic Microparticles Powered by Megahertz Ultrasound. *ACS Nano* **2017**, *11*, 12668–12676.

(32) Ahmed, S.; Wang, W.; Bai, L.; Gentekos, D. T.; Hoyos, M.; Mallouk, T. E. Density and Shape Effects in the Acoustic Propulsion of Bimetallic Nanorod Motors. *ACS Nano* **2016**, *10*, 4763–4769.

- (33) Nadal, F.; Lauga, E. Asymmetric Steady Streaming as a Mechanism for Acoustic Propulsion of Rigid Bodies. *Phys. Phys. Fluids* **2014**, *26*, 082001.
- (34) Collis, J. F.; Chakraborty, D.; Sader, J. E. Autonomous Propulsion of Nanorods Trapped in an Acoustic Field. *J. Fluid Mech.* **2017**, *825*, 29–48.
- (35) Sabrina, S.; Tasinkevych, M.; Ahmed, S.; Brooks, A. M.; Olvera de la Cruz, M.; Mallouk, T. E.; Bishop, K. J. M. Shape-Directed Microspinners Powered by Ultrasound. *ACS Nano* **2018**, *12*, 2939–2947.
- (36) Bernard, I.; Doinikov, A. A.; Marmottant, P.; Rabaud, D.; Poulain, C.; Thibault, P. Controlled Rotation and Translation of Spherical Particles or Living Cells by Surface Acoustic Waves. *Lab Chip* **2017**, *17*, 2470–2480.
- (37) Balk, A. L.; Mair, L. O.; Mathai, P. P.; Patrone, P. N.; Wang, W.; Ahmed, S.; Mallouk, T. E.; Liddle, J. A.; Stavis, S. M. Kilohertz Rotation of Nanorods Propelled by Ultrasound, Traced by Microvortex Advection of Nanoparticles. *ACS Nano* **2014**, *8*, 8300–8309.
- (38) Ahmed, S.; Wang, W.; Mair, L. O.; Fraleigh, R. D.; Li, S.; Castro, L. A.; Hoyos, M.; Huang, T. J.; Mallouk, T. E. Steering Acoustically Propelled Nanowire Motors toward Cells in a Biologically Compatible Environment Using Magnetic Fields. *Langmuir* **2013**, *29*, 16113–16118.
- (39) Li, Z.; Bai, L.; Zhou, C.; Yan, X.; Mair, L.; Zhang, A.; Zhang, L.; Wang, W. Highly Acid-Resistant, Magnetically Steerable Acoustic Micromotors Prepared by Coating Gold Microrods with Fe₃O₄ Nanoparticles via pH Adjustment. *Part. Part. Syst. Charact.* **2017**, *34*, 1600277.
- (40) Wang, W.; Li, S.; Mair, L.; Ahmed, S.; Huang, T. J.; Mallouk, T. E. Acoustic Propulsion of Nanorod Motors inside Living Cells. *Angew. Chem., Int. Ed.* **2014**, *53*, 3201–3204.
- (41) Hansen-Bruhn, M.; de Ávila, B. E.-F.; Beltrán-Gastélum, M.; Zhao, J.; Ramírez-Herrera, D. E.; Angsantikul, P.; Vesteraer Gothelf, K.; Zhang, L.; Wang, J. Active Intracellular Delivery of a Cas9/SgRNA Complex Using Ultrasound-Propelled Nanomotors. *Angew. Chem., Int. Ed.* **2018**, *57*, 2657–2661.
- (42) Esteban-Fernández De Ávila, B.; Angell, C.; Soto, F.; Lopez-Ramirez, M. A.; Báez, D. F.; Xie, S.; Wang, J.; Chen, Y. Acoustically Propelled Nanomotors for Intracellular SiRNA Delivery. *ACS Nano* **2016**, *10*, 4997–5005.
- (43) Wang, W.; Duan, W.; Zhang, Z.; Sun, M.; Sen, A.; Mallouk, T. E. A Tale of Two Forces: Simultaneous Chemical and Acoustic Propulsion of Bimetallic Micromotors. *Chem. Commun.* **2015**, *51*, 1020–1023.
- (44) Gao, W.; Manesh, K. M.; Hua, J.; Sattayasamitsathit, S.; Wang, J. Hybrid Nanomotor: A Catalytically/Magnetically Powered Adaptive Nanowire Swimmer. *Small* **2011**, *7*, 2047–2051.
- (45) Li, J.; Li, T.; Xu, T.; Kiristi, M.; Liu, W.; Wu, Z.; Wang, J. Magneto-Acoustic Hybrid Nanomotor. *Nano Lett.* **2015**, *15*, 4814–4821.
- (46) Tottori, S.; Zhang, L.; Qiu, F.; Krawczyk, K. K.; Franco-Obregón, A.; Nelson, B. J. Magnetic Helical Micromachines: Fabrication, Controlled Swimming, and Cargo Transport. *Adv. Mater.* **2012**, *24*, 811–816.
- (47) Ahmed, S.; Gentekos, D. T.; Fink, C. A.; Mallouk, T. E. Self-Assembly of Nanorod Motors into Geometrically Regular Multimers and Their Propulsion by Ultrasound. *ACS Nano* **2014**, *8*, 11053–11060.
- (48) Xu, T.; Soto, F.; Gao, W.; Dong, R.; Garcia-Gradilla, V.; Magaña, E.; Zhang, X.; Wang, J. Reversible Swarming and Separation of Self-Propelled Chemically Powered Nanomotors under Acoustic Fields. *J. Am. Chem. Soc.* **2015**, *137*, 2163–2166.
- (49) Xu, T.; Soto, F.; Gao, W.; Garcia-Gradilla, V.; Li, J.; Zhang, X.; Wang, J. Ultrasound-Modulated Bubble Propulsion of Chemically Powered Microengines. *J. Am. Chem. Soc.* **2014**, *136*, 8552–8555.
- (50) Takatori, S. C.; De Dier, R.; Vermant, J.; Brady, J. F. Acoustic Trapping of Active Matter. *Nat. Commun.* **2016**, *7*, 10694.
- (51) Wei, M.; Zhou, C.; Tang, J.; Wang, W. Catalytic Micromotors Moving Near Polyelectrolyte-Modified Substrates: The Roles of Surface Charges, Morphology, and Released Ions. *ACS Appl. Mater. Interfaces* **2018**, *10*, 2249–2252.
- (52) Zhou, C.; Zhang, H. P.; Tang, J.; Wang, W. Photochemically Powered AgCl Janus Micromotors as a Model System to Understand Ionic Self-Diffusiophoresis. *Langmuir* **2018**, *34*, 3289–3295.
- (53) Melde, K.; Mark, A. G.; Qiu, T.; Fischer, P. Holograms for Acoustics. *Nature* **2016**, *537*, 518–522.
- (54) Chen, Y.; Ding, X.; Steven Lin, S. C.; Yang, S.; Huang, P. H.; Nama, N.; Zhao, Y.; Nawaz, A. A.; Guo, F.; Wang, W.; Gu, Y.; Mallouk, T. E.; Huang, T. J. Tunable Nanowire Patterning Using Standing Surface Acoustic Waves. *ACS Nano* **2013**, *7*, 3306–3314.