Recent Advances in Field-Controlled Micro–Nano Manipulations and Micro–Nano Robots

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Field-controlled micro–nano manipulations and micro–nano robots have attracted increasing attention in the fields of medicine, environment, engineering, and energy due to their outstanding characteristics which include small size, strong controllability, cluster action, and strong penetrability; thus, they have gradually become an important research focus in micro–nano manufacturing and in vivo detection. However, precise cluster control, targeted drug delivery in vivo, and cellular micro–nano operation remain challenges. Herein, the scientific research results produced in recent years to meet these challenges are studied. Considering the current research enthusiasm and application challenges, the micro–nano manipulations and micro–nano robots driven by physical fields (magnetic field, sound field, and light field) are mainly discussed. This review includes detailed analysis of control mechanism, control objectives, and supporting technologies; analysis of recent research results, and advantages and future development trends driven by physical fields, etc. This review involves the crossover and integration of multiple disciplines (including microelectronic technology, micro–nano processing technology, biology, physics, chemistry, machinery, and automation, etc.), hoping to inspire relevant practitioners to create new research perspectives, and promote the development of micro–nano robotics.

1. Introduction

Since the birth of human civilization, robotics has advanced in the direction of intelligence, precision, and miniaturization. Owing to the rapid developments of micro–nano technology, micro–nano operation technology based on external field control has emerged,[1] including the subsequent micro–nano robotics. In 1959, Richard Feynman, the Nobel Prize winner and theoretical physicist, pioneered the use of microrobots to treat diseases.[2] Feynman’s prediction of micro–nano technology began to approach reality in the 1980s, and remarkable progress has been made over the last two decades. Micro–nano robots are a unique and attractive research prospect as they integrate the interdisciplinary advantages of micro–nano technology and robotics. According to different application scenarios, related discipline also include biology, medicine, materials, and artificial intelligence, etc., whereas micro–nano robots are gradually emerging in these fields.[3] Phenomenon on the micro–nano scale is often significantly different from that at the macro level, which has a strong influence on the strategy, algorithm, operation, movement and control software, and hardware of the robots.[4] Cells, biomolecules, and life processes all have micro–nano characteristics. Artificial devices can interact closely with biological systems at the micro–nano scale. They can provide novel scientific insights and new tools for disease detection and treatment.

1.1. Overview of Micro–Nano Robots

As the deduction and application of science and technology in understanding and manufacturing new materials and devices, micro–nano technology has gradually advanced toward maturity and stability since the 21st century. Nanotechnology is still in its infancy in international exchange and competition.[5] A comparison of the scale of micro–nano robots is shown in Figure 1A. The diameter of hair is about 100 μm. Micro–nano robots are now smaller than the diameter of hair, and they are gradually developing to the nanoscale. This article mainly focuses on robots below the millimeter level, i.e., those with three-directional dimensions (length, width, and height) less than 1 mm. The
The earliest research and conceptual design of microrobots was conducted and classified by American intelligence agencies in the early 1970s.\(^6\) The movement mode of micro–nano robots mainly depends on the research purpose and application scenarios. At the submicrometer scale, the dominant force changes, and gravity, inertial force and other effects will be minimal. On the contrary, due to the large surface area to volume ratio, surface tension and viscous resistance will play a decisive role in the change. In the microfluidic environment, the Reynolds number of micro–nano robot is less than 1, and the viscous force dominates the inertial force. Therefore, the main force acting on the micro–nano robot to make it move might be the viscous force instead of the lift force. Movement in fluid requires noncontact control. Optical, magnetic, acoustic, and electric fields are well-developed control methods that can guide micro–nano robots to overcome viscous forces,\(^7,8\) and their mechanisms of action are shown in Figure 1B.

The applications of micro–nano robots are mainly concentrated in the biomedical field,\(^5,9,10\) among them drug delivery has become the most popular application,\(^11\) as shown in

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**Figure 1.** Overview of micro–nano manipulations and micro–nano robots. A) Size comparison of micro–nano robot, approximately close to the diameter of hair. B) Four commonly noncontact activations for micro–nano manipulations and micro–nano robots. C) Four main applications of micro–nano manipulations and micro–nano robots. D) Related sciences for micro–nano manipulations and micro–nano robots.
Figure 1C. Mechanism of cell migration through vascular endothelium (called migration) involves the binding of cell surface receptors to adhesion molecules, the application of promotive forces and the dilation of vascular walls, and the physical deformation of migratory cells. By attaching itself to migrating inflammatory cells, the robot can actually “free ride” through blood vessels without the need for its own complex migration mechanism. Micro–nano technology provides a wide range of new technologies for developing customized methods to optimize drug delivery. However, most nanodrugs are passively targeted and do not have functions such as actual operational control. Magnetic resonance imaging (MRI) guided nanocapsules are potential precursors of nanorobots. The latest progress of nanorobots has been reviewed previously, and the magnetically driven micro–nano robots has also been reviewed. The potential application of robotics in infectious disease management, particularly for the COVID-19 epidemic of the past two years could also be found in recent review. Also, the latest progress on the application of micro–nano robots in cancer treatment has been discussed in a recent review.

Micro–nano robots not only shine in the medical field, but also have immeasurable application value in other popular fields, as shown in Figure 1C. In environmental protection, pollution control and antipollution nanorobots will be put into the polluted environment in large quantities, using sensors to decompose the source of pollution, and set cleaning procedures to effectively address the issue of water and gas pollution. In the engineering field, micro–nano robots are endowed with the ability of small animals such as insects and birds or multispecies through bionics technology, which can serve as not only a reconnaissance and intelligence collection tool, but also an invincible attack weapon. In the energy field, micro–nano robots combine mechanical, chemical and molecular systems. Some scholars believe that petroleum nanorobots can be efficiently used for oil exploration, extraction, and storage.

The development of micromanipulation and micro–nano robots involves the intersection of many disciplines, as shown in Figure 1D. The assembly, observation, and monitoring of micro–nano robots are inseparable from microscale science; micro–nano fluid mechanics includes Brownian motion, diffusion motion, laminar and turbulent flow, stoke flow, and capillary phenomena; in micro–nano scale, it is necessary to consider intermolecular forces, including Vander Waals force, Coulomb force, electrostatic and electrophoretic force, optical dielectrophoretic force. The production of micro–nano robots requires the assistance of materials science technologies. In the design of materials, often, hydrophilicity, contact angle, and other factors often need to be considered. The development of biomimetic surface technology has also expanded the scope of micro–nano robots. The processing, manufacturing, and assembly requirements of micro–nano robots have urged related precision processing and manufacturing technologies, including photolithography, 3D printing, self-assembly, and microfluidics, as shown in Figure 1D.

Optical lithography is currently the most important lithographic technology, and its mainstream status will remain unshakable in the next few years. The advancement of photolithography technology has continuously reduced the feature size of devices, and the integration and performance of chips have been continuously improved. 3D printing technology is a processing method of constructing 3D entities through a layer-by-layer printing method, and has been widely used in the production and molding of artificial organs, blood vessels, and cells. Because of the small size, controllable material, controllable structure, and high efficiency, the droplet wrapping and material molding technologies with microfluidics are the core technologies that have also been used in the manufacturing of micro–nano robots. Self-assembly technology is widely used to synthesize nanostructured material systems. The assembled nanostructured materials not only inherit the characteristics of their structural units (such as nanoparticle, nanowire, etc.), but also have quantum coupling and synergistic effects produced by the combination of nanostructure units. In addition, new derived characteristics, such as performance of the system accepting external field (optical, electrical, magnetic) modulation characteristics. These characteristics are the basis for design and manufacture of nanodevices, sensors or other devices.

### 1.2. Classification of Micro–Nano Robots

Robots have developed into the micro–nano scale. At this scale, the fluid viscous force experienced by the robots is very large, making conventional driving methods extremely difficult to realize accurate control. For this reason, scientists have developed several new effective driving methods including magnetic fields, light waves, ultrasonic waves, biological motors, chemical catalytic reactions, etc. The driving methods of micro–nano robots can be classified into physical, chemical, biological and multiple driving methods, as shown in Table 1. Only a small part of the related references are listed here, and more related documents will be shown in the following description. This field developed so fast in recent years that new research results and technologies will definitely be constantly published during the process of this review, so that they are not collected in this article. We always welcome researchers in related fields to share and discuss research viewpoints with us to promote the vigorous development of micro–nano robots.

In addition to the content listed in the table, temperature-control has also received a lot of attention in recent years. Temperature-controlled micro–nano robots are currently mainly used for temperature-controlled drug release, for instance, during the photothermal therapy. On the other hand, owing to the use of soft and smart materials, temperature could be used to actuate microrobots. Temperature control belongs to the field of intelligent response. Due to biocompatibility and degradability, there is still much room for improvement in the clinical application of temperature-driven nanorobots and temperature control systems. Therefore, it is not the scope of discussion in this article. In the application of micro–nano robots in the biomedical field, the control system often needs to realize multiple functions such as drive control, positioning control, imaging control and displacement control at the same time. However, such as chemical drive and biological drive, real-time displacement control is not yet possible, as shown in the Table 1, so they are not the focus of this article. At present, magnetic, acoustic, and optical controls are the field control systems that can best realize the control of multiple parameters at the same time. They are also...
the research directions that have attracted much attention in recent years, and some of them have been verified in clinical practice. Therefore, they are likely to become the technologies that will change clinical treatment in the future. Based on the above factors, this article will focus on three types of magnetic, acoustic, and optical control that can drive and control motion. Some scholars regard micromanipulation generated by micro-robots as a research module. In this review, micro–nano manipulation can sometimes be regarded as a micro–nano robot, when the structure that realizes the micro–nano manipulation can be regarded as a whole, and the overall size is within the defined range of the micro–nano robot. Therefore, in the following discussion, most of the time the two are collectively referred to as micro–nano robots.

Here, we take stack on the control systems and challenges of different microrobot classes. We explain how the magnetic, acoustic and optical fields control micro–nano robots to complete micro–nano manipulation tasks; these include control system, control target and support technology. The mechanisms of magnetic, acoustic and optic control are introduced. Afterwards, the research trends and progress of these three physical field control system in recent years are summarized and analyzed. Finally, we highlight the importance of control mechanism, hoping to provide a more comprehensive research report for relevant practitioners and make modest contributions to the development of micro–nano robots.

### 2. Field-Control Systems

#### 2.1. Magnetic Control System

The force on micro–nano robots in a fluid with low a Reynolds number is not dominated by inertial forces, and the irregular movement of particles begins to play a role, posing a challenge to the precise driving of micro–nano robots. The driving mechanism of natural organisms provides many examples for the development of micro–nano robots. For instance, biological macromolecules convert chemical energy into mechanical energy to help cells complete transportation tasks; the flagella structure of bacteria and sperm enables them the kinetic energy to swim in fluids, etc. Based on the research biological driving mechanisms, important progress has been made in the self-propelled micromotors. The requirement of biocompatible energy conversion mechanism for noncontact micromotor drive has promoted the research on external magnetic field, electric field and acoustic wave driving methods.

The magnetic system with permanent magnets as the core has become the first choice for micro–nano robot drive due to its large working space, precise and controllable large-scale operating force, small biological tissue influence, and low dependence on external energy lines. In the design of control system, parameters that affect the control accuracy and efficiency mainly include the number of magnets and the position of the magnets, as shown in Figure 2A. By coupling with the manipulator, the programming and reconstruction of the magnetic microrobot is achieved. A more precise trajectory control and cooperative operation is thus realized. Using permanent magnets to drive magnetic actuators in the same space will generate stronger magnetic fields and magnetic field gradients than the electromagnetic coils. Owing to this feature, permanent magnets can meet the control target to achieve 3D directional motion in the viscous fluids such as biological media. As a driving tool, it is widely used in close-accessible in vitro analysis and operation environments such as microfluidic chips, human eye corneal peeling/repair operations, cochlear surgery and other micro manipulations close to the human surface.

Compared with electromagnetic coils, permanent magnets do not require power supply systems or large-scale water-cooling devices, and thus, provide a wide experimental space. The magnetic actuator system driven by permanent magnets is widely
Figure 2. Overview of magnetically activate system. A) Magnetic control methods and techniques. B) Magnetic control targets. C) Supporting technology of magnetic control. A.i: reproduced with permission.\textsuperscript{[42]} Copyright 2020 Elsevier B.V.; A.ii-a: reproduced with permission.\textsuperscript{[51]} Copyright Wiley; A.ii-b: reproduced with permission.\textsuperscript{[53]} Copyright 2019 AIP; A.ii-c: reproduced with permission.\textsuperscript{[52]} Copyright 2018 Elsevier B.V.; B-a: reproduced with permission.\textsuperscript{[59]} Copyright 2019 Wiley; B-b: reproduced with permission.\textsuperscript{[60]} Copyright 2018 Wiley; B-c: reproduced with permission.\textsuperscript{[64]} Copyright 2020 Wiley; B-d: reproduced with permission.\textsuperscript{[61]} Copyright 2016 PNAS; B-e: reproduced with permission.\textsuperscript{[63]} Copyright 2019 Science; B-f: reproduced with permission.\textsuperscript{[56]} Copyright 2009 AIP.
used in in vitro detection and biological tissue manipulations. As an excellent carrier for in vitro manipulation, the microfluidics has the advantages of low pollution, portability, and high integration, as shown in Figure 2A-iv. The use of permanent magnets to construct MMT and the combination of microchannels can be used for frequency control to realize the manipulation of droplets and cells in the microchannels. Magnets and ultrasonic waves are used to control magneto-actuators and biomimetic robots to drive biological particles in microchannels. To control the buoyancy force, a micro gripper with a hollow structure was designed. The magnetic actuators are combined with ultrasonic stage to realize oscillation and levitation control, arrangement outside the microchannel are more conducive to cell/particle transportation, rotation, enucleation, and injection.

A magnetic field can exert force and torque on any magnetic object without any mechanical connection between the object and the external field. The electromagnetically driven magnetic field has the advantages of high speed, accuracy, and easy control, which are conducive for computers to achieve the operation and control of micro–nano robot in vivo. The magnetic field generated by the electromagnetic coil has the following advantages: 1) size and direction of the magnetic field can be adjusted easily and quickly; 2) coupling of the multicoil magnetic field can obtain a magnetic field in any direction in a 3D space; 3) by adjusting the current of each coil, complicated magnetic fields can be obtained, such as gradient fields, rotating magnetic fields, oscillating magnetic fields, etc.; 4) the produced magnetic field has high-speed responsiveness and can achieve more precise control. As shown in Figure 2A-ii, a tetrahedron arranged magnetic field can be used to control an octopus-inspired millirobot, and a rotating magnetic field could be established to control a magnetic helical microswimmer and a wheel-shaped flaky microswimmer. Electromagnetic coil-based systems can be used to control a variety of magnetic targets to accomplish complex tasks.

At present, researchers have constructed different magnetic fields based on different driving methods. According to the driving mode of robots in the magnetic field, the driving methods can be roughly divided into gradient field driving, uniform magnetic field driving, oscillating magnetic field driving, rotating magnetic field driving, and cluster driving, as shown in Figure 2A-iii (B means the magnetic field, $\nabla B$ means the magnetic field gradient). The magnetic field can act on any magnetic substance placed in it. For example, when a magnetic robot is placed in a uniform magnetic field, it will generate a torque, causing the robot to rotate; but when the magnetic field acts in a gradient, it will generate a magnetic force on the robot. The function attracts robot to move along the magnetic force. In a gradient-based magnetic field, the magnetic field can be superimposed by multiple coils, and the current in coils can be altered to change direction of the magnetic field, thus changing force direction of the robot and realizing multiple degrees of freedom motion. The oscillating magnetic field refers to a magnetic field whose size or direction changes periodically. Using structural characteristics of the robot, shape of the robot periodically changes with the oscillating magnetic field; thus, the robot generates forward power and realizes the specific functions. The rotating magnetic field is characterized by the magnetic field vector which rotates completely and continuously around the axis. Generally, the field vector rotates in a plane perpendicular to the rotation axis. In addition, the rotating magnetic field also includes a conical magnetic field rotating magnetic field. The driving method based on the rotating magnetic field has been widely used in the control of spiral robots and spherical robots. For micro–nano robots, complex tasks can be achieved by clusters of robots. The magnetic field can act on any magnetic substance placed in it, which enables magnetic field an unparalleled advantage in cluster control.

With the development of control technology, the control objectives of magnetic field have also been diversified. This diversification is evident from the initial simple particle control to currently used magnetic actuators and bionic microrobots, as shown in Figure 2B. Aiming to application scenarios, especially drug loading needs in targeted therapy, diverse magnetic objectives have emerged in recent years, including the spiral microrobot, spherical robot, ceramic microrobot, and capsule microrobots controlled by rotating magnetic field, deformable jellyfish robots, soft robots, and foldable robots controlled by oscillating magnetic field; circular hollow robots and soft robots controlled by gradient magnetic field. Given the in vivo application of magnetic objectives, biocompatibility is an important principle in the design of micro–nano robots in recent years, and therefore the concept of cellular robots has been derived. The existing research involves the use of red blood cells, immune cells, platelets, stem cells, endothelial cells, activated fibroblasts, and cancer cell membranes. These cellular robots have potential application value in targeted drug delivery, biosensors, vaccination, detoxification, and virus detection.

micro–nano robots need to navigate in viscous fluids, and thus, their motion design of micro–nano robots needs to generate a driving force. The motion design and control capabilities of these robots need to be carried out in a microfluidic environment that meets the application scenarios. Therefore, the development of micro–nano robots cannot be separated from the experimental environment constructed by microfluidic chips which include the construction of flow fields, and the coupling design of flow fields with external fields. First, microfluidic chip provides a good controllable environment in terms of flow and boundary conditions to realize the physical condition design of micro–nano robots. Second, microfluidic chip provides a challenging experimental platform for the functional realization of micro–nano robots. Finally, microfluidic chips are a general platform that needs to be manipulated and characterized at the micrometer level, and micro–nano robots can help meet this need. As shown in Figure 2C, microfluidic chips have been successfully implemented in several structures including planar channels, blood vessel channels, obstacle channels, 3D channels, and bifurcated channels to meet the requirements of micro–nano robots and micro–nano manipulations.

2.2. Optic Control System

2.2.1. Optical Tweezers (OT)

Optical tweezers is a major invention of laser technology, and currently it is an important tool for micro–nano
It focuses a laser beam through an objective lens to form an optical trap at the focus of laser. Micro–nano objects are restrained in the optical trap by light pressure (as shown in Figure 3A-i). Therefore, this control method might be called as light control or optical control. The plane movement then controls the micro–nano objects to move with the plane of optical trap, and the optical trap moves in a vertical direction to the focal point. The optical pressure of the laser is the change in momentum caused by light passing through the control object, which in turn creates the trapping force. Therefore, the wavelength of light, the size of the object, and the optical properties of the object are important factors for laser trapped. The force

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Figure 3. Overview of optically activate system. A) Optic control mechanisms and technologies. B) Targets of optic control, from single beads to bulky particles and bacteria. C) Support technologies of optic control: optical system and wireless control platform. C-i: reproduced with permission.© 2021 MDPI.
generated by optical tweezers is in the range of sub-piconewtons to nanonewtons, which facilitates position detection at the nanometer scale.[72] In addition, the intrinsic properties of the light field (energy and momentum) and the spatial distribution of characteristic parameters (intensity gradient of the light field) jointly determine the effect of light on the matter. Therefore, the different effects of light on matter[73] and manipulation of light on complex particles[74] can be achieved by adjusting the properties of these light fields. Under the microscope, optical tweezers technology can be used for motion control and microsurgery operations on micro–nano objects (such as viruses, bacteria, intracellular organelles, etc.)[72]

Since the study by Ashkin et al.[75] which reported the first single-beam optical tweezers in 1986, optical tweezers have evolved from simple micron cell manipulation to single-molecule and submicrometer precision measurements. With technological innovation and progress, optical tweezers have been widely used in biology, soft matter colloidal science, and physical nanoscience.[72] For example, detecting the elasticity of cell membrane,[76] elucidating the potential energy of particle interaction.[77] Optical tweezers have also emerged in physics, such as nanotechnology[78] and quantum mechanics.[79] Currently, the mainstream of optical tweezers includes single-point optical tweezers, holographic optical tweezers, magneto-optical tweezers, and electro-optical tweezers. Especially, holographic optical tweezers belongs to multibeam optical tweezers, which is formed by using holographic elements to construct a light field.[80]

There are still some challenges that need to be further solved on optical tweezers, including the interaction between the single-beam gradient force trap and the particles, the control of optical particles, the new optical trap characteristics formed after the new beam is focused, and the optical field distortion encountered in the design and application.

2.2.2. Optical Electrical Tweezers (OET)

Although optical tweezers can manipulate individual particles flexibly and have advantages in physical quantity measurement, the required light intensity and power are relatively high, which are likely to damage the controlled objects. Optical tweezers uses the principle of light pressure to capture micro–nano particles. A new type of manipulation technology, optoelectronic tweezers, which combines optics and electrodynamics, has been proposed.[81] Optoelectronic tweezers use light pattern induced space electric field to polarize particles to form dielectrophoretic forces (DEP forces), which can then manipulate micro–nano particles, as shown in Figure 3A-ii. In an OET, the subject is encapsulated in a microfluidic chip, a chamber composed of an upper bottom plate covered with a conductive layer made of a photosensitive material. In dark or low light conditions, conductivity of the conductive layer is low and the impedance is large. When a voltage is applied across the chip, the potential of bottom plate is greatly reduced, and the intensity of the electric field in the liquid medium of the chamber is small. When a light beam irradiates the conductive layer, the conductivity of irradiated part increases, which leads to the formation of a “virtual electrode.” The electric field strength of the liquid medium above the irradiated portion also increases, and a nonuniform electric field is formed in the medium. Particles will be polarized in the electric field, and the nonuniform electric field interacts with the particles, thereby generating attractive or repulsive forces on the particles. By changing the light position or changing the optical pattern, the directional control of the particles can be achieved, as shown in Figure 3A-ii.

OET uses the photoelectric effect of crystals and combines the characteristics of OT and dielectrophoretic control. Weak light intensity is needed to form virtual electrodes on the surface of the conductive layer, which reduces the power requirement, avoids the manufacturing of complex electrodes, and achieves flexible manipulation of micro–nano particles.[82] OET is a new micromanipulation method that has broadened the traditional scope of micromanipulation. It has the advantages of noncontact, small damage, and closed system. For living biological cells, organelles, and other particles that need to be cultured in a specific media, this noncontact aseptic manipulation method can avoid damaging the experimental environment, maintain cell viability, and reduce any external interference.

OT and OET are collectively referred to as the driving mode of optical control in the subsequent sections. With the improvements in related technologies, the targets of optical control have also evolved gradually from simplified to complex, cluster, and biological goals. As shown in Figure 3B, the main known targets of optical control include nanometer particles,[83] proteins,[84] micro–nano robots,[85–87] hydrogels,[88] cells,[89] algae and worms,[90] bacteria,[91] and carbon nanotubes.[92]

The basic structure construction of optical control system for OET is shown in Figure 3C-i.[92] For real-time display and observation of the optical path, the image of the photoelectric microfluidic chip passes through the objective lens and form a parallel optical path. The size of the optical path is scaled through a set of lens groups, to a size consistent with the effective area of image sensor charge-coupled device (CCD). For the real-time projection of light path, the designed manipulated pattern is projected through the projector, which is first scaled by the lens, and then scaled to the same size as the optical aperture of the objective lens. Finally, the optical pattern is converged and projected onto microfluidic chip through the objective lens.

The basis of the original optoelectronic tweezers structure, as shown in Figure 3C-ii. Cross-platform graphical user interface (GUI) using iPad and PC as interactive terminals was also implemented. The GUI program could integrate tasks, for instance, real-time monitoring of CCD camera, design and control of projection graphics, postprocessing of acquired microscope images, and display of recognition results. The optical projection pattern in the projection imaging module could also be designed on the iPad GUI, and the data is sent to the execution terminal computer through the cloud server. Thus, the flexibility of the devices improves manifold.

2.3. Acoustic Control System

Acoustic drive is a noncontact manipulation method designed to meet the latest demands of micro–nano actuation functions.[93] It uses various physical effects of sound waves to control micro–nano solids, liquids, gases and soft substances.[94] The commonly
used frequency of sound waves in micro–nano controls is in the ultrasonic range (20 kHz), and it can also be used in the audio or infrasonic ranges. Compared with other common driving methods for micro–nano robots, acoustic drive has the following advantages: 1) the generation and excitation equipment for sound wave are well developed, the device structure is relatively simple and compact, the frequency and amplitude control of the sound wave are easy to achieve, and the operation personnel does not require long-term training; 2) acoustic drive is a noncontact operation mode (that is, there is no direct contact with fluids), there are no specifications for the nature of the operating object (geometry, electromagnetics, optics, chemistry, etc.), and the driving process. The nature of the medium remains unchanged which indicates good bio-compatibility; 3) based on its inherent nonlinear characteristics, acoustic drive is designed for high efficiency, high energy, clean (noncontaminating fluid), and low-cost means. The complex control of micro–nano robots could be achieved through the acoustic structure which provides a new route for micro–nano robots to move in biological media with high viscosity and high plasma intensity.

Generally speaking, there are three main kinds of microoperation principles based on acoustic drive including traveling wave fundamental acoustic field drive (traveling wave tweezers, TWT), standing wave fundamental acoustic wave drive (standing wave tweezers, SWT) and acoustic flow fundamental acoustic wave drive (acoustic current tweezers, ACT), as shown in Figure 4A. Both traveling wave and standing wave tweezers directly act on particles or fluids through the acoustic radiation force exerted by the acoustic field, while acoustic flow tweezers indirectly acts on particles through the sound field to induce local fluid flow. Active traveling wave tweezers is more flexible, but usually requires multiple transducers and relatively high transmission systems. While, the control mechanism of passive traveling wave tweezers is simple and easy to implement, there is a single sound field mode, and the calculations for simulation are extremely difficult. SWT of bulk acoustic wave (BAW) has high flux, but their accuracy is limited, and the operation requires high power along with the higher requirements for related accessories. Surface acoustic wave (SAW) of SWT has high precision for manipulating nanoparticles and has a simple structure. However, its flux is low, sound field mode is limited along with cumbersome manufacturing steps, which hinder the experimental progress. Acoustic flow tweezers based on microbubbles have several modes of sound field, but the control accuracy depends on the size and stability of the bubbles, and the reproducibility is often poor. Relatively, the acoustic flow tweezers based on solid microstructures have high stability and repeatability, but the microstructures are difficult to change during the experiment, and hence the sound field mode is restricted. Taken together with the requirements for control accuracy, surface acoustic waves have received greater attention and have advanced rapidly.

Acoustic streaming refers to the time-averaged stable migration of sound-field energy due to viscous dissipation and absorption by the fluid, which is a typical nonlinear problem. The essence of acoustic flow is the local flow caused by the gradient force of the acoustic momentum flux in the fluid in the time average. It is a powerful tool for microfluidic applications.\[93–98\]

According to the different location of acoustic flow generation, the acoustic streaming can be divided into boundary-layer-driven acoustic streaming and body acoustic streaming, as shown in Figure 4A-iii. Both of these mechanisms stem from the attenuation of sound energy flux, which in turn leads to a momentum flux gradient, and thus generates acoustic streaming. When the sound current is driven, the capture position and rotation mode of the cells or particles can be controlled by regulating the frequency of the sound waves. Boundary acoustic streaming is an important control mechanism produced by the rapid dissipation of sound waves at the solid boundary. The particle size is a critical factor for determining the dominant force between the acoustic radiation force and the acoustic flow-induced resistance. Beyond the critical particle size, acoustic radiation becomes the dominant force. Functionally, the hydrodynamic effect of acoustic streaming can be utilized for different basic fluid functions, including mixing, micropumping, particle aggregation, and convergence.

In the research of acoustic micro–nano manipulation technology, acoustic radiation force is defined as the force exerted on the whole object to drive its motion. Objects in different spatial positions will receive uneven kinetic energy density and potential energy density, the sound field produces sound radiation force on the objects due to the momentum transmission of the sound field.\[99\] An object with a volume of V placed in the sound field experiences a sound radiation force generated by the exchange of momentum between the field and the object. The acoustic radiation force acts on the entire volume of the object, but due to the conservation of overall momentum, the problem is attributed to the force acting on the object surface. Acoustic radiation force can be divided into primary acoustic radiation force and secondary acoustic radiation force. Acoustic radiation force affects particles (including beads, cells, or bubbles) in the fluid by pushing or convergence. In the standing wave model when two traveling waves are superimposed, the primary acoustic radiation force directly moves the particles to the pressure node or antinode. The secondary acoustic radiation force is realized by the interaction between particles and can be used to concentrate particles. The primary acoustic radiation force mainly acts on the compressible spherical objects in the standing wave mode and in viscous fluids.

The current sound field-driven objects mainly include particles,\[100\] cells,\[101\] nanowires,\[102\] metal rods,\[103\] nano robots,\[104\] and bionic micro robots,\[105\] as shown in Figure 4B. The detailed mechanism and progress are described in the following chapters. Acoustic flow is a stable flow driven by the absorption of high-amplitude acoustic oscillations in a fluid. It describes the dissipation and attenuation of sound field energy absorbed by the fluid to form a stable migration motion under time average, which is a typical nonlinear effect. The acoustic flow in a microchannel is generated by vibrating microbubbles or vibrating solid microstructures, as shown in Figure 4C. As a carrier of the micro–nano structure, the microfluidic chip is an indispensable supporting technology for acoustic flow drive. The bubble channel and the liquid channel are constructed by intersecting multiple channels. The target particles/cells flow through the main liquid channel and then through the bubbles generated by the bubble channel. The transducer generates a vortex in the bubbles and consequently rotates the targeted particles/cells. The solid microstructure has a similar mechanism of action, and microfluidic chip provides the microstructure and the main liquid channel.\[105,106\] The microfluidic chip also provides pits and
protrusions for sound waves, which act as loads for body waves to capture the targeted particles/cells. In addition, the microfluidic chip works with surface acoustic waves to concentrate and capture high-precision particles. The microfluidic chip plays an indispensable role in the development of acoustic wave driving, from auxiliary positioning to auxiliary precise control.

Figure 4. Overview of acoustically activate system. A) Mechanisms and technologies of acoustic control. B) Targets of acoustic control. C) Supporting technologies of acoustic control. B-b: reproduced with permission. Copyright 2012 ACS. B-c: reproduced with permission. Copyright 2016 ACS. B-d: reproduced with permission. Copyright 2016 RSC.
3. Recent Research Highlights and Applications of Field-Control System

3.1. Magnetic Control

Magnetically driven microrobots have gained widespread attention in the field of minimally invasive tasks due to their remote access to enclosed small spaces. Recently, Dong et al.\cite{107} proposed a 2D method to control the external magnetic field at the air–water interface or solid surface. They programmed the external magnetic potential energy with ferromagnetism to achieve the control of the external magnetic field with a diameter of 100–350 μm. The collective mobility control of microrobots is shown in Figure 5A. These results are technically innovative and helpful to realize multiobjective control and cooperative transport of multiple objects in the field of biomedicine, as well as higher throughput and fast parallel operation. As future application prospects, to exert the strongest effect of the control mechanism, the authors indicated that 3D motion control will remain a challenge. This method has potential applicability in driving control method of smaller particles for the noncontact drug loading control in the blood vessel.

Microrobots in blood vessels have also been the research focus in recent years for the treatment of vascular diseases. Based on the control mode of wireless transmission, precise and high degree of freedom operations are possible. Lee et al.\cite{107} have proposed a microrobot that can perform drilling functions and have motion capabilities in a 3D space. It has a characteristic precise manipulation performance in the fluid channel of the simulated blood vessel network. It is embodied in the realization of multiple selection and movement of the desired path at the channel junction, and the drilling of the artificial thrombus in the artificial 3D vessel, as shown in Figure 5B. The results are innovative in terms of precise operation and drilling performance in control methods, which not only help in the accurately treat of thrombus, but also take into account the biocompatibility of the material in the future. Hence, it can be used in vivo, and is more likely to have an important role in the effective operation of human blood vessels.

The surface interface force between liquid and solid expands the target range of magnetic field drive. An Li et al.\cite{108} recently proposed a control method of driving liquid droplets using a steel ball in a programmable magnetic field. This method is simple and reliable. The size and position of the steel ball adjust the structure of the robot, and then affect the front and rear resistance of the droplet, and realize different behaviors such as transportation, splitting, release, rotation and combination of the droplet. And the type of droplets is not limited to water. This control method can also realize the manipulation of oil, gas and other fluids. The magnetic field is driven in such a way that in a confined space, anhydrous, anaerobic environment, as shown in Figure 5C. The research results are relatively innovative in control methods, especially the programmable and automated operation of droplets, which are expected to play a greater role in the fields of material transportation, micro–nano processing, and bio-medicine in the future.

Liquid manipulation is similar to cluster control. It is very challenging to condense the cluster control into a micron-level droplet and achieve multiple collective modes with strong environmental adaptability. Xie et al.\cite{109} used alternating magnetic fields to achieve such control. Driven by different input magnetic fields, a single microrobot exhibits multiple dynamic modes such as oscillation, rolling, tumbling, and rotation, which then triggers a group of microrobots to self-organize into corresponding liquids, chains (rolling columns), and belts (rolling) and swirling group forms. Similarly, Fan et al.\cite{110} demonstrated a ferrofluid droplets with high deformability with the help of magnetic control technology, as shown in Figure 5D. The liquid microrobot monomer can be resembled into various shapes and realize many complex operations, which could be applied to monitor target delivery.

Although drug delivery is expected to treat a variety of diseases, it is a very big obstacle for ophthalmic diseases. Although magnetic field drive is minimally invasive and solves the problem of difficult ocular drug injection, magnetic nanoparticles drive residual magnetic nanoparticles after drug treatment, thus causing secondary damage to eyes. In response to this problem, Dong-In Kim et al.\cite{111} recently proposed a two-layer hydrogel microrobot that could recover after drug delivery. The robot consists of a magnetic nanoparticle layer and a hydrogel layer. The particles serve as the dynamic layer and the hydrogel layer as the treatment layer. The dissolution of the hydrogel is controlled by the alternating magnetic field to achieve the purpose of drug release. After the drug is released, the power layer and the drug layer are completely separated, and then the power layer, that is, the magnetic nanoparticles, can be moved to a fixed position by the magnetic field, so as to achieve the purpose of recovery, which also reduces the secondary burden on the eyes, as shown in Figure 5E. The research results are highly innovative in terms of magnetic assembly and alternating magnetic field control. Combined with the characteristics of hydrogels, it solves the limitations of traditional microrobots in obtaining magnetic nanoparticles after drug delivery, while maintaining the performance of the traditional microrobots.

Accurate drug delivery is expected to play a greater clinical role in the treatment of eye diseases in the future. Hyperthermia micro–nano robots play an important role in drug delivery, release and treatment. Magnetically controlled thermal degradation micro–nano robots provide powerful tools for targeted therapy due to their small size, minimal invasiveness and precise wireless control. In this context, Park et al.\cite{112} proposed a method consisting of polyethylene glycol diacrylate (PEGDA) and pentaerythritol triacrylate (PETA), and containing magnetic Fe$_3$O$_4$, nanoparticles (MNP) and 5-fluorouracil. The (5-FU) hyperthermia microrobot is biodegradable. Remote precise control is realized by rotating magnetic field, heating of hyperthermia microrobot is realized by alternating magnetic field, drug release mode is controlled, and multidirection anticancer is realized. The viability of the cells is shown in Figure 5F. The research results are highly innovative in the structure of magnetic microrobots, and have great potential in vitro targeted drug delivery and hyperthermia treatment in the future.

Multi-structure and multifunctional magnetic microrobots are currently the research hotspots of magnetic-driven targeted therapy. However, large-scale manufacturing of local precision-propelled and excellent therapeutic microrobots remains a huge challenge. Wang et al.\cite{57} recently proposed a composite magnetic microrobot, which used spirulina as a biological template.
**Figure 5.** Recent research and applications of magnetic control. A) 2D microrobot swarms for cooperative manipulations. Reproduced with permission.[47] Copyright 2020, SAGE. B) 3D magnetic navigation for precise thrombus treatment. Reproduced with permission.[102] Copyright 2018, Springer Nature. C) Microrobot manipulates the droplets for various fluids manipulation. Reproduced with permission.[103] Copyright 2020, AAAS. D) 3D deformable microrobots for target delivery. Reproduced with permission.[110] Copyright 2020, Wiley-VCH. E) Magnetic hydrogel microrobot for drug delivery and retrieval. Reproduced with permission.[111] Copyright 2020, Wiley-VCH. F) Magnetic degradable microrobots for drug release. Reproduced with permission.[112] Copyright 2019, Wiley-VCH. G) Microrobots on spirulina templates for targeted delivery. Reproduced with permission.[113] Copyright 2019 ACS. H) Cell-based microrobot controlled by magnetic field for tumor therapy. Reproduced with permission.[114] Copyright 2020 IROS publications.
to synthesize nanoparticles by a chemical method to act as a light-to-heat conversion agent. The magnetic nanoparticles are deposited on the surface through condensation. The colloidal sol process is driven by magnetism, and the anticancer drugs are loaded on the microrobot, giving it chemotherapy effects. The prepared magnetic microrobot has efficient propulsion performance in a rotating magnetic field, and has synergistic chemotherapy-photothermal therapy effect, as shown in Figure 5G. The research results are highly innovative in the structure and control speed of the magnetic microrobot, which are expected to become a future platform for efficient drug delivery, targeted delivery and photothermal therapy. It seems that micro–nano robots with multiple functions are no longer a challenge.\[113\]

Aiming at targeted therapy, micro–nano robots are playing their advantages. Feng et al.,\[114\] proposed a cell-based microrobot controlled by a high-gradient magnetic field, which can simultaneously perform precise movement of micro–nano robots and release targeted drugs, and has achieved good results in in vivo experiments, as shown in Figure 5H. Encapsulating magnetic nanoparticles in macrophages not only achieves biocompatibility and degradability at the same time, but also has a high drivability. It has a relatively innovative high magnetic field and in vivo experimental results.

### 3.2. Acoustic Control

The acoustic wave can not only drive the microstructure to rotate, but also drive the microstructure forward in the narrow channel to realize the physical function of multiple degrees of freedom. Qiu et al.,\[115\] proposed a micro–nano robot driven by ultrasonic power supply, which can be used as a small endoscope, as shown in Figure 6A. The surface consists of an array of microbubbles that vibrate to produce energy when driven by ultrasonic waves. Multiple degrees of freedom are generated by controlling the power through the bubble size. The research results are highly innovative in the structure of micro–nano robots and have high medical value in the future medical field of minimally invasive surgery. The main feature of sound waves is their ability to control nanoscale targets. With the rapid development of research on the micro–nano robots, it is more and more important to develop bionic micro–nano robots with biocompatibility. Berta Esteban-Fernandez de Avila et al.,\[102\] developed an ultrasound-driven bionic nanorobot with dual cell membrane functionalization capable of targeting removal of bacteria and toxins. Feng et al.,\[116\] realized the rotation of microbeads and oocytes with the help of acoustic control technology, as shown in Figure 6B. The results are highly innovative on cell rotation approach in acoustic fluid and can be applied to single cell analysis. Li et al. further achieved highly stable fixation and rotation related to the size and density of the microbeads.\[117\]

Targeted delivery and release capability is the focus of research in the most promising field of biomedical applications of micro–nano robots. To solve the current challenge of precise on-demand motion control, Lu et al.,\[118\] proposed a microrobot used interface that could quickly recognize user commands to realize the delay free drive of microrobots, as shown in Figure 6C. The method is implemented on an acoustic driven platform. The speed and direction of the controlled microrobot can be adjusted, which can quickly respond to instructions with high precision, and can realize instant communication and directional transportation of the microrobot. The research results are highly innovative in terms of control methods and human-machine interface, and can be applied to the development of intelligent microrobot system platform and microcell analysis factory in the future.

Micro–nano robots with certain autonomous movement ability often have strong propulsion force, with key applications in targeted therapy, noninvasive surgery and other fields. As an important branch of artificial swimmers, sound-driven micro–nano robots with autonomous movement ability can be better applied in the physiological environment of human body. Daniel Ahmed et al.,\[104\] proposed a nanoscale swimmer using structural resonance with high efficiency when operating in vivo. The tail of the nanorobots uses a flagella structure that vibrates small amounts in response to sound waves to generate propulsion. The rigid structure of the head allows the nanobot to move faster, while the flexible structure of the tail allows it to respond to sound waves. The structural resonance can produce a large propulsion force, which can play a role in the field of targeted drug delivery in the body physiological environment in the future. For the precise control process in the targeted drug delivery process, Han-Sol Lee et al.,\[119\] proposed a new ultrasonic driven mechanism that could realize the operation of drug particles/cells and move within the human body to achieve accurate diagnosis and treatment, as shown in Figure 6D. The results are highly innovative in terms of control techniques that could be used in the future to operate microrobots inserted into peripheral blood vessels and targeted drug delivery.

The frequency is the key parameter affecting the driving force. Therefore, generating a large driving force at a smaller frequency is the research focus of acoustic drive. Kaynak et al.,\[106\] achieved high-speed rotation of microstructures in microchannels using in-situ fabrication and simple sonic driving techniques. Piezoelectric transducers use sound waves to drive the edge structure to vibrate, which generates microflow and then induces rapid rotation. This simple and controllable method is expected to help microfluidic technology shine in the fields of biomedical, physics and chemistry in the future. In view of the ability of acoustic waves to control fluids and microstructures, Kaynak et al.,\[120\] proposed a soft micromechanical structure driven by acoustic waves, which uses the performance of acoustic hydrogel to drive fluids. The compound micromechanical can be connected to multiple pumps for work and can be remotely controlled, as shown in Figure 6E. This research provides a new idea for the development of miniaturized automata, which can be used as soft microrobots for minimally invasive diagnosis and targeted therapy in the future. The development of microoperating systems enables mechanical engineers to operate and control targets with high precision at the cellular level. For this reason, Guo et al.,\[21\] proposed a platform based on acoustic flow control. By adjusting the intensity and wave form, cell control on a micro scale is realized, as shown in Figure 6F. The control has high flexibility and precision, and the control of fluid has reached an unprecedented height. The results of this study are innovative in terms of control methods and can be used to study precise cell mechanical operation and cell characteristics in the future.
3.3. Optic Control

Because of their technical characteristics including flexibility, easy to integrate, easy to be combined with other manipulation and detection technology, OT and OET for microfluidic chip laboratory and cell control have become a global hot spot in recent years. Especially in biological science, nanotechnology, and micro–nano manufacturing, a wide range of application

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Figure 6. Recent research and applications of acoustic control. A) Acoustic controlled RBC-PL-robot for removal of pathogenic bacteria and toxins. Reproduced with permission.\textsuperscript{[115]} Copyright 2017, ACS. B) Acoustic controlled rotation of microbeads and oocytes. Reproduced with permission.\textsuperscript{[116]} Copyright 2019, AIP. C) Acoustic controlled nanoswimmer for propulsion to maneuver micro-/nanosized objects. Reproduced with permission.\textsuperscript{[118]} Copyright 2019, ACS. D) An untethered ultrasound-controlled actuator for targeted drug delivery. Reproduced with permission.\textsuperscript{[119]} Copyright 2019, Springer Nature. E) Acoustic controlled micro rotor in PDMS channel for microelectromechanical systems. Reproduced with permission.\textsuperscript{[120]} Copyright 2020 Wiley. F) Ultrasound control surface actuator for flexible endoscope. Reproduced with permission.\textsuperscript{[121]} Copyright 2020, Wiley.
proposed. In addition, OWT because of its low power, low energy consumption, and flexible control pattern characteristics have gained immense traction in the biological field for cell analysis, screening, physical quantity measurement, DNA molecular genetic manipulation, pathological detection, and drug efficacy detection. Advances in micro–nano manufacturing can promote further development of micromechanical assembly technology.

OT can be used for noncontact manipulation of nanoscale objects, but there are high requirements for material types that can be captured. Būtaitė et al.\[123\] put forward an optical trapping platform combined of optics and hydrodynamics, reduce the requirement for material type, in vivo biological specimens using optical tweezers, as shown in Figure 7A. The image shows the principle of controlling a single target. Light is used to control the rotation of the microrobot to form a local fluid motion flow field. The coupling of the flow field traps the target particle, and the movement of target particle in the flow field is fed back to the control driven by the microrobot; thus a closed-loop control is formed. The results are highly innovative in terms of control technology, and can be used to expand the optical tweezers platform in the future, to stabilize and study biological systems in minimally invasive technology.

There are different difficulties in using light-controlled micro–nano robots in blood vessels and in water. The physiological environment in blood vessels is a fluid environment with high viscosity. It is still a great challenge to drive micro–nano robots at a high speed in a viscous medium. Li et al.\[125\] put forward a new kind of micro stage rocket type robot, which uses all-optical drive and can be driven in the bloodstream with the resolution of the microscale, as shown in Figure 7B. The rocket-shaped structure gives it high driving force and moving speed, and the optical imaging system developed can also track the micro–nano robot in the blood flow, which solves the positioning problem of the micro–nano robot after entering the human body. The research results are highly innovative in the design and positioning of microrobots, which could broaden the application range of micro–nano robots in the biomedical field in the future.

An important concept of robotics is the ability to achieve multifunctional changes and perform complex and diversified tasks according to operational requirements, and this is no exception for micro–nano robots. To achieve high biocompatibility for light-controlled microrobots in complex environments, Xin et al.\[122\] recently proposed an optically controlled algae microrobot capable of performing multiple tasks and working efficiently in coordination and synchronization, as shown in Figure 7C. The central beam is constructed to capture the light trap, the boundary of the beam and the curved red arrows are constructed to create the annular scanning light trap. The small diagram on the right is 2D, with the red dots representing the light trap, where the flagellum of both arms replaces the function of the process work, and performs complex tasks. The research results are highly innovative in terms of robot structure, and can be used in in vitro biomedicine such as target manipulation and biological aggregate removal in the future.

Although the light-controlled robot can achieve several functions, it has certain limitations, for instance, the stability of driving smaller targets, the high requirements of driving and control software when driving parallel, etc. These have facilitated the development of the OET technology. Zhang et al.\[124\] proposed an OET-controlled microrobot that uses light to generate dielectrophoretic force instead of photonic force, thus produces stronger force for manipulation. The optical control system adopted in the control process is generated by an optical projector, which greatly reduces the cost consumption and makes the parallel operation simple and feasible. As shown in Figure 7D, the microrobot is simple and easy to manufacture with unlimited shape, and can be programmed to carry out complex multi-axis operation with less damage to cells. The results show that the design and control techniques of micro–nano robots are convenient and highly innovative, which can be widely used in the future micro-manipulation of cells. The manipulation of cell and other biological micro–nano robots is a revolution of field-controlled robotics and has increasingly gained importance in the field of biomedicine.

Based on the characteristics of noncontact field control in optical induced dielectrophoresis, OT can manipulate micro–nano particles in parallel under low intensity light; thus, it plays a greater role in noncontact micro–nano assembly scenarios. Using this feature, Lim et al.\[123\] proposed a self-assembly method of graphene oxide sheets based on OET control, as shown in Figure 7E. The arrangement of graphene sheets and programming of various patterns can be customized, and the control method of OET is simple and easy to implement. The results of this study are highly innovative in terms of control targets and control techniques, which may increase the possibility of the future application of graphene in energy storage and other fields. In addition, as a label-free, nondestructive, light-inducing technique, optoelectronic tweezers are often used to manipulate cells, but are limited to microfluidic chips. Zhang et al.\[122\] recently isolated cancer cells from normal epithelial cells using OET, as shown in Figure 7F. This label-free technique preserves the integrity of cell membrane and activity during the isolation and characterization of gastric cancer cells. The method has high sensitivity, and it is the first time that the OET method has been applied to the separation of clinical gastric cancer ascites samples. In addition, the control platform is equipped with the cell membrane capacitance testing technology, which can quickly detect the cell membrane capacitance during the process and serve as a biomarker for determining the status of cancer cells. The research results are highly innovative in terms of control technology, and can be applied to the future research on the mechanism of cell membrane metastasis of gastric cancer and the subsequent research of cancer cells.

### 3.4. Control by Multiple Fields

OT can be used to capture and manipulate moving microorganisms, however, high-intensity lasers can cause light damage, and the optical equipment is complex and expensive. Magnetic tweezers do not cause additional damage to biological targets but require the target to have additional magnetic tags. Acoustic tweezers are often used to accurately capture static organisms, but the ability to capture dynamic organisms has not been demonstrated.\[124\] Each capture method has its own advantages, but at the same time, they also have some limitations. With the development of micro–nano manufacturing technology, the
combination of multiple field control modes has piqued the interests of researchers. Two or three fields can be combined to control different functions, respectively, for precise and complex tasks.

Owing to the popularity of photodynamic therapy in tumor therapy, the multiple field-controlled drive mode of photomagnetic field emerged and was applied. First, both magnetic control and light control can be used as power systems, and the hybrid...
control of microorganism transportation can reduce the damage of microorganism caused by light and meet the requirement of magnetic field intensity. Second, using magnetic control as the power system and optical control to control the release and therapeutic effect of drugs, the multiple field-control system offers great advantages in its applicability. Zhong et al. have proposed a photosynthetic biological hybrid magnetic microswimming microrobot as a new strategy for targeted therapy, as shown in Figure 8A. The magnetic material acts as an actuator for directional motion and as a contrast agent for magnetic resonance imaging. CD-ROM drive is the treatment method, and the photosensitizer carried by the microrobot can produce cytotoxic reactive oxygen species under the irradiation of laser, thus inhibiting the growth of tumor. At the same time, the special photosensitizer proposed in this article can also assist fluorescence imaging, which can be used to image tumor microenvironment and detect the therapeutic effect of tumor. The results of this study are highly innovative in terms of driving mode and micro–nano robot structure, which can be used in the future for tumor diagnosis and synergistic targeted therapy. The light source can not only be used as the power source of drug release to assist the therapeutic effect of micro–nano robots, but also can be used as the driving source of motion, which can cooperate with other external fields to generate greater propulsion force and accomplish more complex tasks. Villa et al. proposed a magnetic/optical cooperatively driven propulsion microrobot that can be used to push and capture yeast cells, as shown in Figure 8B. The surface of the microrobot is coated with magnetic nanoparticles for driving the magnetic field. Due to the photocatalytic nature of the design of the microrobot, it can produce strong photo-mobility under visible light irradiation, and then produce greater swimming ability to push yeast cells. The research results are innovative in terms of the structural design and application scenarios of microrobots, and the proposed autonomously propelled microrobots open up new application possibilities in the field of food.

Remote manipulation and directional movement in complex biological fluids are the focus of research on micro–nano robots. Bioactive microrobots are promising candidate technologies. Aiming at this technology, Xing et al. proposed a biological hybrid microrobot, which used the hybrid control mode of magnetic field drive and light field trigger to achieve the targeted treatment of tumor, as shown in Figure 8C. The magnetic structure was designed by clustering control method to improve the enrichment degree of the microrobot in the tumor site. The on-demand light-controlled structure design realizes the laser irradiation of tumor hyperthermia, which can eliminate tumor and reduce the potential side effects. Furthermore, after the completion of the treatment task, the microrobot can be removed by laser hyperthermia of other modes, thus reducing the side effects of biological residues on the human body with good biological safety. The research results are innovative in the material design of microrobots and have high application value in the remote control and directional transport of biological circulation system in the future.

Due to the poor tissue penetration ability, it is difficult to operate and guide photo-controlled drug release in vivo, and high light intensity is easy to cause damage to biological tissues. In addition to photomagnetic hybrid drive, acoustic magnetic hybrid drive is another research hotspot. Compared to optical tweezers, acoustic and magnetic tweezers have significant advantages in terms of biocompatibility and depth of penetration, and as a biocompatible energy, acoustic field driven by microswimmer tends to move faster than magnetic field and can be implemented in simpler devices. Magnetic field can often provide more convenient steering control. Ren et al. proposed a kind of micro–nano robot based on acoustic dynamic bubble, as shown in Figure 8D. Driven by acoustic wave, great propulsion speed can be generated. Driven by magnetic field, the direction and mode of motion can be controlled to produce autonomous motion in 3D space, which is acoustic/magnetic dual field control mode. The microswimmer has been developed with high control accuracy and close control to perform complex tasks in a multiphase biological environment. The research results are highly innovative in terms of the control mode and the structure of the microrobot, and the multifunctional micro–nano robot control technology may play an important role in the advanced biomedical research and clinical treatment in the future. Similarly, Aghakhani et al. put forward a kind of acoustic/magnetic hybrid driven bubble micro robot. As shown in Figure 8E, bubbles generate resonance through sound waves to drive them horizontally at high speed. The surface anisotropy is coated with soft magnetic nanofilms to provide the steering ability for the microrobot driven by the magnetic field. Different from the research of Ren et al., the magnetic field here only provides steering drive rather than forward drive, and the sound field alone can produce a high propulsion speed. The research in Figure 8E mainly uses the interaction between the microrobots near the wall to generate high acoustic driving force and driving speed. The research results are innovative in terms of robot structure design and driving mode, and can be applied to drive and navigate the microrobots into the restricted position of the organism with minimum invasion. Similar bubble-assisted fluid assembly methods have also been used to fabricate microvascular structures of different shapes.

Due to the strong influence of sound field on microstructure and microfluidics, voice control is minimally invasive and biocompatible in targeted therapy, resulting in many combination modes of sound field and magnetic field. Park et al. recently proposed a magnetically driven porous spiral microrobot. The encapsulated magnetic nanoparticles are used to achieve wireless drive in a rotating magnetic field. The porous structure design can respond to acoustic field control, release drugs in different modes, and achieve a high cancer treatment effect, as shown in Figure 8F. Different from the aforementioned light-controlled drug release, the voice-controlled drug release here can produce a higher tissue penetration ability, and improve the release speed, concentration and stability of the drug without damaging the biological tissue, so as to achieve a higher therapeutic effect. The research results are highly innovative in terms of control mode, which lays a foundation for microrobot as a targeted drug delivery platform for ultrasound-assisted drug release control.

To better understand the characteristics and innovations of recent research progress, we summarized the above content into Table 2. In the process of publishing our papers, more advanced technology and research progress continue to be published. For instance, Liu et al. proposed a new structure to realize magnetic micromanipulation. Bai et al. proposed a new acoustic field structure to realize efficient capture of tumor cells. Chen
Figure 8. Recent research and applications of multiple fields control. A) Dual magnetic/optic powered hybrid microrobots for radio-photodynamic synergetic therapy. Reproduced with permission. Copyright 2020, Wiley. B) Dual magnetic/optic-powered hybrid microrobots for preventing microbial contamination in beer. Reproduced with permission. Copyright 2020, Springer Nature. C) Magneto-actuated and optic triggered bio-microrobots for targeted cancer therapy. Reproduced with permission. Copyright 2020, Wiley. D) 3D steerable acoustically powered and magnetically steered microswimmers for single-particle manipulation. Reproduced with permission. Copyright 2019, AAAS. E) Acoustic powering and magnetic steering for actuating and navigating microrobots. Reproduced with permission. Copyright 2020, PNAS. F) Acoustically mediated, magnetically powered and laser-synthetic microrobots for targeted therapy. Reproduced with permission. Copyright 2020, Wiley.
Table 2. Characteristics and innovations of recent research on field-control.

| Field       | Characteristics and innovations                                                                                                                                   | Applied direction                      | Ref. |
|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|------|
| Magnetic    | Realized high and fast cooperative transport of multiple objects. Innovative control mechanism.                                                                 | Non-contact drug loading control.      | [43] |
|             | Realized the drilling of artificial thrombus in a 3D space. Innovative robot structure, and precise operation.                                                      | Effective vessel operation.            | [107]|
|             | Realized simple and programmable control of liquid droplets using a steel ball. Innovative control methods.                                                       | Material transportation.               | [108]|
|             | Realized complex shapes and operations of liquid microrobot. Innovative cluster control mechanism.                                                              | Target delivery.                      | [110]|
|             | Realized the control of hydrogel microrobot. Innovative assembly of two magnetic systems and recovery of microrobots.                                            | Drug delivery.                        | [111]|
|             | Realized assemblies of multiple magnetic systems and multidirection anticancer. Innovative structure.                                                            | Targeted therapy.                     | [112]|
|             | Realized efficient propulsion performance therapy effect in a rotating magnetic field. Innovative structure and control speed.                                | Targeted delivery.                    | [57]  |
|             | Realized biocompatibility, degradation and therapeutic effects of cell microrobot. Innovative high magnetic field and in vivo experiments.                   | Targeted precision therapy.           | [114]|
| Acoustic    | Realized multi-degree-of-freedom control of endoscope-structured microrobot. Innovative structure control mechanism.                                              | Minimally invasive surgery.           | [115]|
|             | Realized rotation of microbeads and oocytes. Innovative control mechanism.                                                                                     | Single cell analysis.                 | [106]|
|             | Realized instant communication and directional transportation with high precision. Innovative control method.                                                    | Micro-cell analysis factory.          | [118]|
|             | Realized operation of drug particles and move within human body. Innovative control mechanism.                                                                  | Targeted drug delivery.               | [119]|
|             | Realized multicore of soft micromechanical structure. Innovative structure and control method.                                                                    | Targeted therapy.                     | [120]|
|             | Realized cell control on micro scale. Innovative control method.                                                                                               | Precise cell manipulation.            | [121]|
| Optic       | Realized closed-loop control of fluids and optics. Innovative control method.                                                                                   | Minimally invasive technology         | [86]  |
|             | Realized all-optical drive and positioning in bloodstream. Innovative robot structure.                                                                           | Biomedical therapy.                   | [87]  |
|             | Realized efficient coordination and synchronization of multitask control. Innovative robot structure.                                                           | In vivo target manipulation.           | [122]|
|             | Realized the use of light to generate dielectrophoretic force. Innovative control mechanism.                                                                    | Biomedicine.                          | [85]  |
|             | Realized programming control of graphene oxide sheets. Innovative control mechanism.                                                                              | Energy storage.                       | [123]|
|             | Realized isolation and characteristic calibration of cancer cells. Innovative control platform.                                                                  | Single cell analysis.                 | [89]  |
| Multiple    | Realized dual functions of driving and imaging through magnetic and optical control. Innovative control mode and robot structure.                                 | Targeted therapy.                     | [126]|
|             | Realized push and capture of yeast cells through magnetic and optical controls. Innovative robot structure.                                                       | Food.                                 | [127]|
|             | Realized targeted treatment of tumor using a biological hybrid microrobot. Innovative material design.                                                            | Directional transport.                | [128]|
|             | Realized precise motion in 3D space through acoustic &magnetic controls. Innovative control mode and robot structure.                                               | Clinical treatment.                   | [98]  |
|             | Realized high driving force and speed through acoustic and magnetic control. Innovative robot structure and driving mode.                                        | Minimum invasion.                     | [96]  |
|             | Realized high release speed and concentration of drug through acoustic and magnetic control. Innovative control mode.                                               | Targeted therapy.                     | [112]|

et al.\cite{135} realized a control of ferrofluid-based robot with high motion accuracy, and high measured output force. Tanyong Wei et al.\cite{136} proposed a magnetic controlled microrobot with simultaneously improved degradability and mechanical strength through innovative structure design.

4. Discussion

This article reviews the recent research progress of micro–nano manipulations and micro–nano robots driven and controlled by physical fields (magnetic, acoustic, and optical fields), mainly surrounding the application prospects of micro–nano robots in biomedical field. By comparing these three driving methods, we can find that: 1) magnetic field does not cause additional injury to the biological objectives but require the objectives to have an additional magnetic tag; 2) acoustic field is often used to accurately capture static organisms but the ability to capture dynamic objectives needs to be further verified;\cite{124} 3) optical field can be used to capture and manipulate the moving micro-organism but the high-strength laser could cause light damage, and the optical equipment is both complex and expensive; Compared to optical control, magnetic and acoustic controls have significant advantages in biocompatibility and depth of
penetration. As a biocompatible power source, acoustic control could generate faster speed than magnetic control. Magnetic control could often provide more convenient steering manipulation. Each manipulation method has its own advantages and limitations. Aiming at the pursuit of precise and complex tasks, future research will mainly focus on the way of multiple-fields control. Current observation in vivo is still a very tricky challenge. Traditional imaging methods have limitations, for instance, ultrasound technology has low resolution, magnetic resonance imaging (MRI) technology cannot achieve real-time imaging, CT and other related methods have large radioactivity, barium meal, and other gastroscopic methods have great human discomfort. Magnetic particle imaging (MPI) may become the next technology to solve the problem of real-time observation in vivo. Integrating MPI and magnetic control system to realize precision and real-time observations in vivo will be an important area. There is less related research, and special attention is needed in the future. In the next step, the driving mode of physical fields has a lot of space to study from the perspective of multifield combination, such as various acousto-optical and electromagnetic couplings, which can achieve more accurate control and human–computer interaction. In addition, solving the problem of real entry into the human body in the field of bio-based materials is also a direction that requires special attention.

Precise delivery of micro–nano robots to the desired site in vivo is very important in precision therapy. When referring to the application of micro–nano robots in biological treatment and diagnosis, biocompatibility and degradability are issues that must be discussed together. Biocompatibility ensures that the micro–nano robots can enter the in vivo environment, and the degradability ensures the safety of the in vivo after the micro–nano robot completes its task, and the two complement each other. The current research on bio-based micro–nano robots guarantees its biocompatibility, but the degradability is still not an easy-to-achieve operation. Therefore, most of the current micro–nano robots are generally biocompatible but not degradable, and therefore their application in clinical treatment is limited.[117] Biocompatible materials have been developed into synthetic polymer materials, proteins and DNA, etc. Some researchers are also trying to use composite materials with special structures or extractions to test the degradability of micro–nano robots in vitro,[118–140] but there are not plentiful related studies. Research in this field is still in the early stages of development, and is therefore an area that urgently needs to expand research efforts in the future. In addition to solving the problem of exploration of biodegradable materials, it is necessary to consider whether or not the rate of degradation and degradable products are good in biocompatibility. Yang et al.[141] recently reported a magnetic microswimmer with biocompatible and biodegradable components. On the other hand, because of the advantages of insensitivity to biological tissues, precision control and positioning, magnetic fields have become the preferred driving source for biodegradable micro–nano robots.[142]  

5. Conclusion

The research shows that energy field driving technology and intelligent material technology are widely used in the field of microrobots. In energy field driving technology, magnetic control has attracted more and more attention because of its advantages such as convenient control method, large output force, no direction and relatively easy generation. In contrast, light waves, microwaves, and ultrasonic waves are highly directional and limited in application. Moreover, when applied to medical examination in vivo, they have certain side effects on organism. Micro–nano robot system is a structural unit integrating sensing, control, execution and energy. It is the results of the cross integration of computer, material, machinery, electronics, control and biomedicine and other multidisciplinary technologies, which is characterized by small structure size, precise devices and micro-operation. In the future, the main development and research directions of micro–nano robots include: reducing energy consumption, simplifying structure, large displacement output and force output, excellent performance of wire control, small size, and little response time.

Acknowledgements

The authors thank the National Natural Science Foundation of China (Grant No. 52005019), the National Key R&D Program of China (No. 2019YFB1309700 and No. 2019YFB1309702), the Beijing Nova Program of Science and Technology (Grant No. Z19110000119003), and China Postdoctoral Science Foundation (Grant No. 2019M650419).

Conflict of Interest

The authors declare no conflict of interest.

Keywords

biomedicine, field control, microfluidics, micro–nano manipulation, micro–nano robots

Received: June 10, 2021
Revised: August 26, 2021
Published online: November 5, 2021

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