Emerging Micro/Nanomotor-Based Platforms for Biomedical Therapy

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Highly efficient and versatile natural motors play a pivotal role in biological processes. Inspired by these biological motors, researchers developed their synthetic counterparts that can convert various energies into locomotion. With the potential to revolutionize the biomedical treatment process, these micro/nanomotors have been attracting a booming research enthusiasm since the birth of the first micro/nanomotor 15 years ago (since 2004). First, typical motion mechanisms are elucidated and a detailed comparison is provided regarding their efficiency in a biological context. Next, cutting-edge proof-of-concept biomedical applications of the motors are overviewed, including on-demand drug dispensing, cell transporting, and precise microsurgery. Current achievements and remaining bottlenecks are discussed, to spur more collaboration among chemistry, nanoengineering, and the biomedical fields. With increasing attention and continuing innovation of the field, clinical translation of micro/nanomotors is possible in the next 15 years.

1. Introduction

Natural motors that can convert fuels into mechanical motion,[1] accomplishing complicated function have attracted and amazed the public and researchers for a long time. As early as in 1966, people envisioned a miniaturized submarine that can sail in human blood and perform delicate mechanical work in the movie Fantastic Voyage. Yet, for actual versatile synthetic micro/nanomotors that would enable the therapeutic process at micro/nanoscale, it was not until 2002, the artificial micro/nanomotors prototype, or “catalytic boat” at centimeter scale, was developed by a pioneering team at Harvard University. [2] After that, Sen and coworkers [3,4] at Pennsylvania State University reported the first catalytic micro/nanomotors in 2004. [5,6] In general, a motor is a micro/nanodevice that converts chemical, optical, acoustic, or other forms of energy into mechanical motion and performs complex tasks. [7] In terms of the energy sources, motors can be classified as chemically propelled [8,9] and nonchemically propelled [10-12] motors (Figure 1).

For chemical-driving motors, metal/enzyme-catalyzed chemical reactions or surface decomposition of local fuel is relied. These local fuels include hydrogen peroxide (H2O2) [13] and glucose [14] whereas for nonchemical (external field)-driving motors, micro-ultrasonic [15] light [16,17] magnetic field [18] and electric field [19] provide the energy input. With an attempt to counterpart the natural motors, researchers set out to explore possible biofunctions of these micro/nanomotors. Yet, after 15 years of exploration of the field, it is now understood that not all mechanisms are suitable for each biomedical application, which means there is an application scope for a certain type of micro/nanomotors. For instance, typical self-electrophoresis-powered motors are asymmetry conductive bimetallic rods, which are rigid and can interfere with the flow of the bloodstream. Self-diffusiophoresis propulsion will be severely attenuated in highly concentrated biofluid. Bubble-propelled micro/nanomotors may present potential harm of gas embolism despite their advantage in relatively high velocity. For external-field-driven motor without the concern of fuel/product compatibility and environmental impact, they demonstrate relatively good biocompatibility and robustness. However, there are also some concerns. For example, for light-driven motors, it is less powerful with deep tissue application when compared with their magnetically driven counterparts, as light penetration ability is limited. Therefore, an in-depth analysis of the motor mechanisms in the context of their application scopes is presented as the first section of this review, followed by showcasing the state-of-art biomedical applications of the micro/nanomotors in Section 3. In this part, representative micro/nanomotors exhibiting a great versatility and distinct advantages in various biomedical applications are shown. These advantages rely upon the efficient propulsion capability of the motors. Such propulsion at a remarkable speed, can significantly shorten the time cost and increase the efficiency of cargo delivery (such as drug, gene, and protein), as well as sensing, detoxification, etc. Yet, challenges remain. Insufficient propulsion in biofluids, limited biocompatibility, and biodegradability are still roadblocks that lie ahead.

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Therefore, in the end, we provide an overview of the recent progress of micro/nanomotors in both mechanisms and biomedical applications, including drug delivery, cell transportation, biosensing, detoxification, surgery, and separation, as well as providing an insight into the limitations of this field. With this, we hope to attract multidisciplinary attention to address the field challenges and accelerate the development of this booming field in the next 15 years.

2. Motion Mechanism

The propulsion mechanisms of micro/nanomotors have a great impact on their velocity, locomotion efficiency, and environmental compatibility. All the aforementioned factors will thus influence their performance in biological environment significantly. Therefore, in this section, we will discuss the motion mechanisms based on the energy sources (chemical propulsion, nonchemical/external field propulsion) and provide a detailed analysis of their efficiency in the biological context.

2.1. Chemical-Driven Motor

In general, chemical-driving motors consist of two components: an active (mostly catalytical) part and an inactive segment. At the surface of the active segment, a chemical or biochemical reaction is induced, ensuring a gradient force around the active-inert Janus structure and leading to propulsion. Herein, we present three typical chemical-driving micro/nanomotors: self-electrophoresis-, self-diffusiophoresis-, and bubble-driven motor systems.

2.1.1. Self-Electrophoresis-Driven Motor

Self-electrophoresis propulsion is due to a local microelectric field generated within an asymmetric conductive bimetallic rod motor. The bimetallic motor acts as an independent electrochemical battery, with one metal end serving as the anode and the other as the cathode. One of the earliest self-electrophoresis-driven motor was proposed by Paxton et al.\textsuperscript{[14]} They devised a platinum/gold (Pt/Au) nanorod motor (370 nm in diameter and \textapprox 2 \mu m in length). The propulsion is due to the electrochemical decomposition of H\textsubscript{2}O\textsubscript{2} at the platinum (anode, oxidation reaction) and gold (cathode, reduction reaction) ends of the rod. A local microelectric gradient was generated from the oxidoredox reaction and a migration of electrons/ions was induced on the rod’s surface. The electrons can migrate from Pt side to Au side, while propelling the Pt–Au nanorod motor to move with Pt as head and Au as tail. After that, Wong and Sen\textsuperscript{[15]} fabricated bimetallic rod Ag/Pt nanomotor, which utilized the reversible reaction between silver and iodide (I\textsubscript{2}). When Ag was converted to AgI, the Ag/Pt nanorod was propelled (Figure 2A). On the surface of the nanorod, the side of negatively charged could cause electro-osmotic fluid flow. Such fluid flow along the rod was consistent with the direction of the electric field (Ag to Pt). In 113 \mu m, Ag/Pt nanorod could move at the speed...
of 20 μm s⁻¹. Compared with previous motor of Au-Pt/H₂O₂, Ag-Pt/I₂ motor demonstrated higher efficiency. The self-generated electric field propels the charged rod in a similar process as “electrophoresis,” thus termed as self-electrophoresis.

Later, researchers set out to explore the speed-influencing factors of these self-electrophoresis-driven motors. Paxton et al. [8] experimentally showed that current could be produced between Pt plated- and Au-interdigitated microelectrode in H₂O₂ solution or H₂O₂/ethanol mixture solution. They found that the current density decreases with the lowering of H₂O₂ concentration. With an increase in ethanol concentration, there was a decrease in the catalytically generated current density and the speed of bimetallic nanorod. With increasing of ion concentration and solution conductivity, the velocity of motors sharply decreased. Such current density, along with the bulk solution conductivity, determining the efficiency of electric field, was found to have a significant influence on the migration speed of motors. In biofluids, solution conductivity is relatively high; therefore, the moving ability of the self-electrophoresis-driven motor is severely impaired. More importantly, researchers [39] could calculate the speed of prolate spheroidal nanomotor induced by self-electrophoresis. They proved that motor speed was dependent on the motor shape. What is more, theoretically, calculation of speed they proposed could be applied for spherical and rod-like shape. Based on this, a new strategy occurred that the velocity of nanomotor propelled via self-electrophoresis could be controlled by the shape of nanomotor.

In addition to the factors influencing speed, the factors determining moving direction are also investigated. Wang and coworkers [39] fabricated a variety of bimetallic nanorods, such as Au–Pt, Ni–Au, Pd–Au, Pt–Rh, and Ru–Au nanorods via electroplating method. The group determined the anode–cathode and potential by comparing the H₂O₂ reaction rate for each metal (Au, Pt, Rh, Ni, Ru, and Pd). In general, the electrons flow from anode to cathode. The motion direction was found to be always opposite from the electrons flow direction (i.e., for the Au–Pt motor, the Pt end move forward while the electrons flow from anode Pt to cathode Au) for the bimetallic nanorod motor systems. These findings in principle allowed prediction of the motion direction for all combinations of bimetal. They also demonstrated that single metal rod motor based on (poly(pyrrole)-Au nanorods (Ppy-Au) exhibited only Brownian movement in H₂O₂ solutions, giving support to electrochemical propulsion mechanism (self-electrophoresis) for bipolar metal motors.

2.1.2. Self-Diffusiophoresis-Driven Motor

For the self-diffusiophoresis-powered motors, the reaction products accumulate at one side of asymmetric motor, which leads to a concentration gradient between the active/inert side, thus inducing product outer diffusion and propulsion. Compared with the aforementioned self-electrophoresis-powered motors, self-diffusiophoresis-driven motors can also possess asymmetric structure (yet, not necessary). For self-electrophoresis-driven motor, asymmetric bimetallic rods are needed, whereas for self-diffusiophoresis-driven motor, just one metal or one active material was required. In addition, for propulsion, the self-electrophoresis-driven motor generated a local micro-electric

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Figure 2. Representative examples of chemical-driving motor. A) Self-electrophoresis-driven motor. The reaction between Ag and I₂ generating electron formed micro-electric field. Reproduced with permission [35] Copyright 2016, American Chemical Society. B) Self-diffusiophoresis-driven motor. Urea as fuel was decomposed to CO₂ and NH₃ in the presence of urease. Reproduced with permission [36] Copyright 2016, American Chemical Society. C) Bubble-driven motor. a) The Mg-based micromotor in gastric fluid-generated hydrogen to propel motor motion. b) Images for the propulsion of the Mg-based micromotors taken at 2 min interval. Reproduced with permission [37] Copyright 2017, Nature Publishing Group.
field which was lacking in the case of self-diffusiophoresis-driven motor. With these, one could differentiate the self-diffusiophoresis-driven motor from the self-electrophoresis-powered motor.

As mentioned earlier, for self-diffusiophoresis-driven motors, a concentration gradient is derived from a chemical reaction on the motor surface: the depletion of reactants and the accumulation of products. The outer diffusion of the self-generated products (can be ionic or nonionic) induced locomotion of the motor, which is called self-diffusiophoresis. The diffusiophoresis phenomenon was first observed by Ebel et al.[40] In their experiment, 0.1 μm diameter polystyrene latex spheres were placed in an electrolyte solution (lithium chloride, sodium chloride, or potassium chloride). By creating an electrolyte concentration gradient, the accumulation of particles at one side and the depletion at the other side was observed, thus diffusiophoresis.

For self-diffusiophoresis-driven motor, the solute gradient is self-generated from reaction, therefore, termed as “self-diffusiophoresis.” One typical example of this type of motor was developed by Kagan et al. They prepared Au microparticles (MPs) motors of 0.8–1.5 μm and shape of disk.[41] The movement was induced by a local product gradient from the Au-catalyzed hydrazine and H₂O₂ decomposition. Near the catalytic Au surface, the decomposition of hydrazine and H₂O₂ led to accumulation and outer diffusion of ionic products (H⁺, N₂H₃⁺, and OH⁻ ions). Such diffusion induced the autonomous motion of Au MPs. The Au MPs speed can reach 16 μm s⁻¹ in the H₂O₂/hydrazine solution.

In addition, Au MPs, a 2 μm-diameter Ag₃PO₄ MP was also reported to be propelling in NH₃ solution via self-diffusiophoresis.[42] In NH₃ solution, Ag₃PO₄ MPs can generate ions, such as OH⁻, HPO₄²⁻, and Ag(NH₃)₂⁺. It was the outer diffusion of such ions (self-diffusiophoresis) that drove the Ag₃PO₄ MPs. Interestingly, the movement of particles can be induced by both the concentration gradient generated from themselves or their neighbors. In addition, the reaction and dispersion/clustering of these ions are reversible, enabling the motor system to act as a NOR logic gate with NH₃ as input. In the presence/absence of NH₃ light, the transition of expulsion and attraction between Ag₃PO₄ MPs can be realized. Other typical examples of self-diffusiophoresis-driven motors involve enzyme-powered motors, the diffusion of enzyme reaction products is responsible for propulsion. With the degradability and naturally occurring feature, enzyme-driven motor is regarded as one of the most promising biocompatible motors. Researchers already explored the use of urease, glucose oxidase (GOx)/catalase (Cat)[14], and lipase[43] as the catalytic component of motors. For example, urease-functionalized Janus hollow mesoporous silica microparticles (JHPS)[36] was fabricated (Figure 2B). The decomposition products (CO₂ and NH₄) of urea by urease, could generate a concentration gradient at the surface of JHPS, consequently power the motion of JHP-urease (self-generated diffusiophoresis). Such micromotors propelled by biologically available urea are of full biocompatibility, which are attractive for biomedical application.

In general, biofluids such as blood, urea, and lymph fluid, consist of high level of electrolytes, proteins, and sugars. Yet to be noted, for self-diffusiophoresis-driven motors, the presence of high-concentration solute/electrolyte can interfere with the self-generated solute gradient, thus undermining the moving abilities.[44] The impaired moving and performing abilities of self-diffusiophoresis-powered motor in biological environment present a hurdle for practical bioapplications. Exploring motors powered via two or more (less affected) mechanisms may alleviate this problem.

2.1.3. Bubble-Driven Motor

Bubble propulsion could be realized by gas-generating reactions taking place at the surface of micro/nanomotors. In most trials, H₂O₂ was chosen as chemical fuel, which can be decomposed into oxygen. Once exceeding solubility limit, oxygen bubbles are produced, inducing propulsion. Kovtyukhova[45] placed catalytic bimetallic (Pt and Rh) nanorods of 2–7 μm long in a H₂O₂ solution (3–30 wt%) and observed directional motion of the motors. It was found that the oxygen bubbles evolved from the rod surface. With the departure of oxygen bubbles, the momentum exchange between such a “tilted” rod and water flow can drive the directional movement of the rods.

In addition, rod motor, rolled-up Ti/Fe/Pt (10/5/2 nm thickness, respectively) microtubes could also be powered via microbubbles. This motor system was fabricated by Schmidt and co-workers.[46] Ti is a substrate and Pt is the catalyst to decompose H₂O₂ to O₂ bubbles. Cargos such as polystyrene (5 μm in diameter) and Tj/Fe/Pt nanolopes (25 nm thick and 50 μm wide) could be transported by these microbots in 5 wt% H₂O₂, 0.005% surfactant and 1 vol% isopropanol (for decreasing surface tension of H₂O₂) solution. The group found that with higher concentration of H₂O₂ (such as 15 wt%), the O₂ bubbles could be generated at a high bubble frequency (f = 38 Hz). Conversely, bubbles were generated with a lower frequency (f = 8 Hz) with lower fuel concentration. Higher bubble frequency can result in improved moving speed and performance.[47] The speed is also relevant with the cargo amount. With increased cargos, the speed of the microtubes experienced a decline from 80 to 18 μm s⁻¹ as the resistance increased. The incorporation of Fe in the system allowed guided motion by external magnetic field. However, a disadvantage of this system is the use of nonbiodegradable materials.

Other factors that influence the motor speed include external stimuli. Ultrasound field was also found to have a direct effect upon the evolution of the oxygen microbubbles, capable of rapid and reversible motion control of microengine. The presence of an ultrasound field can disturb the evolution of bubbles[48] at the opening of the tubular micromotors, which can result in greatly hindered bubble propulsion.

Temperature can also be used as a stimuli to control the on/off of motion.[9] Tu et al. fabricated a Pt-loaded bowl-shaped polymeric vesicle nanomotor. They functionalized the nanomotor with a temperature-responsive poly (N-isopropyl acrylamide) (PNIPAM) polymer brush via surface-initiated atom-transfer radical polymerization (SI-ATRP). The lower critical solution temperature (LCST) of PNIPAM is determined as 35 °C. When the temperature is above the LCST of PNIPAM, the PNIPAM brushes are hydrophobic and inhibit the entry of fuel into the catalytic position of bowl-shaped polymeric nanomotors. When the temperature is below the LCST of PNIPAM, the PNIPAM brushes are switched to hydrophilic state and allow
the catalysis reaction, thus the bubble release for propulsion. Therefore, the on/off of nanomotor can be reversibly controlled.

In addition to O₂ bubbles, H₂ bubbles can also propel motors. Micromotor, composed of TiO₂-coated Mg (20 ± 5 μm in diameter), was proposed. The micromotor was propelled by the H₂ bubble from the reaction of Mg and gastric fluid (Figure 2C). The speed of Mg-based micromotors could reach up to 120 μm s⁻¹, which is remarkable when compared with self-electrophoresis or self-diffusiophoresis motors.

In 2012, a water-powered Ti-Al/Ga Janus micromotors were developed. The motor system was propelled by hydrogen gas generated from H₂O-splitting reaction. The evolution of hydrogen bubble provided strong propulsion, leading to a linear movement with a speed of 3 mm s⁻¹. Such motor was obviously faster than that of particles propelled by H₂O₂ decomposition, whereas the use of biofriendly water as fuel represents an important step toward biocompatible motor system. Yet, the release of the Al⁺⁺ (which may cause renal or other organ dysfunction), from the reaction needs more attention.

As mentioned earlier, the bubble-powered motor is characterized with a high speed and suffer little from biological medium. Compared with motors propelled by self-electrophoresis and self-diffusiophoresis, which could be paralyzed in a high ionic strength biological medium, motors induced by bubble propulsion are advantageous, showing potential for realistic biomedical application. However, the potential harm of introducing bubble-propelled motors into the blood stream should be cautioned. The accumulation of gas bubbles may cause unwanted embolism.

2.2. Nonchemical (External Field)-Driven Motor

In this section, external field-driven (fuel free) micro/nanomotors will be covered. These types of motors can circumvent the potential toxicity posed by chemical fuels and the problem of local fuel shortage. In addition, the constant external input ensures the robustness of the motor system. This is because the energy conversion process of the external-powered systems is more independent from the local environment. The systems are less influenced by the ion/solute species in the biological environment. In addition, fuel-free micro/nanomotors exhibit advantages of high controllability, long lifetime, and relatively good biocompatibility. In the following sections, we will provide a detailed discussion of the ultrasound, light, magnet, and electricity propulsion mechanisms as well as their relevancy in the context of bioenvironment.

2.2.1. Ultrasound-Driven Motor

Under illumination, photoactive materials (such as TiO₂) can absorb light energy, and undergo photocatalytic reactions. By devising a Janus photoactive particle and building up reaction products asymmetrically around the particle, the particle can be propelled. For instance, Hong et al. fabricated a motor system based on SiO₂–TiO₂ Janus particle. They observed that in the presence of UV light, SiO₂–TiO₂ Janus particles can migrate and be faster than the individual SiO₂ or TiO₂ particles. When UV light was removed, SiO₂–TiO₂ Janus particles would repel each other, showing particle expansion. These expansion and contraction are reversible. Diffusiophoretic force was considered responsible for the movement. In a model they proposed, the locomotion may be resulted from the outer diffusion of chemical species, O₂⁻, OH⁻, H⁺, OH⁻ (photo induced by TiO₂) at different speeds. Similarly, via self-diffusiophoresis, a matchlike photocatalytic nanomotor (SiO₂-coated Ag nanowire with an AgCl tail) was propelled. Upon UV illumination, AgCl underwent photodegradation and generated a concentration gradient of proton and chloride ion, thus self-diffusiophoresis. The Ag-based nanomotor could be used as surface enhanced Raman spectroscopy probe, providing a novel nanomotor-based surface enhanced Raman spectroscopy biosensing platform.

Using the same UV light (365 nm), the isotropic semiconductor TiO₂ micromotors (1.2 μm in diameter) were propelled by O₂ concentration gradient generated from the self-catalyzed decomposition of H₂O₂. The direction of this motor is always along with the coming light direction, minimally interrupted by the Brownian movement and the local flow. More interestingly, the velocity of motor could be precisely controlled by incident light intensity.
Other UV-powered motor systems include titania–silica Janus spheres[56] (1.5 μm in diameter). The system was powered by photocatalytic decomposition of \( \text{H}_2\text{O}_2 \) at the \( \text{TiO}_2 \) surface. When the light is on, these colloids particles move toward each other and form clusters, whereas with the light off, the clusters melt as Brownian diffusion takes over. These active–passive systems open up a new way to form new assembly that cannot be acquired in conventional passive systems.

In most trials, UV light is the most common light source. Yet, the potential damage of high-energy UV with deoxyribonucleic acid (DNA)/ribonucleic acid (RNA) limits the biomedical applications of these motors. Palacci et al.[16] verified that blue light can also be an energy source for light-driven motors. They can change the phoretic and osmotic force conveniently by switching on/off blue light. Their system is based on an active colloid (hematite embedded 3-methacryloxypropyl trimethoxysilane/TPM). Without blue light, the particles were dispersed randomly in solution. With the illumination of blue-violet light (\( \lambda \approx 430–490 \text{ nm} \)) through the microscope objective, the particles achieved self-propulsion with a speed up to \( 15 \text{ μm s}^{-1} \). More importantly, a visible-light (\( \lambda < 700 \text{ nm} \)) photocatalytic micromotor[56] can be propelled at a speed of 18.71 μm s\(^{-1}\) with glucose as fuel. Such micromotor was composed of cuprous oxide (Cu\(_2\)O) (photocatalytic active material) and 1.35% N-doped carbon nanotubes (N-CNTs) (improving catalytic activity). Through photocatalytic decomposition of glucose, the products, neutral molecules (\( \text{C}_6\text{H}_10\text{O}_5 \), \( \text{C}_2\text{H}_4\text{O}_4 \), \( \text{C}_2\text{H}_5\text{O}_3 \), HCOOH, and \( \text{H}_2 \)) and ionic species (HCOO\(^+\), H\(^-\)) accumulated at one side of the micromotor where glucose enriched (Figure 3B). Consequently, a concentration gradient was generated due to the different diffusion speed of products species, inducing propulsion. With glucose as fuel and visible light as energy source, this system was attractive due to the higher biocompatibility compared with previous systems relying on hazardous fuel (\( \text{H}_2\text{O}_2 \)) and high energy light (UV light). In addition, it is possible to control the direction via visible light. Such biocompatibility and wireless controllability are highly desirable for the biomedical application. Unfortunately, the photocatalytic material used in the system was nondegradable.

In addition to light-induced self-diffusiophoresis, light-assisted electrophoresis is another approach to promote motion. Mou et al.[57] fabricated a TiO\(_2\)/Pt Janus sub-micromotor (average size 800 nm). A platinum layer was asymmetrically coated on the anatase TiO\(_2\) sub-microspheres. Under UV irradiation (368 nm), the TiO\(_2\)/Pt Janus sub-micromotor asymmetrically catalyzed the water oxidation and reduction, generating a local electrical field to propel the sub-micromotor. The velocity could reach 21 μm s\(^{-1}\). In addition, by adjusting the irradiation intensity and mode (pulsed/continuous), the behaviors of the Janus TiO\(_2\)/Pt sub-micromotor, including the motion state, speed, and aggregation/separation, can be reversibly and remotely controlled. For this system, water was used as fuel, which can improve the biocompatibility of the motor system.

After that, Wang et al.[58] prepared n\(^-\)/p \( \text{Si} \) and p\(^+\)/n\(^-\) \( \text{Si} \) silicon nanowire (400 μm in length) motors by vapor–liquid–solid (VLS) growth method and observed the motion of these silicon...
nanowire photoelectrode motors. Compared with the examples mentioned earlier, the single silicon nanowire motor can be driven by a visible even near-infrared (NIR) light, which is more attractive concerning biocompatibility.

In addition to light-induced electrophoresis, light-induced temperature gradient is another way to promote motion. Qian et al.\(^6^\) observed that a gold-polystyrene Janus microsphere (\(\approx 1\) μm in diameter) particle population could migrate in the presence of 532 nm laser. The movement was considered to be derived from a laser-induced temperature asymmetry (higher temperature at the Au side than the polystyrene side) at the particle surface.

In addition to visible light-induced motion, Wu et al.\(^6^\) proposed a gold nanoshells (AuNSs)-loaded polymeric tubular rocket motor powered by NIR light. They fabricated this rocket with poly (styrenesulfonic acid) (PSS) (negative charge) and poly (allylamine hydrochloride) (PAH) (positive charge) via layer-by-layer technique. Then, by a seeding-growth method, AuNSs were grown inside the polymeric rocket, forming (PSS/PAH)\(_{20}\) AuNS rocket. In the NIR region, due to the stronger plasma resonance absorption of AuNSs, local temperature gradients are formed between the internal and external surfaces of asymmetric AuNSs. These temperature gradients and the asymmetric structure of the rockets lead to thermophoretic forces difference around the rockets, thus propelling them. The speed of AuNS rockets could be as high as 160 μm s\(^{-1}\).

A detailed theoretical study of the self-thermophoresis nanomotor was later provided by the same group.\(^6^\) They pointed out that for this type of motors, motion is induced by overcoming Brownian motion with self-thermophoresis force. By theoretical simulation of thermophoresis force distribution, they determined that the maximum thermophoresis force was located at the interface of AuNSs and water. Hot molecules around the semispherical AuNSs of the Janus particles could push the Janus particles to the cold side. Both self-thermophoresis force and Brownian force would affect the moving behavior of nanosized motors.

As for microsized motors\(^6^\) powered by NIR light, the Brownian motion could be ignored due to their larger diameter than the average Brownian path. Thus, the motion of micro-motors is determined by self-thermophoresis force alone. Steeper temperature gradients could generate stronger self-thermophoresis force, which allows the smaller micromotors to move at higher speed.

### 2.2.3. Magnet-Driven Motor

Magnet could be regarded as one of the safest, most feasible, and versatile way to propel motors. Compared with other external field-driven motors, motors powered by magnetic field are more flexible because of the fine tunability of the field strength and direction.

By connecting a magnetically active “magnetic beads flagellum” (giving propulsion) and a red blood cell (RBC) (being transported), Dreyfus et al.\(^1^0^\) proposed a synthetic-biological hybrid motor and demonstrated the locomotion of RBC with the flagellum. The motion arose from the deformations of the time-reversal invariance of the filament in the magnetic field. Two factors (the dipolar interactions between the beads and the interaction between the dipole and the external field) allowed the pivoting of filament following the magnetic field.

Magnetic energy could be transferred into cyclic mechanical deformations with a fully synthetic motor. Gao et al.\(^6^\) demonstrated the locomotion of the Au/Ag/Ni nanowires (with gold as “head” and ferromagnetic nickel as “tail”) induced by an external rotating magnetic field. By varying the length of the Ni/Au segments and adjusting the magnetic field direction, forward (“pushing”) backward (“pulling”) motion of Au/Ag/Ni (Au “head” and Ni “tail”), and an accurate “on/off” control could be realized. Such nanowire motors modulated by external magnetic field do not require the presence of local fuel and are of relatively good biocompatibility.

Recently, a magnetic surface walker,\(^5^1^\) which was composed of two Ni/SiO\(_2\) (15-nm Ni coated 3-μm SiO\(_2\)) Janus microspheres, was fabricated (Figure 3C). In an oscillating magnetic field (2.7 mT), the velocity of this magnetic surface walker could be up to 18.6 μm s\(^{-1}\) (\(=4\) body length s\(^{-1}\)). The speed could be easily regulated by changing the field strength and frequency. In this work, the oscillating magnetic field can not only propel the Janus microspheres but also precisely guide these surface walkers.

In addition to motors driven by pure magnetic force, Baraban et al.\(^6^\) showed a Permalloy (Py, Fe\(_{90}\)Ni\(_{10}\), alloys)-based motor propelled via a magnetic-induced thermophoretic force. When the particle was exposed to the alternating magnetic field, the thermophoretic force generated by the alternating magnetic field can drive the Janus particle.

In general, for magnetically driven motors, the energy conversion process is independent from the local environment, therefore, this type of motors is less influenced by the ionic and complicated biological media. With this advantage, the main bioapplication hurdles for the chemical-powered motors, that is, limited application scope, is circumvented. However, separation and selective control of single motor in the motor systems remains a challenge.

#### 2.2.4. Electricity-Driven Motor

Using electric field to drive micro/nanomotors is attractive due to the high controllability and nonpolluting property of the electric field.

An electric-powered system composed of Au/Ni/Au nanowire rotating motor (with a diameter of 150–400 nm and a length of 800 nm–10 μm) and Au/M/Cr (M represents magnetic materials such as Ni and Co) nanomagnet thin film was developed.\(^1^9^\) This thin film is composed of three layers, the bottom layer Cr facilitating adherence to the substrate, the middle layer M providing magnetic field, and the top layer Au with varied thickness allowing for adjusting magnetic attraction. Via magnetic interaction, the nanowire motors were positioned on the top of the nanomagnet thin film. The system was then connected to quadrupole electrodes, which provided stable alternating current (AC) electric field. In an AC electric field, these nanomagnets could rotate. They found that by narrowing the gap distance between the quadrupole electrodes and increasing the intensity of AC electric field, the speed of nanomotors can increase to at least 18 000 rpm (which can be classified as ultrahigh speed).
In addition to pure metal-based electric-driven motor, Yan et al. devised a metal-coated (35 nm-thick titanium) SiO₂ Janus sphere motor (3 μm in diameter) that could rotate in an electric field.[65] They found a relationship between moving direction and field frequency. By increasing the frequency from 5 to 30 kHz and 1 MHz, the direction of Janus particles can be changed. It was due to that the magnitude of electric field frequency has a strong impact on ionic screening effect and dipolar interactions between motors, thus the swimming direction of particles.

In the same year, Zhang et al.[52] selected a system based on mixtures of pure silica (4 μm) and Janus particles (3 μm), which can move and form out-of-equilibrium self-assembled structure in an electric field. When exposed to AC electric field (40 kHz), one inert (pure silica) particle is slightly raised from the bottom of the sample cell, attracting either three or four Janus particles, which can form chiral tetrahedral rotors (low activity) or square pyramidal rotors (high activity). The structures can be induced to rotate (either clockwise or counter clockwise) in the field (Figure 3D).

Recently, a nanomotor precisely controlled by electric field has been devised.[66] This nanomotor (250 nm in diameter) is composed of 2 μm-length Pt and 3 μm-length Au. They found that the peak voltage of 10 V AC was sufficient to align catalytic nanomotors and trigger the movement. Importantly, the velocity of the nanomotors was dependent on their position in the electric field. As well, the nanomotor direction could be reversed. It was demonstrated that the speed increase of nanomotor was induced by direct current (DC) electric field. Different from previous work, the author achieved precise manipulation of nanomotors by changing the AC electric field and DC electric field. This breakthrough offers us a new method to complete complex tasks.

While the electric field provide a versatile approach for propelling and guiding motors, the compatibility of electric-powered motors with highly conductive biological medium remains practical concerns. Typical medium required for electric-powered motors is nonionic isosmotic solution of medium is highly ionic and conductive, which would severely hinder the motion. Other concerns involve the safety issues of high voltage of electric field.

3. Biomedical Applications of Micro/Nanomotors

Thanks to the combined efforts of researchers from multidisciplinary fields, both chemical-driving motors and external field-propelled motors, are demonstrating their potentials in biomedicine. In this section, we provide an in-depth summary of various motor applications in the biomedical field, including drug delivery, cell transportation, biosensing, detoxification, surgery, and separation.

3.1. Drug Delivery

Passive drug carriers depend on systemic circulation to reach the disease area. These drug delivery agents usually lack the navigation ability, which is necessary for precise targeted delivery. It was also pointed out that the tissue penetration ability of passive nanoparticle (NP) delivery agent was poor; whereas, for micro/nanomotor-based drug delivery systems, motors are capable of active navigation and can penetrate deep into targeted diseased tissues, thus improving the therapeutic efficacy and reducing the side effects.[67]

In addition, micro/nanomotors possess features such as fast movement and strong towing force. With these capabilities, micro/nanomotors-based drug carriers can transport therapeutic payloads to the location in an efficient manner.

One of the initial trials was demonstrated by Kagan et al.[20] They endeavored active and precise transportation of therapeutic particles with motor system. Drug-loaded poly(lactic-co-glycolic acid) (PLGA) particles (containing small magnetic iron oxide NPs) were attached to the alloy (Ni/(Au₅₀/Ag₅₀)/Ni/Pt) nanomotors and quickly delivered to their destination. The fast locomotion of motors facilitates the efficient delivery. This represents an important step toward “active” drug delivery. It was also demonstrated that the nanomotors can rapidly pick-up, transport, and release therapeutic payloads of varied size from a loading area to a target site through a predetermined route. With this highly controllable navigation ability, the motor systems provide a solution to the current problems in passive NP-based drug delivery, that is, “off-targeting.”

The loaded cargo was found to be influencing the propulsion speed and trajectory of the motor due to the increased dragging force.[18] The same group later also demonstrated the drug delivery toward HeLa cancer cell with a flexible magnetic nickel–silver nanoswimmer.

In addition to motors driven only by one energy source, dually powered motors offer possibilities to broaden the application scope. Gao et al.[68] fabricated a multifunctional Janus micromotor by a one-step emulsion solvent evaporation method. The Janus micromotors consisting of polycaprolactone (PCL), Pt NPs, and Fe₃O₄ NPs were loaded with coumarin, the model drug. As PCL was degraded in the solution of Pseudomonas cepacia, micromotors disassembled and released coumarin simultaneously. In addition, the coumarin could be released within 2 h. For this Fe₃O₄-loaded system, the moving trajectories of micromotors could be controlled by magnetic field so that coumarin was released along the predetermined route. These micromotors demonstrate great potential for drug delivery due to their biodegradability and controllability. In addition to PCL polymeric motors, Peng et al. explored the possibility of drug delivery in a tumor tissue model with a dually driven polymeric nanomotor. Catalytic platinum and magnetic nickel were situated in the stomach of the self-assembled bowl-shaped poly(ethylene glycol)-b-polystyrene (PEG-PS) vesicles. The presence of both particles allows the motor to be driven by both chemical fuels (H₂O₂) and magnetic field. With the external magnetic field, the bowl-shaped doxorubicin/platinum–nickel-loaded stomatocytes could be guided toward the direction of the tumor tissue model and transport antitumor doxorubicin to the target region (Figure 4A). This work demonstrates the applicability of nanomotors in a biological-relevant environment.[69] In this system, biocompatible poly (ethylene glycol) (PEG) segments increase the stability of motors and decrease the possibilities of immune attack and clearance. Yet, Pt/Ni NPs were non-biodegradable and non-biocompatible.
In addition to catalytic Pt, the biological enzyme could also be utilized to propel the motor system for drug delivery. For instance, Sánchez and coworkers fabricated an urease-functionalized mesoporous silica nanobot, which was powered by the decomposition of urea into ammonia and carbon dioxide. Importantly, these urease-powered nanomotor could be propelled in ionic media. When Dox-loaded urease nanobots and Dox-loaded nanobots (without urease) were coincubated with HeLa cell for 6 h, Dox-loaded urease nanobots demonstrated four times more release of Dox into HeLa cell than their counterparts. These nanobots propelled by urease possessed good biocompatibility and their products (NH$_3$ and CO$_2$) were harmless and biocompatible. Most importantly, the efficiency of Dox-loaded nanobots' drug release was higher than passive counterpart, which was very attractive for biomedical application. Yet, for this motor, direction control was still lacking.

In the previous trial, biological enzyme was used as the catalytic segment. Researchers also explored the possibility of using biological segments as the shell of the nanomotors. Recently, a virus-like spherical motor has been fabricated for drug delivery. This Janus virus-like nanomotors (25–30 nm in diameter) (JVN)s) were composed of brome mosaic virus (BMV), cowpea chlorotic mottle virus (CCMV), and catalytic Pt (coated on half sphere of the NP). The system could be propelled by catalytic decomposition of H$_2$O$_2$ at a speed of 9 μm s$^{-1}$. The chemotherapeutic drug tamoxifen could be carried by virus-like nanomotors and delivered into the breast tumor cells. Moreover, the therapeutic payload could be released at pH 4.5. The virus-like structure in this work can greatly increase the capacity of cargo. Different cargoes including inorganic NPs, proteins, enzymes, and drugs can be carried. In addition, the main body of the virus-like nanomotor is degradable, highly desirable for bioapplications.

### 3.2. Cell Transportation

Researchers attach importance to cell transportation as guided migration or delivery of sperm cell, immune cell, and stem cells, may facilitate fertility, cancer therapy, and body renewal, respectively.

For reproduction assistance, hybrid sperm cell motors were proposed. A sperm was first loaded to a ferromagnetic micro-motor (polymeric microhelix coated with NiTi soft-magnetic bilayer) by confining the tail of the sperm to the inside of the microhelix. The ferromagnetic Ni allows for remote control through an external magnetic field. Transportation of the sperm was achieved by magnet-actuated motion of the helix. The velocity could reach 17.6 ± 3.53 μm s$^{-1}$. Upon approaching an oocyte cell, the sperm was released from the microhelix via reversal of the magnetic field rotation. Eventually, successful fertilization was achieved when sperm cells fused with the oocyte cell (Figure 4B).

In addition to magnetic-driven motor, the bubble-driven polyelectrolyte multilayer (PEM) Fe$_3$O$_4$-Pt microplates was also
explored for cell transport.\textsuperscript{[71]} With Pt, the motor catalytically decomposed H$_2$O$_2$ into oxygen bubble and be propelled, achieving transport of HeLa cells. With a magnetic field and the Fe$_3$O$_4$, guided delivery is obtained. The cells could survive approximately 22 min in 5\% H$_2$O$_2$ solution. Yet, with an increased hydrodynamic drag force and a decreased diffusion of H$_2$O$_2$ to the micrometer, the cell attachment reduces the speed of the micromotor by 90\%.

### 3.3. Biosensing

As for biosensing, effective recognition, pick-up, and isolation are favorable. Fortunately, micro/nanomotors can fulfill this requirement. With the fast moving and strong towing feature, micro/nanomotors can pick up targets rapidly and efficiently. In addition, high controllability enables the targeted and precise biosensing of micro/nanomotors in the biological environment.

In situ analysis and detection of target, such as protein, nucleic acids, and cancer cell, can be realized with the micro/nanomotor system. Wu et al.\textsuperscript{[24]} proposed an Au–Pt nanowire motor-based approach for the detection of DNA and \textit{Escherichia coli} 16S rRNA. A substrate was first coated with thiolates capture probe (SH-CP). The presence of a target complementary nucleic acid (DNA or RNA) leads to duplex formation and subsequent capture of an SH-DP-Ag NP detector probe. After addition of H$_2$O$_2$, the captured Ag NP is dissolved into silver ions. The higher the DNA/RNA level, the more captured Ag NP/Ag$^+$. The silver ion amount is positively correlated with the nanomotor speed. By incubating the silver ions solution with the Au–Pt motor and reading out the motor speed, the amount of specific DNA/RNA in the environment can be determined.

In addition to the detection of biomolecules randomly dispersed in the solution, Xu et al.\textsuperscript{[25]} demonstrated the targeted cell biosensing with a motor system. The group developed plasmonic-magnetic NPs (PM-NPs) motors with enhanced optical and magnetic properties. A quasi-one-dimensional PM nanotube was first fabricated by uniformly distributing plasmonic Ag NPs on silica–nickel nanotubes. The magnetic nickel segment of the system allowed for precise manipulation of the moving direction, thus the possibility of single-cell level sensing. Under the guidance of an external magnetic field, the motors moved toward a target living Chinese hamster ovary cell (CHO cell). The Ag segment of the motors facilitated surface enhanced Raman scattering to detect the surface molecules of the cell. They showed that PM nanotubes have great compatibility with biological cells due to their unique longitudinal geometry and nanoscale diameters, which is important for molecule-level biosensing and detection.

In addition to the magnetic field, light field can also be a guiding cue for the nanomotors to reach the target site for sensing. Ma and coworkers\textsuperscript{[26]} fabricated a silicon-coated silver matchlike nanomotor (AgNW@SiO$_2$), which could move by self-diffusiophoretic force under UV light. Under the UV light, the motor can demonstrate guided movement, phototaxis behavior. With the guidance of UV light, this matchlike nanomotor could reach the targeted MCF-7 breast cancer cells. This AgNW@SiO$_2$ can serve as surface enhanced Raman spectroscopy probes and achieve smart biochemical sensing with micro/nanoscale precision. They found that Raman signal increased three times after the UV light-guided nanomotor aggregation at the cell.

### 3.4. Detoxification

Micro/nanomotors are promising in the field of detoxification. With the fast movement feature, self-propelled motors can capture and eliminate toxin rapidly, cleaning environment in an efficient way. Natural components including RBC membrane can absorb toxin. Hu et al. used an extrusion approach to fuse RBC membrane with PLGA NP to prepare the nanospheres\textsuperscript{[26]} particles (Figure 4C). The α-toxin-neutralizing ability of nanospheres was confirmed with both in vitro RBC hemolysis experiment and mice experiment.

Highly stable RBC membrane-coated gold nanowire motors were shown to absorb membrane-damaging toxins/α-toxin even more efficiently than the passive RBC membrane-coated particle.\textsuperscript{[27]} The ultrasound-driven RBC membrane-wrapped gold nanowire motors were used as a decoy to attract, capture, and neutralize toxins. With the fast moving and strong propulsion capabilities, the ultrasound-propelled nanowire motors demonstrated higher effectiveness of absorbing and neutralizing toxins than that of nonpropelled membrane-covered nanowire and bare motors.

In addition to ultrasound-driven motor, RBC membrane-coated magnesium (RBC-Mg) Janus motors powered by water can efficiently remove cell membrane damaging toxin/α-toxin.\textsuperscript{[28]} The Janus motors were prepared by introducing RBC membrane, gold NPs (AuNPs) and alginate (ALG) to the half exposed surface of magnesium MPs. This type of RBC-Mg Janus motors could be self-propelled in water, by the hydrogen bubble from Mg-water reaction. For determining the detoxification capability of the RBC-Mg Janus motors, they mixed motors and toxin in a 5\% albumin solution. They found that RBC membrane-functionalized motor can interrupt the nonspecific absorption of α-toxin onto the RBCs, thus avoiding hemolysis. A sharp decrease in the relative hemolysis, was observed for both the RBC-coated SiO$_2$ particles and RBC-Mg Janus motors group. There was a stronger detoxification ability of RBC-Mg Janus micromotors than nonpropelled RBC-coated SiO$_2$.

By novel 3D printing (microscale continuous optical printing, μCOP) approach, a hydrogel microfish motor capable of detoxification was fabricated.\textsuperscript{[24]} The technique allows rapid and efficient motor production. With the μCOP technology, they incorporated three different types of functional NPs into the motor system. Pt NPs are used for propulsion, Fe$_3$O$_4$ NPs for guiding in magnetic field, whereas polydiacetylene (PDA) NPs for neutralizing toxin melittin. With this approach, multifunctional segments can be incorporated into this platform, broadening the application scope of micro/nanomotors in complex biological environment.

### 3.5. Surgery

The micro/nanomotors possess the properties of fast and controlled moving. These motors afford high accuracy, flexibility, and controllability, which are highly demanded to performing complex surgery. In addition, the micro/nanoscale motors can...
reach precisely the destination where manual operation cannot reach. The resulted thrust from the fast movement allows for strong penetration into the tissue. The concept of robot-assisted surgery was then proposed.[39] These remote-controlled robotic surgical devices can facilitate the minimally invasive surgery/laparoscopic surgery procedures. Compared with conventional surgery, the robot-assisted surgery is characteristic of shorter hospital stays, less postoperative pain, and lower risks of infection. In addition, robot-assisted surgery liberates the hands of doctors, provides convenience and precision.

With the micro/nanosized propelling robots (motor), researchers are allowed to perform delicate and complex operation at micro/nanoscale remotely. Gultepe et al.[30] used a local stimuli responsive μ-gripper motor (≥980 μm tip-to-tip) for surgery. This μ-gripper was composed of Si (bottom layer), Cr, Au, Cu, Ni (middle layer), and temperature responsive polymer (top layer). A Cr film of thickness 60 nm and a Au film of thickness 100 nm were for resisting stress. Ni (8 μm) and Au (1 μm) were the rigid segments for strengthening. In addition, with Ni, a ferromagnetic material, in the μ-gripper, the grippers can be guided by an external magnetic field to the target tissue. A mixture (5:1 v/v) of SC1805 and SC1813 acted as the thermoresponsive layer, which could be actuated at the selected temperature. In response to body temperature cues, these μ-grippers can obtain mechanical energy from residual stress and close/grip. In the experiment, more than 1560 μ-grippers were injected into the bile duct of the porcine liver through the catheter. After that, these μ-grippers were visualized via the endoscopic camera when they went into the biliary orifice. At the biliary orifice, the catheter was deployed for 10 min. During that time, the μ-grippers were allowed to close in response to body temperature. Then, the deployment catheter was replaced with the retrieval catheter wrapped with a magnetic tip to retrieve the μ-grippers. It was a successful demonstration of tissue (relatively dense bile duct) extraction with the μ-grippers which were only about 160 nm-thick. For the first time, these μ-grippers can cut tissue samples (the bile duct of the porcine liver) from real organs of an animal which is hard to reach by other approach. They also demonstrated that extracting intact cells and high-quality RNA and DNA from the retrieved tissue was fully possible. This can be used for diagnosis of cancer, inflammation, or other diseases.

Furthermore, Nelson et al.[31] proposed a tethered system composed of polyurethane catheter with a cylindrical neodymium–iron–boron (NdFeB) magnet inside the injection needle. These structures were manipulated by magnetic field and can be used for posterior eye operation. This ophthalmic surgery is advantageous with high precision and force feedback. The magnetic fields strength and gradients of the magnetic manipulation system, are also important. This system allows lower magnetic strength with precise ophthalmic surgery, which could minimize the danger of surgery and maximize the safety of patients. These magnetically robotic systems allowed more flexibility, stability and accuracy, and reduced risk of tissue perforation.

3.6. Separation

The moving feature of micro/nanomotors can also be used for separation. The micro/nanomotors-based platform can achieve efficient separation, such as removing circulating cancer cells from the blood.

Using microrocket motors, circulating tumor cells (CTC) without sample pretreatment could be directly detected and isolated in situ.[32] Via N’-(3-dimethylaminopropyl)-N-ethylcarbodiimide/N-hydroxysuccinimide (EDC/NHS) chemistry, the anti-carcinoembryonic antigen (anti-CEA) monoclonal antibody (mAb) was coupled to the outer gold surface of the Ti/Fe/Au/Pt microtube microrockets. When the anti-CEA mAb-modified microrockets interact with the cell, the microrockets could bind to the CEA antigens on the surface of target cancer cells. Then, the microrockets picked up the cancer cell and transported it to the target area (Figure 4D).

A nucleic acid probe functionalized Ti/Ni/Au/Pt tubular motor was proposed to selectively capture and separate target nucleic acids directly from biological samples. In this work, the micro/nanomotors modified with a single strand DNA probe move freely in a biological sample containing H2O2 fuel. Upon interacting with the fluorescently labeled target nucleic acid, one-step separation of the target nucleic acid was achieved.[33]

Recently, MnO2 PEI/Ni/Au/aptamer K12 motors were used to isolate human promyelocytic leukemia cells (HL-60 cancer cells) from the human serum sample.[74] In the magnetic field, the Ni-incorporated nanomotor could be guided toward HL-60 HL-60 cancer cells in the human serum sample. The presence of aptamer K12 allows specific recognition and interaction with the target cell. The HL-60 cancer cells were then successfully isolated by the nanomotor.

4. Conclusion

Over the past 15 years, micro/nanomotors have emerged as novel platforms for biomedical therapy. With strong towing force, fast moving capability, these micro/nanodevices have revolutionized people’s perception about the therapeutic process. Despite great progresses that have been made in the field, hurdles remain along the road toward clinical translation.

One remaining problem is the toxicity associated with micro/nanomotors. H2O2, the most widely used fuel, may pose oxidative pressure to the biological entities. For the motors themselves, the metallic components of motor systems upon dissolution and release can cause immune reaction in the human body. In an effort to address these obstacles, research groups are starting to explore biocompatible water, glucose, and so forth as power source and biodegradable materials as framework of micro/nanomotor. Yet, current choice of biocompatible fuels and materials is limited.

In addition, the speed and efficiency of motor demand improvement. Recombinant biological enzymes may provide a higher catalytic efficiency, and thus a solution. Attention should also be given to the relationship between the motor size/shape and the motor performance. In this respect, precise control of moving direction needs to be taken into consideration. Certain relationship may exist between the moving motor size/shape/direction. For example, with the motor size shrunk to nanoscale, the moving motor direction could be easily randomized by Brownian force. It remains unsolved how the motor size/shape influence motor properties. In the future, more
attention should be directed to clarify these relationships, especially in biological environments.

The application scope of the micro/nanomotors needs to be extended. The fast movement feature and strong towing property of motor has been used for shortening time of various biomedical applications, including delivery, cell transportation, sensing, detoxification, separation, and surgery. Yet, other aspects of the motor, such as the energy conversion capability and mechanical property need to be explored. It would also be exciting to explore the possibility of mechanotreatment with the emergent micro/nanomotor platform.

The complicated environments of high viscosity and ions, in the human body remain a hurdle. The performance of motors driven by self-electrophoresis and self-diffusiophoresis is inherently impaired in such a media. Only a few motors can exert their motion in the highly viscous and ionic human blood. Even if the viscosity problem was overcome, many other issues, including the interference of fast blood flow (1–20 mm s⁻¹) with motion, will also need to be taken into consideration.

Overcoming the bottlenecks of the field mentioned earlier, we expect that we will get closer to the clinical translation of micro/nanomotors.

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Conflict of Interest

The authors declare no conflict of interest.

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