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Increasingly Intelligent Micromachines

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Abstract

Intelligent micromachines, with dimensions ranging from a few millimeters down to hundreds of nanometers, are miniature systems capable of performing specific tasks autonomously at small scales. Enhancing the intelligence of micromachines to tackle the uncertainty and variability in complex microenvironments has applications in minimally invasive medicine, bioengineering, water cleaning, analytical chemistry, and more. Over the past decade, significant progress has been made in the construction of intelligent micromachines, evolving from simple micromachines to soft, compound, reconfigurable, encodable, multifunctional, and integrated micromachines, as well as from individual to multiagent, multiscale, hierarchical, self-organizing, and swarm micromachines. The field leverages two important trends in robotics research—the miniaturization and intelligentization of machines—but a compelling combination of these two features has yet to be realized. The core technologies required to make such tiny machines intelligent include information media, transduction, processing, exchange, and energy supply, but embedding all of these functions into a system at the micro- or nanoscale is challenging. This article offers a comprehensive introduction to the state-of-the-art technologies used to create intelligence for micromachines and provides insight into the construction of next-generation intelligent micromachines that can adapt to diverse scenarios for use in emerging fields.

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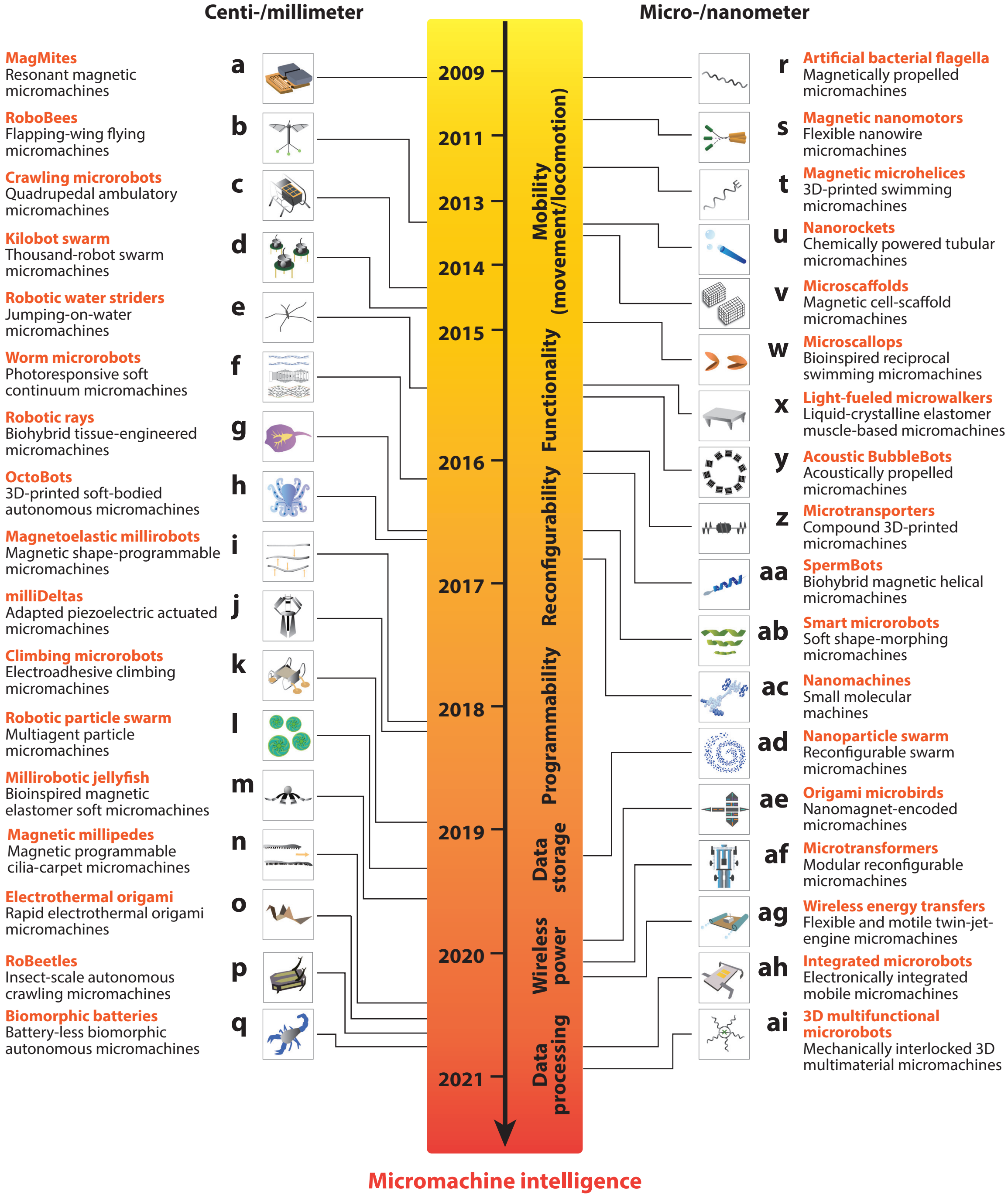
1. ADVANCES IN INTELLIGENT MICROMACHINES

Machines have been created for hundreds of thousands of years to augment and enhance human capabilities in order to liberate us from laborious tasks and harsh working conditions, evolving from the simplest machines (such as digging tools, hand axes, wheels, and levers) to complex mechanical systems (such as engines and automobiles) and automated, intelligent machines (such as autonomous robots). While machines have become increasingly capable and intelligent, particularly with the rise of artificial intelligence (AI), researchers have begun to develop advanced robotics to completely restructure machines at small scales. Compared with their macroscale counterparts, micromachines are tiny enough to access narrow and confined spaces inside the human body. They are highly integrated, portable, and minimally invasive; consume little energy; can be mass manufactured; and exhibit high performance with atomic-level accuracy and precision, enhanced stability, and robustness, as well as incredible sensitivity and responsiveness. However, the miniaturization of machines requires more demanding manufacturing and assembly techniques and poses tremendous design challenges due to nonintuitive microscale effects, such as energy dissipation (e.g., heat transfer), electromagnetism (e.g., electrostatic charges and micromagnetism), fluid dynamics (e.g., viscosity or surface tension), and more.

One of the first to explicitly propose tiny machines was Richard Feynman, who delivered an epoch-making speech at Caltech on December 29, 1959, titled "There's Plenty of Room at the Bottom" (1). According to Feynman (1, p. 900), the "very wild" idea of "swallowing the surgeon" was originally proposed by mathematician Albert Hibbs for Feynman's theoretical micromachines, and he pointed out that "other small machines might be permanently incorporated in the body to assist some inadequately-functioning organ." Based on this concept, the plot of a submarine and its crew shrunk to "about the size of a microbe" and injected into the human body to repair brain damage appeared in the science fiction movie *Fantastic Voyage*, released in 1966. Decades later, MagMite (2), a submillimeter-scale robot wirelessly powered by oscillating magnetic fields that can move on a flat surface and produce sufficient force to push microscale objects (see **Figure 1*a***), was created by Nelson's group at ETH Zurich in 2008**.** It succeeded in responding to one of Feynman's tentative ideas: "How many times when you are working on something frustratingly tiny. . .have you said to yourself, 'If I could only train an ant to do this!' What I would like to suggest is the possibility of training an ant to train a mite to do this" (1, p. 898). While this was considered to be a fantasy for decades, significant progress has been made in materials science, nanotechnology, and robotics in developing micromachines with advanced technology to revolutionize a broad range of engineering fields, including precision medicine (3–5), bioengineering (6), soft micro- and nanorobotics (7), advanced manufacturing (8), water cleaning (9–11), and analytical chemistry (12).

The world of micromachines embraces a wide variety of state-of-the-art microdevices with dimensions ranging from a few millimeters down to nanometers, such as micro- and nanoelectromechanical systems (e.g., microsensors and microactuators), microelectronic circuits (e.g., microcontrollers), energy storage microdevices (e.g., microbatteries and supercapacitors), labs on a chip (e.g., microfluidic channel systems), and human–micromachine interfaces (e.g., neural dust), as well as micro- and nanorobots (e.g., microswimmers and nanomotors). From the overall perspective of machine evolution, these existing micromachines have incorporated all the necessary functions required to constitute an intelligent system that not only can run automatically but also can perceive and respond to the world around it. All components, including mechanisms, sensors, controllers, actuators, power sources, and interfaces, are ready to merge into a new, fully intelligent micromachine. Of course, in engineering there are trade-offs between the downscaling of the machine and the degree of functional components that can be effectively integrated. It is highly desirable for micromachines to establish feedback mechanisms of information while interacting



(*Caption appears on following page*)

Figure 1 (*Figure appears on preceding page*)

Development trends in intelligent micromachines since 2009. At the centi- and millimeter scales (*top*): (*a*) MagMites (2), (*b*) RoboBees (13), (*c*) crawling microrobots (14), (*d*) kilobot swarm (25), (*e*) robotic water striders (15), (*f*) worm microrobots (19), (*g*) robotic rays (20), (*h*) OctoBots (21), (*i*) magnetoelastic millirobots (22), (*j*) milliDeltas (171), (*k*) climbing microrobots (16), (*l*) robotic particle swarm (26), (*m*) millirobotic jellyfish (23), (*n*) magnetic millipedes (24), (*o*) electrothermal origami (90), (*p*) RoBeetles (17), and (*q*) biomorphic batteries (18). At the micro- and nanometer scales (*bottom*): (*r*) artificial bacterial flagella (27), (*s*) magnetic nanomotors (33), (*t*) magnetic microhelices (28), (*u*) nanorockets (29), (*v*) microscaffolds (30), (*w*) microscallops (34), (*x*) light-fueled microwalkers (35), (*y*) acoustic BubbleBots (31), (*z*) microtransporters (32), (*aa*) SpermBots (42), (*ab*) smart microrobots (36), (*ac*) nanomachines (40), (*ad*) nanoparticle swarm (41), (*ae*) origami microbirds (39), (*af*) microtransformers (37), (*ag*) wireless energy transfers (40), (*ah*) integrated microrobots (41), and (*ai*) 3D multifunctional microrobots (38).

with their environment, humans, and other intelligent microagents. It is still challenging to create intelligence for machines at small scales that enables them to perform multiple tasks and deal with complex situations, since the scales usually exceed the minimal size at which machine intelligence can be effectively achieved through embedding programmable integrated circuits.

The term intelligent micromachine refers to complex microsystems that can accomplish specific goals or missions autonomously at small scales in the presence of the uncertainty and variability inherent to the microscale world. Intelligent micromachines leverage the two most significant trends of robotics research, miniaturization and intelligentization, but a compelling combination of these two trends has yet to be realized. Throughout the past decade of representative studies, as depicted in **Figure 1**, two alternative strategies have been used to create intelligent micromachines: the top-down and bottom-up approaches. The top-down approach of establishing an intelligent micromachine starts with devising an integral system framework to miniaturize intelligent machines while ensuring their versatile functionalities. For example, recent technologies have enabled centi- and millimeter-scale autonomous robotic systems, such as insect-inspired micromachines (13–18), soft-bodied micromachines (19–24), and multiagent systems (25, 26).

By contrast, the bottom-up approach first builds single-functional components to a minimal size and then upgrades and augments their functions by integrating new parts by degrees until an intelligent micromachine has been achieved. At micro- and nanoscales, this method involves exploring some of the most advanced nanotechnologies to progressively strengthen the capabilities of micromachines, such as mobility/locomotion, functionality/mechanical advantage, flexibility/adaptability, programmability/reconfigurability, reprogrammability/data storage, multimaterials/multifunctionality, wireless power transfer/communication, and data processing/computing, as depicted in **Figure 2**.

Progress has clearly outlined an evolutionary course toward increasingly intelligent micromachines in many aspects: from rigid (27–32) to flexible (33, 34), soft (35–37), and smart (35–38) materials; from simple (27, 29) to compound (28, 32–34, 38), reconfigurable (36, 37, 39), and integrated (40, 41) mechanisms; from basic principles (29, 30) to bioinspired (27, 34), biohybrid (42), and modular (37) design strategies; from single-functional (27, 29–31, 33–35) to multifunctional (28, 32, 36–38, 42), multimodal (37, 39, 40, 43), and encodable (39) actuators or sensors; and from individual micromachines (27–42, 44) to cooperative (45) and collective (28, 43, 46) systems. Studies in this field are continuously evolving toward the ultimate goal of creating intelligence for machines at small scales.

The main goal of this review is to illuminate a new and promising field of advanced robotics, intelligent micromachines, by outlining the evolution of this field, describing the general definition of intelligent micromachines, and classifying existing studies. **Figure 3** summarizes research directions and core techniques discussed below. From the perspective of intelligent systems, we define micromachine intelligence (μ-AI) and discuss state-of-the-art technologies and methodologies for the intelligentization of micromachines. In the last sections of the review, we provide

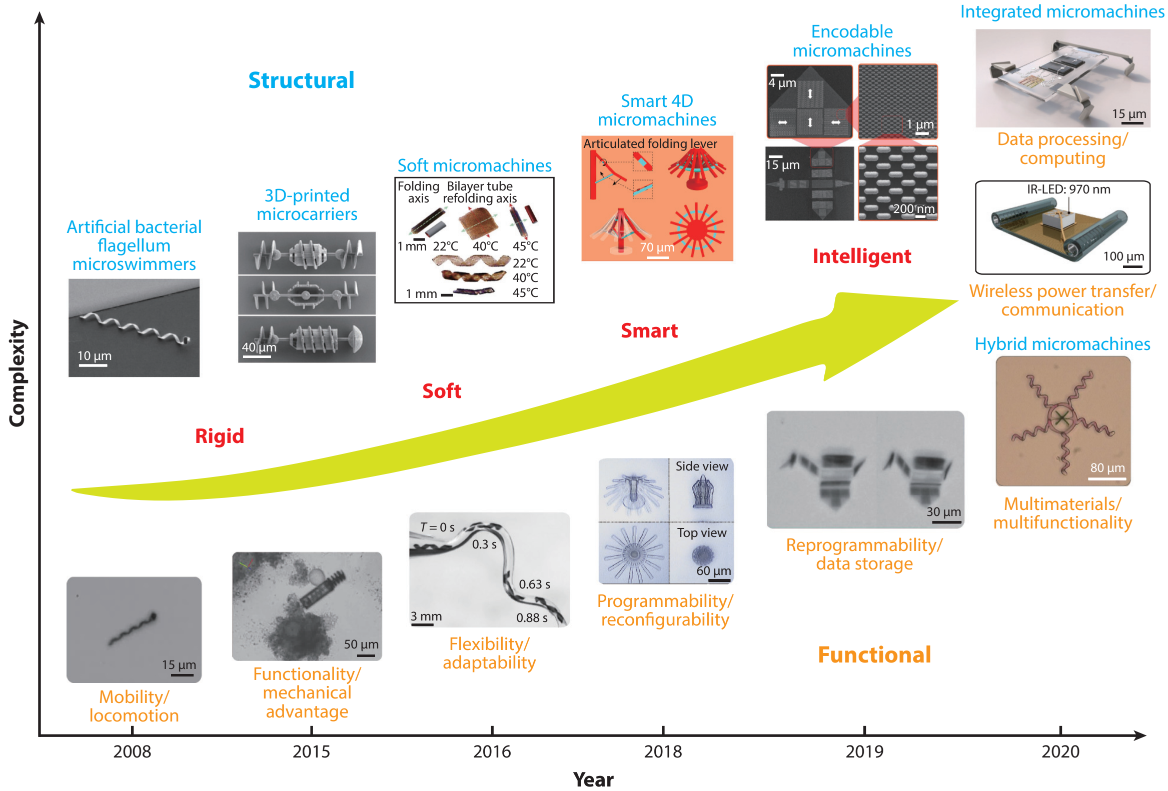


Figure 2

The overall evolution of the field of micrometer-scale machines since 2008, showing artificial bacterial flagellum microswimmers (27), 3D-printed microcarriers (32), soft micromachines (36, 71), smart 4D micromachines (60), encodable micromachines (39), hybrid micromachines (38), and integrated micromachines (40, 41). Soft micromachines and smart 4D micromachines images adapted from References 36 and 60, respectively, under a CC BY 4.0 license; top integrated micromachines image provided by I. Cohen/Cornell University; bottom integrated micromachines image adapted with permission from Reference 40 (copyright 2020 Springer Nature Limited).

insight into the development of next-generation intelligent micromachines for a wide range of engineering applications.

2. CLASSIFICATION OF EXISTING INTELLIGENT MICROMACHINES

2.1. Mobile Micromachines: Mobility and Locomotion

One of the major goals in this field is to develop capabilities for micromachines to manipulate and transport micro- and nanoscale objects such as droplets (47) and drug molecules (48, 49); biological materials such as DNA (50), proteins (51), and cells (30, 32, 42); and microorganisms or nanorobotic swarms (32). A mobile micromachine must produce enough force to counteract drag, friction, inertia, or gravity and shape the mechanisms in the appropriate fashion to locomote according to specific environmental media or interfaces. To achieve autonomous flight, researchers at Harvard (13) created intelligent flapping-wing micromachines through a series of technical innovations using lightweight materials, precise pop-up assembly, high-frequency piezoelectric

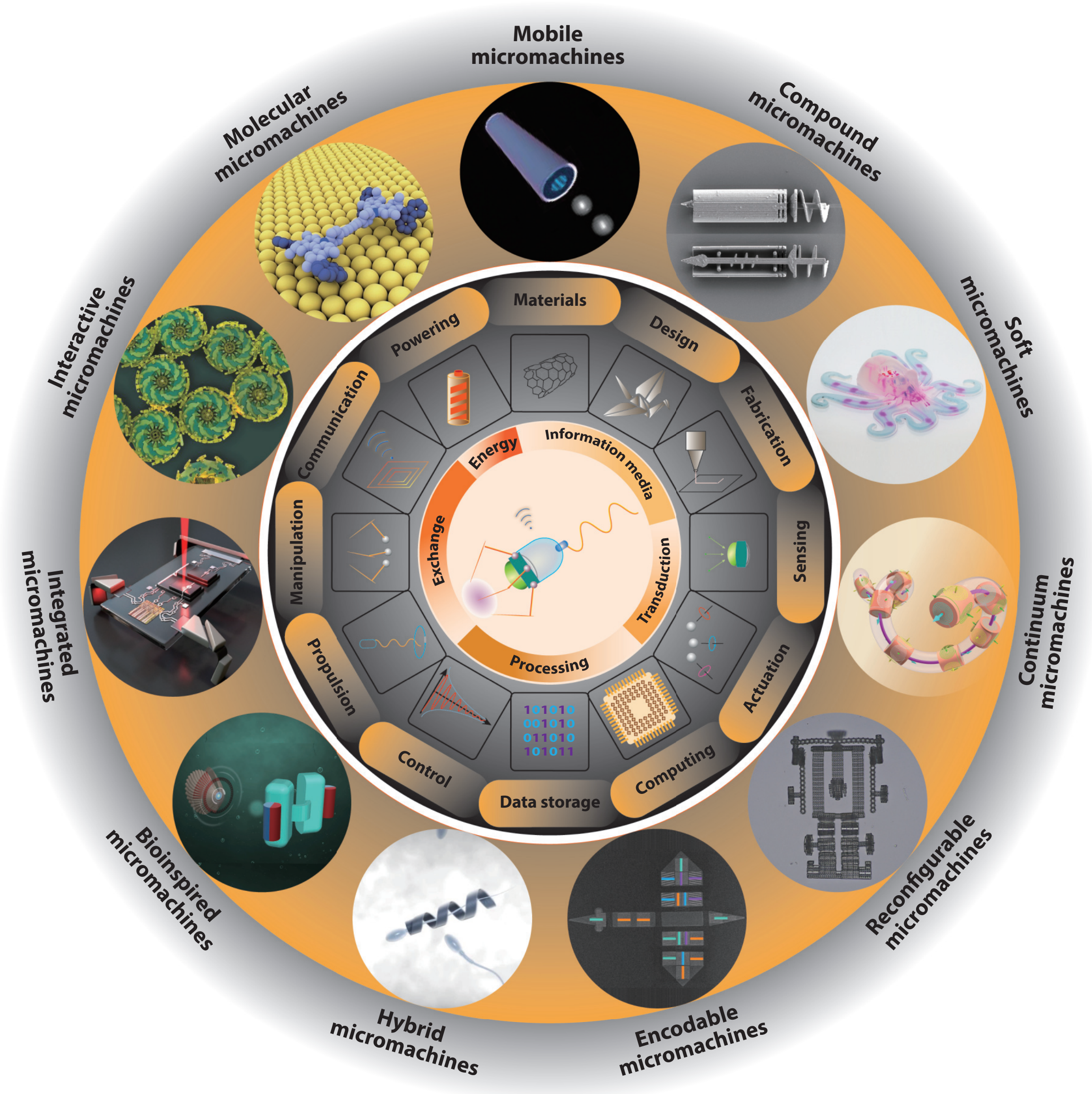


Figure 3

Research directions and core techniques of intelligent micromachines. The major research directions can be classified as mobile (172), compound (32), soft (21), continuum, reconfigurable (37), encodable (39), hybrid (42), bioinspired (34), integrated (41), interactive (26), and molecular (44) micromachines. According to the functionality of the micromachines, the core techniques of constructing intelligent micromachines can be divided into materials, design, fabrication, sensing, actuation, computing, data storage, control, propulsion, manipulation, communication, and powering. These aspects in turn correspond to the five steps of micromachine intelligentization: information media, transduction, processing, exchange, and energy supply. Mobile micromachines image adapted with permission from Reference 172 (copyright 2012 American Chemical Society); soft micromachines image adapted with permission from Reference 21 (copyright 2016 Macmillan Publishers Limited, part of Springer Nature; all rights reserved); hybrid micromachines image adapted with permission from Reference 42 (copyright 2016 American Chemical Society); bioinspired micromachines image provided by A. Posada, P. Fischer, and T. Qiu; integrated micromachines image provided by I. Cohen/Cornell University; interactive micromachines image adapted with permission from Reference 26 (copyright 2019 Springer Nature Limited); molecular micromachines image adapted with permission from Reference 44 (copyright 2016 American Association for the Advancement of Science).

actuators, and bioinspired aerodynamics. Further developments also enabled quadrupedal ambulatory micromachines capable of crawling (14, 17, 18, 52) or climbing (16) on rough terrain, jumping on water (15), and so on. In addition, soft-bodied micromachines with highly adaptive morphologies have been developed for various locomotion mechanisms, including the traveling-wave motion of light-actuated worms (19), biohybrid rays (20), and magnetic millipedes (24); the multimodal locomotion of magnetic shape-programmable micromachines (22); and millirobotic jellyfish-like swimming (23).

As the sizes scale down to micrometers, mobile micromachines exist mostly in liquid environments where viscosity dominates inertia and must avoid reciprocal motion when propelling forward in Newtonian liquids (53). Inspired by the propulsion mechanism of bacteria flagella, researchers have developed magnetic helical micromachines and thoroughly investigated their propulsion mechanism, fabrication method, control strategy, and biomedical applications (27, 28, 32, 36, 50, 54, 55). The corkscrew motion of these microhelices is one of the most popular methods to break the time-reversal symmetry in Stokes flow. Other locomotion methods in low-Reynolds-number environments include tumbling/wobbling of rotating nanowires (56), undulatory locomotion of multilink nanoswimmers (57), walking liquid-crystalline elastomer muscle-based micromachines (35), slipping acoustic micromachines (58), bubble propulsion of chemically (29, 40) or acoustically (31) powered micromachines, and multimodal locomotion of nanomagnet-encoded micromachines (39) or reconfigurable swarms (43). An alternative strategy to locomote at small scales uses a reciprocal motion, similar to that of scallops, in non-Newtonian liquids (34).

2.2. Compound Micromachines: Functionality and Mechanical Advantage

Compound micromachines offer a simple strategy by integrating basic mechanisms into intelligent micromachines. These mechanisms, such as levers and screws, can function as the building blocks to adjust the direction and magnitude of output force under the conservation of energy. Combining different mechanisms enables numerous functional micromachines for a wide range of complex tasks. For example, a magnetic helical micromachine with a microholder can be regarded as the first prototype of a compound micromachine (28), and an artificial bacterial flagellum is widely known as a basic micromachine with a helical body (27). Subsequently, multifunctional compound microtransporters, with the coordinated mechanism of a turbine head, an Archimedean screw pump, and a screw tail, were engineered for selective collection, 3D transport, and on-demand release of microparticles and encapsulated cells, as well as magnetic nanohelices (32). Simultaneously, compound compliant mechanisms have been employed to engineer 3D-printed microgrippers with integrated force sensors (59). Smart hydrogel materials allow the development of stimulus-responsive micromachine elements such as active origami sheets (36), and 4D direct laser writing allows the construction of 4D micro–building blocks for 3D-to-3D shape-morphing micromachines (37). These complex 3D reconfigurable compound micromachines also exhibit enhanced deformation-amplifying effects from the introduction of mechanical advantage (60). Other candidates for various engineering applications can also be considered, including compound acoustic (61), mechanically interlocked (38), and self-locking (62) micromachines.

2.3. Soft Micromachines: Flexibility, Adaptability, and Compatibility

Soft micromachines are becoming an important emerging subfield of intelligent micromachines, focusing on developing adaptive mechanisms at small scales. Highly analogous to nature's soft-bodied organisms, adaptive micromechanisms are typically soft, easily deformable, and capable of sensing and responding to environmental stimuli such as magnetic (2, 57), acoustic (63), electrical (64, 65), heat (36), light (19, 35), mechanical (59), and chemical (21, 66) signals. Various adaptive micromechanisms have been engineered for different purposes, including flexible hinges (57) and springs (2), soft grippers (59, 67), active origami (36) and kirigami (68), and smart joints (66), as well as compliant sensors (69) and entirely soft actuators such as artificial muscles (64, 65), skeletal muscles (70), liquid-crystal elastomers (19, 35), and so on. In contrast to rigid components (27), soft mechanisms with variable morphologies have greater flexibility or adaptability (22, 71), enhanced functionality (22), and increased robustness (52) or durability (72), and can undertake complex tasks (22) and adapt to extreme scenarios (65, 71). Moreover, a strategy to minimize their fluidic resistance via morphological transformations reflects the ability of soft micromachines to function in a viscous fluid, particularly at small scales (71, 73). At present, despite the substantial challenges in materials, design, modeling, fabrication, and control, soft micromachines have shown great potential for application in various fields, including biomedicine (74), search and rescue missions (64, 68), exploration (65), and multimodal locomotion (22, 24, 36). Soft micromachines could further enable intelligent micromachines to be integrated with flexible microelectronics that facilitate information perception, data storage and processing, and complex logical operations.

2.4. Continuum Micromachines: Compliance, Dexterity, and Redundancy

Continuum micromachines, also known as steerable microcatheters (75), are slender, compliant, multisegmented micromachines with highly flexible bodies and kinematic redundancy, allowing them to maneuver like snakes along complex curvilinear pathways in narrow, confined, and unstructured spaces. Inspired by elephant trunks, snakes, and mollusk tentacles or arms (76), continuum micromachines not only inherit flexibility and adaptability from soft micromachines but also give rise to compliance, dexterity, and redundancy through the coordination of controllable deformation units connected in series. Based on modular design methods (37), precise kinematic and mechanics models can be successfully established for the 3D motion planning of discrete multisegmented structures (77). Fully continuous micromachines can offer greater flexibility but have more complex models due to the nonlinear coupling of motions and forces.

Inevitable trade-offs in flexibility, accuracy, and functionality usually exist in structural designs and control for complex navigation (78). Conventional tethered actuation, such as mechanical pulling, employs external wires to control functional units, causing an increase in size as more units are added. As the size decreases, substantial increases in chamber pressure can disable pneumatic or hydraulic actuation mechanisms and cause unpredictable safety risks. Untethered magnetic actuation allows the miniaturization of existing continuum micromachines to the submillimeter scale, with external magnetic fields that exert torque on tiny embedded supermagnets (79) or microparticle composites (80). Recently, in combination with micrograppers (59, 67), microsensors (81, 82), and microactuators (79), significant efforts have been made to create intelligent continuum micromachines at small scales with high aspect ratios (length to depth) and many degrees of freedom. The more integrated units are revolutionizing techniques and approaches for minimally invasive surgery (77, 78, 83, 84).

2.5. Reconfigurable Micromachines: Programmability, Modularity, and Robustness

Reconfigurable micromachines, also called microscale transformer robots, are intelligent micromachines that can rearrange aspects of their own configurations, such as shape (36, 60, 85–87), stiffness (79), color (88), or other factors (89), to adapt to diverse scenarios, handle multiple tasks, and repair themselves by replacing fatally damaged components. Reconfiguring a micromachine requires its components to be changeable and, more critically, programmable. In comparison with soft micromachines that passively sense and respond to specific stimuli, reconfigurable micromachines place more emphasis on creating active, dynamic interactions with the external environment through the reconstruction of micromachines.

In general, there are two different schemes for small-scale reconfiguration of intelligent micromachines: the transformation of component functions and the reorganization of the interaction between components or subsystems. For example, various methods of shape transformations, such as active micro-origami (36, 86, 90–93), programmable matter (19, 22, 85), and 4D microprinting (38, 60, 94, 95), have been widely used to create shape-reconfigurable micromachines, also called shape-morphing microrobots. Modular reconfigurable robotics (96) was first developed years ago; however, establishing programmable interconnected mechanisms for each heterogeneous module at small scales presents a major challenge for current nanotechnology (97). Nevertheless, magnetic microparticle swarms are regarded as homogeneous modular systems that can be transformed into multiple collective formations by using alternating magnetic fields to remotely regulate the attraction and repulsion interactions between particles (43). As the complexity of reconfigurable interactions increases, some intelligent micromachines with collective functions (e.g., self-assembly, self-organization, self-repair, or even self-replication) could be further investigated in this field.

2.6. Encodable Micromachines: Reprogrammability, Encoding and Decoding, and Data Storage

Encodable micromachines are intelligent micromachines with internal data storage, where information is converted into code (or machine language) and repeatedly written into the micromachines. For current 4D microprinting techniques, shape-morphing information can be programmed into the micromachines (e.g., through adjustable ultrafast lasers) but cannot be modified after manufacture (60), similar to read-only memory, e.g., in a CD-ROM optical disk. Ferromagnets are widely used as data storage material because of their large hysteresis loop, which can be magnetized through an external magnetic field.

Several methods to process composite materials with hard magnetic microparticles, such as shape-programmable materials (22, 98), arbitrary 3D magnetization (99), and 3D printing (80, 85), have been developed for fast shape transformation of intelligent micromachines. Although it might be possible to magnetize the composite materials using a strong external magnetic field, precise control of the magnetization of individual randomly distributed magnetic particles is extremely challenging. However, with stable remanent magnetization and tunable magnetic anisotropy, single-domain nanomagnets (39) have been employed to fabricate encodable magnetic memory for intelligent shape-morphing micromachines. Based on this, a nanomagnetic encoding technique was developed to write a series of zeros and ones into a micromachine that contains shape-morphing information. With this method, four types of nanomagnets oriented along the x and y directions allow 8-bit magnetic data to be stored, giving 256 different configurations.

Other types of encoding technologies include light encoding (19), programming anisotropy of magnetic nanoparticles (100), magnetic quadrupole assemblies (101), color barcoding of magnetic microparticles (102), and DNA aptamer-encoded logic gates (103), among others. Micromachine encoding/decoding and data storage are indispensable for developing a human–environment–machine interface for complex interactions among information from different sources. This technique can serve as the first stage of information processing to further facilitate the advancement of intelligent micromachines toward multi-information fusions and micromachine learning.

2.7. Hybrid Micromachines: Multifunctionality and Hybrid Advantage

The term hybrid micromachines generally refers to intelligent systems composed of diverse hybridized micromachine elements derived from distinctly different sources, e.g., hybrid organic–inorganic composites (48, 104), biological and human-made components (105), hybrid design methodologies (106), multiphysical actuation fields (107), hybrid control strategies, and so on. Through the fusion of seemingly incompatible elements, micromachines will synergize the benefits of different types of methods and techniques, exhibiting a hybrid advantage superior to the performance and functionality of more homogeneous micromachines. Metal–organic frameworks (108) have been used as designable hybrid materials for creating smart biomedical micromachines with tailorable compositions, high responsiveness to stimuli, and excellent cargo-loading porosity, as well as biodegradability and biocompatibility. These porous hybrids, composed of metal ions linked with organic ligands, combine the respective benefits of the inorganic (e.g., rigidity and thermal stability) and organic (e.g., flexibility and ductility) materials and nurture the emergence of enhanced properties and multiple new functionalities (e.g., electrocatalytic, ferroelectric, and ferromagnetic).

Several multistep fabrications (35) with multimaterial designs (38) have been developed for rapid prototyping of hybrid micromachines. However, synthetic micromachines do not always satisfy the requirements of interactions at small scales, and an alternative would be to incorporate biologically engineered components (e.g., living tissues cultured by neurons and cardiac muscle cells) as microsensors or microactuators into biohybrid micromachines (105, 109). For some biohybrid micromachines, such as SpermBots, which are physical hybrids of artificial bacterial flagella and sperm cells (42), their artificial parts can have an enhanced effect on the natural functionality of biological parts. Moreover, hybrid micromachines might encompass multiple sets of redundant components with complementary functions, but with different operation modes or actuation methods that can be switched according to specific situations (110). A greater understanding of interaction mechanisms of hybridized elements will enable us to create multifunctional hybrid micromachines.

2.8. Bioinspired Micromachines: Biomimicry, Bioinspiration, and Optimization

Bioinspired micromachines encompass any micromachine created with designs inspired by biological solutions. Nature has been frequently used as a source of inspiration for designing prototypes of intelligent machines. In general, there are two different methodologies: biomimicry, which derives from biomimetics and directly replicates nature to build something similar, and bioinspiration, which derives from bionics and learns from nature to create something new. Many efforts in biomimetics have been devoted to spawning advanced biomimetic technologies [e.g., from materials (111), functional structures (112), locomotion (13, 19, 20, 22, 23, 33), and fabrication (113)] and consequently constructing micromachines that accurately reproduce functional structures of tiny natural creatures [e.g., robotic insects (13, 15, 17) and soft-bodied micromachines (20–23)]. These micromachines are often called biomimetic micromachines.

Bionics is closely associated with engineering and robotic technology, with an emphasis on imitating bioinspired functions tailored to specific application scenarios rather than solely biological structures. Replicating the biological structures of microorganisms is challenging, particularly at small scales, and the design of microscaled mechanisms and control methods cannot be obtained intuitively. Therefore, bioinspiration is beneficial for advanced micro- and nanorobotics, such as bioinspired microrobots (114), as it allows us to extract principles, theorems, processes, and techniques from natural phenomena to create intelligent micromachines with enhanced functions beyond biological solutions. Among the most successful bioinspired micromachines are artificial bacterial flagella, which are helical microswimmers that mimic the corkscrew motions of *Escherichia coli* bacteria (27, 71), and numerous variants of this micromachine have been engineered for diverse applications.

2.9. Integrated Micromachines: Information Processing and System Integration

Integrated micromachines are a highly integrated intelligent complex of various types of micromachine elements that are organized together to form a complete functional architecture of intelligent systems. Intelligence exists in complex systems, so system integration, in this sense, offers tremendous potential for a further increase in the structural or functional complexity of micromachines and, as a result, helps create μ-AI. Current micro- and nanofabrication techniques, such as 3D direct laser writing, microelectromechanical systems (MEMS), and complementary metal–oxide–semiconductor (CMOS) techniques, offer promising prospects for creating integrated micromachines by enabling the rapid prototyping of miniaturized mechanical (e.g., mechanisms), electromechanical (e.g., sensors or actuators), or electronic (processors or memories) elements. However, their fabrication processes are often incompatible despite originating from the same semiconductor manufacturing techniques. It is, therefore, quite challenging to integrate all of these components into a system as an organized whole. Nevertheless, attempts have been made to integrate simple microelectronic circuits into micromachines, such as p–n-junction integrated micromachines with voltage-controlled electrochemical actuators (41) and microcoil integrated micromachines with wireless energy transfer (40). These micromachines are known as electronically integrated micromachines. Their latent potential may not become manifest until microelectronic integrated circuits (e.g., logic integrated circuits) can be embedded as the brain of a micromachine to form a closed-loop control system along with microscale mechanisms, sensors, actuators, and so on. Moreover, it is highly preferable to develop cutting-edge technologies where flexible microelectronics (115–117) are perfectly integrated to be compatible with adaptive mechanisms of soft micromachines.

2.10. Interactive Micromachines: Communication, Decentralization, Coordination, Cooperation, Self-Organization, and Swarm Intelligence

The term interactive micromachines refers to a wide range of intelligent micromachines capable of interacting with their internal and external environments, where they obtain the knowledge they need. Developing such machines involves creating effective mechanisms for small-scale interactions that have the potential to unleash advanced μ-AI. A micromachine's interactions are a set of feedback loops formed by causally connecting its internal system or subsystems with external systems such as humans, the environment, and micromachine peers, which correspond to four different types of interaction: self-interaction (internal), human–micromachine interaction (external), environment–micromachine interaction (external), and micromachine–micromachine interaction (external). To establish these interactions, it is necessary to formulate mutually acceptable protocols, create feedback mechanisms, and maintain the stability of the overall system during interactions.

An individual micromachine is usually self-centered, demonstrating its intelligence by increasing its complexity of structural functions to adapt to dynamic environments or various tasks assigned by humans. However, this poses a challenge to existing integration techniques at small scales. Group interactions or synergies (i.e., interactions between individuals) tend to decentralize individual competence into the system via their ordered coordination, cooperation, and competition, and thus these individuals can be less complex while spontaneously generating more advanced collective behaviors. As short-range interactions (e.g., electromagnetic or electrostatic interactions between molecules) begin to dominate at small scales, the randomness and weak couplings of multibody interactions, such as Brownian motion, are more conducive to the formation of self-organization that yields the emergence of swarm intelligence. Advances in micromachines have shown a trend toward collective intelligent micromachines (118, 119).

2.11. Molecular Micromachines: Nanomachines, Miniaturization, Self-Assembly, Self-Replication, and Self-Growth

Molecular micromachines are nanometer-scale intelligent machines capable of performing quasi-mechanical movements, rapid transportation, and active morphological transformations (120) in response to changes in environmental conditions. They are constructed from biologically self-assembled (121) or chemical synthetic (122) molecular-level machine elements with atomic detail. In nature, all life starts from biological molecular micromachines, which are hierarchically constructed through DNA or RNA replication. For example, the macromolecule DNA is a precision nanomechanism capable of encoding and storing the genetic instructions required to assemble, maintain, and reproduce active protein complexes. DNA's precise programmability enables the construction of various biologically assembled molecular micromachines for use in many fields, such as targeted drug delivery systems (122), phage therapy (121), nanomanipulation (123), and self-assembly technologies (124, 125). Similar to biological assembled nanomachines, artificial molecular machines can be designed and synthesized based on simple mechanically interlocked molecular elements with controllable locomotion, such as rotaxanes and catenanes. The assembly of these molecular components offers significant potential to create complex nanomechanical systems such as molecular motors, molecular sensors, molecular logic gates, molecular assemblers, and nanocars (124).

3. MICROMACHINE INTELLIGENCE

Existing examples of micromachines have revealed various aspects of intelligent features, but few studies have discussed emergent mechanisms of intelligent behaviors and methodologies used in the intelligentization of micromachines from a system perspective. μ-AI is a micromachine's capability to generate adaptive behavioral responses that maximize the potential to achieve its goals through dynamic interactions with its components, humans, environments, and machine peers. To cope with the uncertainty and variability inherent in complex interactions, for example, an intelligent micromachine is required to take actions under a wide range of conditions and, more importantly, to make reasonable decisions about how to do so. The ability to recognize the complex external world and influence it by establishing dynamic interactions determines the degree of intelligence of these micromachines. μ-AI, therefore, implies the interactions of information at small scales, with a focus on how to trigger the emergence of surprisingly intelligent behaviors. It necessitates an ambitious initiative for micromachines to interact with their internal and external worlds.

In general, the success of creating μ-AI depends greatly on the establishment of three key features of intelligent micromachines: (*a*) control components, which perceive, interpret, process, and react to information gained from different sources; (*b*) adaptive mechanisms, which transmit or suitably modify some forms of information; and (*c*) feedback, which returns information to the system for creating interactions. In recent years, adaptive mechanisms have been widely investigated at small scales, such as soft micromachines (7). The technological innovations in smart printable materials (95, 113, 126, 127) further provide a straightforward but effective strategy to sense and respond to the external environment, and complex 3D shape-morphing (60) or self-reconfiguring modular (37) micromachines can be engineered accordingly. Meanwhile, programmable substances such as ferromagnetic microparticles (22, 24, 85) and nanomagnets (39) have also contributed to the creation of multifunctional micromachines for accomplishing multiple tasks. Unfortunately, most of these micromachines should be more accurately regarded as smart microactuators rather than intelligent micromachines, due to the absence of interactions of information at small scales.

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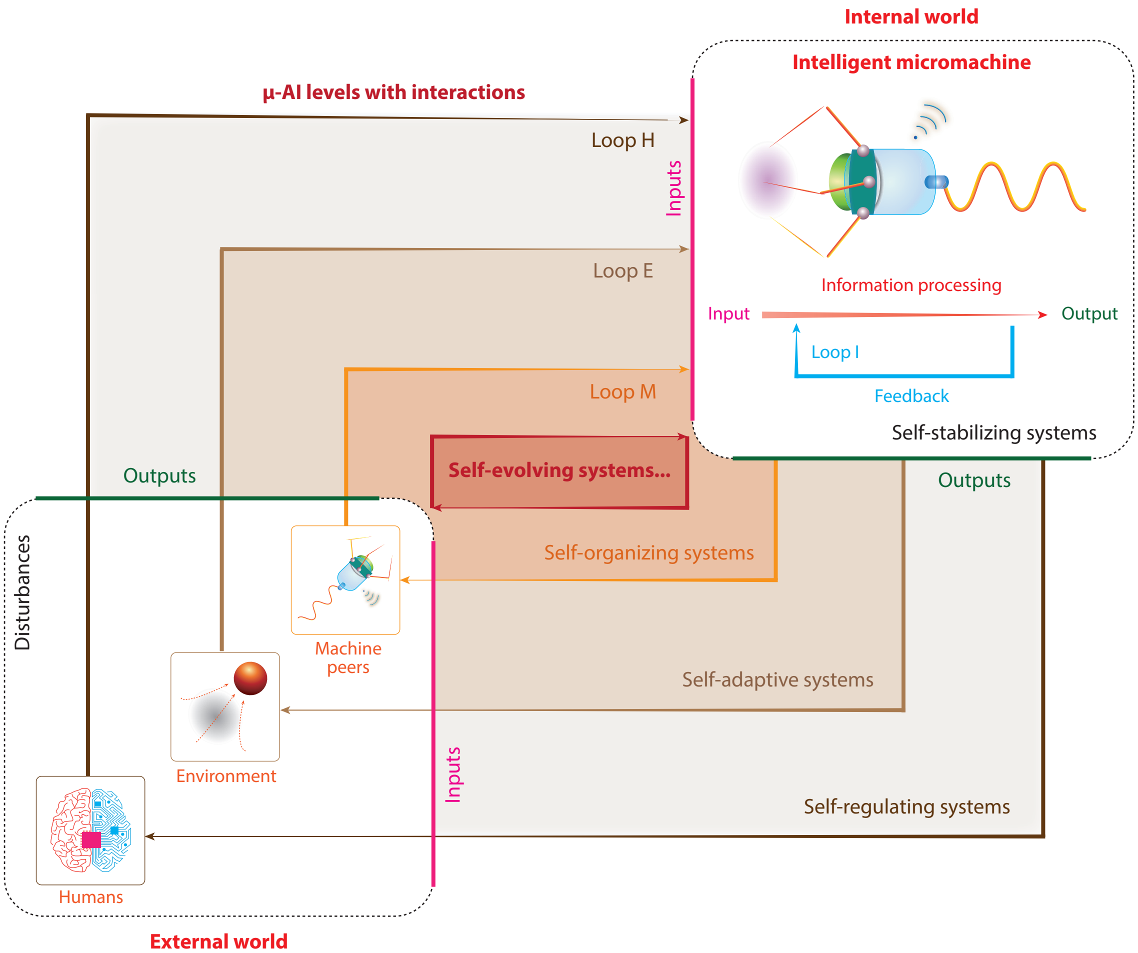

Figure 4

Dynamic interactions of information for creating micromachine intelligence (µ-AI). The four types of interactions are loop I (interaction with itself), loop H (interaction with humans), loop E (interaction with the environment), and loop M (interaction with machine peers). The establishment of interactions depends on feedback that brings information from the output ends (*green*) back to the input ends (*pink*). The combination of these interactions, also called loops IHEM, could lead to the emergence of surprisingly intelligent behaviors. The five µ-AI levels—self-stabilizing systems (level I), self-regulating systems (level II), self-adaptive systems (level III), self-organizing systems (level IV), and self-evolving systems (with artificial intelligence controllers; level V)—hierarchically increase with the change of interactions.

Interaction occurs when a micromachine has two-way causal effects on its internal and external environments, and it is therefore essential that µ-AI forms a feedback loop through at least two reciprocal chains to transfer information from the output of one system to the input of another. Feedback loops represent the most essential feature of intelligent systems, and an intelligent micromachine exhibits four forms of feedback loops, as shown in **Figure 4**: loop I, loop H, loop E, and loop M, corresponding to the micromachine's interactions with itself, humans, the environment, and machine peers, respectively.

Loop I is the fundamental requirement for creating µ-AI, because it allows a micromachine to become a stable system with preset goals to dampen disturbances using negative feedback and amplify stimuli or signals through positive feedback (level I). Based on this, the output can be further set by humans with loop H, thus enabling self-regulating systems, also referred to as automatic control systems, that adjust automatically to the desired output by comparing and synthesizing the output with the knowledge gained from the actual output. Level II μ-AI intelligent micromachines use loop I and loop H. Loop E raises μ-AI to level III, where it can create self-adaptive systems that gently modify control parameters of the system without requiring preset values as the environments change. Level IV is demonstrated by self-organizing systems that can generate spontaneous order arising from local interactions among micromachines, i.e., the emergence of collective intelligent behaviors. Usually, each intelligent micromachine is regarded as an autonomous intelligent agent without any external control, and the emergent mechanism of swarm intelligence could be revealed at this stage. When the interactions become increasingly complex and controllers with advanced AI rules could be integrated into the system with adaptive mechanisms, the potential for creating higher μ-AI levels could far exceed our expectations—e.g., fuzzy logic systems that optimize their performance using AI rules, such as self-assembling, self-learning, self-growing, or self-evolving systems (level V).

4. THE INTELLIGENTIZATION OF MICROMACHINES

To create intelligent micromachines, two core aspects must be considered. The first is functionalization, created by constructing the mechanisms that generate a desired set of outputs according to existing needs. The second is intelligentization, created by introducing a system of control components that regulate or reconfigure the mechanisms to adapt to the changes in needs inherent to internal and external worlds. In recent decades, advanced nanotechnology has made considerable progress in the design and construction of microscale mechanisms, from simple structures (27) to compound mechanisms (32) to complex adaptive mechanisms (36, 60, 94). As micromechanisms become more powerful in functionality and satisfy a certain degree of adaptability and redundancy at small scales, multiple control microcomponents are being integrated with the mechanisms to meet the needs of μ-AI.

For example, helical microswimmers (27) can be considered to be the combination of a magnetic actuator (A) and a propulsion mechanism (M), described as [A+M]. 4D microprinting of smart materials enables the creation of soft micromachines (19, 36, 37), which are active shape-morphing mechanisms that can sense (S) and respond to changes in external stimuli, described as [S+A+M]. The use of single-domain nanomagnets allows micromachines (39) to store data (D) by encoding (E) multiple shape-morphing configurations ([E+D+A+M]), and nanomagnetic logic units (128) have offered the potential to create more intelligent micromachines with a computing (C) function ([E+D+C+A+M]). To some extent, the degree of intelligentization of micromachines is determined by the adaptability of the mechanisms and the integration of control units. The establishment of internal and external interaction mechanisms (i.e., feedback loops) is also an important consideration for micromachine intelligentization. In this section, we explain how to intelligentize micromachines from three perspectives: micromachine elements, the control system framework, and core techniques.

4.1. Micromachine Elements

Figure 5 shows potential functional components of an intelligent micromachine, corresponding to the organ systems of the human body. According to their functionalities, these micromachine elements can be further classified into six categories: control components, adaptive mechanisms, power components, structural components, inputs, and outputs. In this system, control components are described as micromachine elements that embody machine intelligence, with adaptive

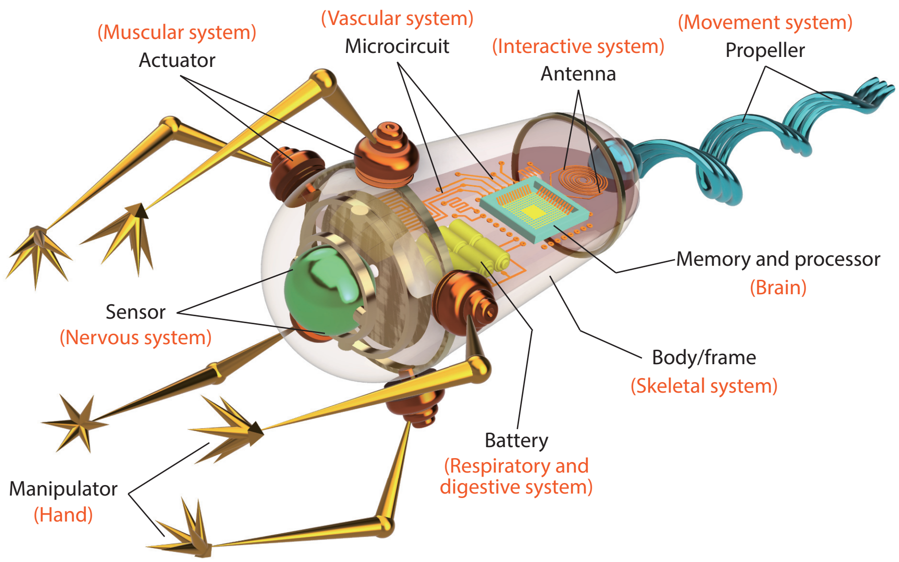

Figure 5

Conceptual illustration of an intelligent micromachine, showing 10 potential functional components: body/frame, manipulator, propeller, sensor, actuator, memory, processor, microcircuit, antenna, and battery. Their functions correspond to some of the functions of the human skeletal system, hand, movement system, nervous system, muscular system, brain, vascular system, interactive system, respiratory system, and digestive system.

mechanisms as primary units that reflect the machine functionality, power components as energy suppliers, structural components as the structural frame, and inputs and outputs as interfaces to bridge the internal and external worlds, as detailed in **Figure 6**.

The control components make up the core of micromachine intelligentization and are required to perceive, fuse, process, and react to information obtained from mutual interactions and automatically maintain the adaptive performance of micromechanisms. As the first step of micromachine intelligentization, perception is responsible for obtaining information through multiple interaction strategies to communicate with the internal and external environments, such as human–machine interfaces, sensors that perceive environmental cues or feedback from the output mechanisms, and receivers that interact with machine peers (e.g., antennae). In the second step, information fusion—the acquired information from different sources—must be further translated into machine-recognized language through a standardized coding process and then integrated into the data that can be processed by the machine. Information processing is the third step, where the data are compared, analyzed, and synthesized by microprocessors to produce reasonable response signals, and necessary information is simultaneously stored in the memory as a previous knowledge reserve. Reaction is the last step of the control process, where the signals are generally converted (e.g., from digital to analog), amplified, and then sent to the microactuators that produce mechanical forces to trigger the movement of the mechanisms. These actuators are engineered to be controllable, coordinated, and programmable according to the design requirements of adaptive mechanisms. In some cases, signals might be directly sent out through transmitters (e.g., antennae) to communicate with other machine agents or receiving devices.

The adaptive mechanisms are functional components capable of generating the desired set of mechanical forces and movement as required. The family of adaptive mechanisms mainly includes

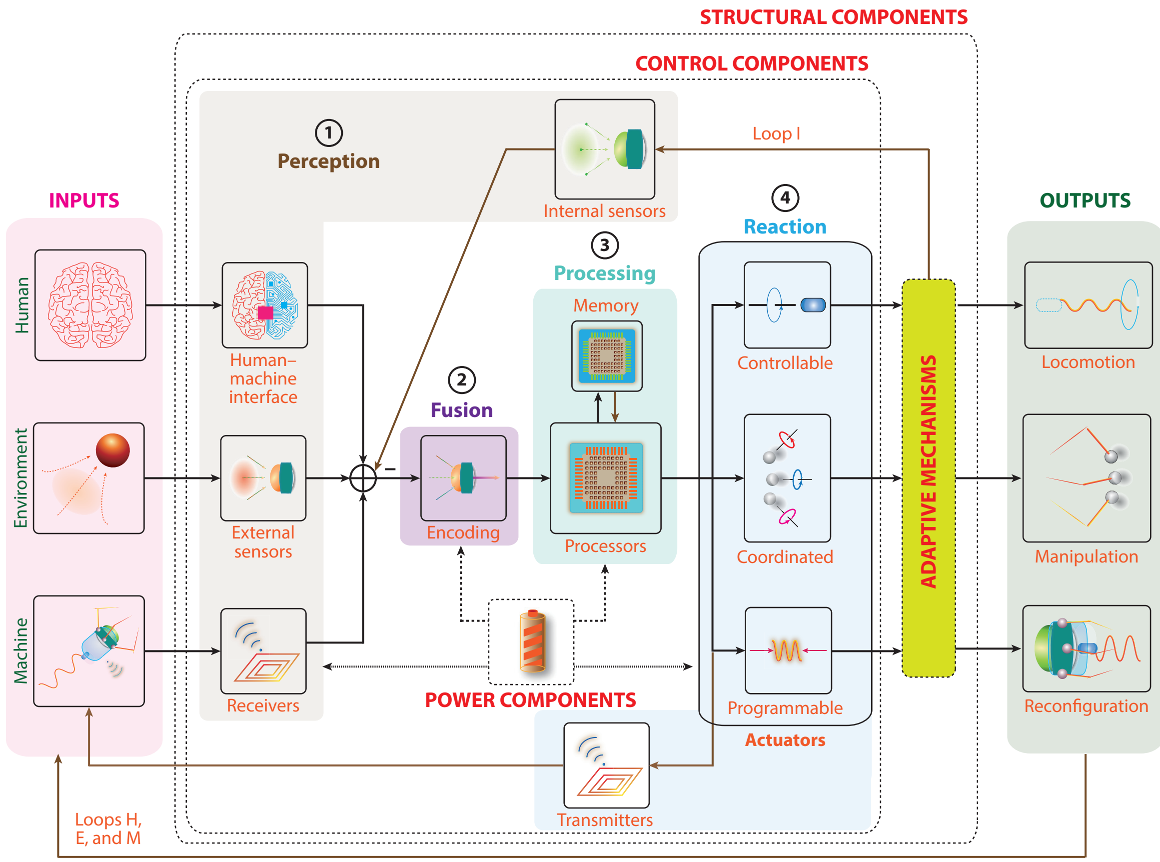

Figure 6

System framework of intelligent micromachines. The main body of this system framework consists of the control components, which cover four key aspects of the micromachine's functionalities: perception, fusion, processing, and reaction. The elements are labeled in all capital letters, and the transmission flows of information and energy between components are depicted as solid and dotted black arrows, respectively. The framework entails four fundamental interactions that intelligent micromachines may potentially have: loop I (internal) and loops H, E, and M (external), indicated with brown arrows.

manipulatory mechanisms (e.g., hands, tentacles, proboscis, and beaks) and locomotion mechanisms (e.g., legs, wings, fins, flagella, and cilia). To adapt to dynamic changes or uncertainty, adaptive mechanisms usually adopt a variable and reconfigurable scheme for the design of structures and functions, such as soft, flexible, deformable, compliant, multisegmented, compound, hybrid, shape-morphing, or self-assembled mechanisms, sometimes packed with the storage and release of mechanical energies as well as the local sensory response.

The power components provide the energy supply for the control components through various manifestations, such as batteries, chemical fuels, transformers, microcircuits, or microchannels. The structural components make up the body frame and are analogous to the human skeletal system (bones and connective tissues), providing support, fixation, and protection for mechanisms or functional components to ensure sufficient space for the normal operation of the whole system.

The inputs and outputs are interfaces between the micromachine and its external world. The inputs potentially contain information gained from interactions with humans, environments, and machine peers, and their outputs can be simply described as three functions: locomotion, manipulation, and reconfiguration.

4.2. System Framework

The system framework is the organizational structure that determines how information or energy flows between elements within an intelligent micromachine system. It is established according to specific requirements on micromachine intelligentization and may have multiple complex feedback loops due to the establishment of interactions with the internal and external environments.

Figure 6 describes a fundamental system framework of intelligent micromachines, which covers the ideal arrangement of all the micromachine elements and four types of potential interactions. Interactions with the external world offer all the necessary knowledge that micromachines need and serve as the inputs of the system to affect the operation of intelligent micromachines. For example, these micromachines interact with humans to adjust responses to specific instructions, with the environment to perform adaptive behaviors, and with peers to execute collective self-organization. The input information is then perceived through various means, such as human–machine interfaces, external sensors, and receivers, and is fused with the internal feedback of the system as the input of the controller. The fused information is computed by the microprocessor, after which some of the obtained data are stored in the memory for later recall and analysis, some are sent back to the receiver in the external environment through the transmitters, and the rest are used as the input signal of the microactuators to control the adaptive mechanisms after power amplification. Eventually, the state of the mechanism is fed back to the system by the internal sensors to maintain the stable operation of the system, and mechanical forces and movements are used as outputs to influence the external environment.

4.3. Core Techniques

From the perspective of the interaction of information at small scales, as shown in **Figure 3**, the core techniques for creating intelligent micromachines can be divided into five categories: information media, transduction, processing, exchange, and energy supply.

Information media provide the physical substrate of μ-AI and carry information and energy. This category focuses mainly on the materials, design, and fabrication of micromachines. Functional materials (129) are the basis for the construction of all intelligent components, which are chosen for their designable and controllable physical or chemical properties (104) and for the capability to sense and respond to various external stimuli, such as magnetic or electrical fields, light, heat, sound, moisture, stress, and pH. Various designs, such as those for smart materials, functional structures, advanced manufacturing processes, and control systems, offer effective optimization methods for all aspects of intelligentization at small scales. Existing design methods that have been widely adapted include biomimetic (18, 111, 113), bioinspired (114), and biohybrid (105) designs; origami designs (86, 90, 91, 93, 120); 4D modular designs (37, 96); and AI-assisted designs, as well as simulation methods for kinetics (60) and kinematics (37). Traditional nanotechnologies such as 2D photolithography and electrochemistry have been widely employed for fabrication (the process of micro- or nanomanufacturing intelligent matter), but advanced 3D microprinting techniques (28, 32, 50, 59) and multimaterial fabrication (38) have allowed rapid prototyping of complex functional microstructures, and additional smart materials (130) and 4D micro- and nanoprinting (37, 60, 94, 95, 126) have been investigated to provide micromachines with intelligent sensing and actuation. Integrated assembly and packaging techniques have also been developed for the systematization of complex intelligent micromachines.

Transduction, or energy transformation, is the process in which a micromachine uses transducers to convert information or signals from one form of energy to another. Normally, information exists in various forms of energy—mechanical (59), electric (41), magnetic (2, 24, 27, 39, 80, 101), chemical (37, 60), sound (31, 58, 61, 63, 110), thermal (90), radiant (19, 35), and so on—and the transformation between different forms of energy primarily involves two major categories concerning μ-AI, sensing and actuation, which are responsible for producing perception and reaction in intelligent systems, respectively. Sensing (4, 12, 82, 131) is the process of perceiving information in some types of energy from the external environment and transferring it into a type of information that micromachines can process, whereas actuation (40, 68, 89, 92, 100, 109, 131) transfers the processed information into other types of energy, particularly mechanical forces and movements that control the mechanisms to interact with the external environment. In particular, some transducers, such as antennae and piezoelectric transducers, have great application prospects because of their bidirectional functions for receiving and transmitting information.

Processing, also called information processing, is the core process of intelligentizing micromachines, where micromachines produce reasonable signals to respond to the external environment by logically comparing and analyzing the obtained data with knowledge stored in memory, such as instructions, parameters, and AI rules. It mainly involves three major techniques: computing, data storage, and control. Computing governs the logical operation of information, which relies on the establishment of logic units. Several techniques have been investigated for computing at small scales, including CMOS-based logic (41), spintronic-based logic (128), and DNA-encoded logic (103). Data storage is responsible for the accumulation of knowledge by encoding, storing, and retrieving information from previous experiences. A nanomagnetic encoding technique has been developed for storing shape-morphing information using single-domain nanomagnets with tunable magnetic anisotropies (39). The high efficiency of data processing further requires an intelligent architecture that maximizes the compatibility of computing and storage units and establishes special communications by introducing controllers that manage the flow of data between units. Here, control describes a process to regulate the output performance of intelligent micromachines using closed-loop feedbacks (131, 132) and covers multiple technical aspects, such as controllers, control algorithms, feedbacks, and control systems.

Exchange, the outward manifestation of μ-AI, is the process for exchanging matter, information, or energy with the external environment, micromachine peers, and humans. The mechanism is one of the components responsible for exchanging and is controlled by actuators to produce the desired forces and motions to act on the external world while receiving responsive effects from the world. Two key techniques for the force and movement of mechanisms are locomotion and manipulation, which involve movement with and without a change in the mechanisms' positions, respectively. Producing effective propulsion and locomotion at small scales for various environmental conditions and optimizing adaptive manipulation strategies for various types of operating objects are the keys to the mechanism design. Some receivers and transmitters also offer the ability to exchange information directly between micromachines. Therefore, real-time remote communication is also considered an essential micromachine technique for information exchange.

Energy supply is the process that provides energy to control the components of the micromachines. Several energy supply strategies for the small-scale actuation of micromachines have already been successfully applied, including rotating or gradient magnetic fields (133), acoustic fields (31, 110, 134), electric fields (135), chemicals (136), light (19, 35), and hybrid methods (48, 105, 110). By contrast, energy supply for computing (128), data storage (39), and active sensing (137, 138) at small scales is limited to various forms of electrical, magnetic, or light energy. Existing technology has not yet enabled the creation of human-made micromachines that can obtain energy completely from their surrounding environments, like biological organisms do, to support the operation of all the components of the entire system (107). Therefore, a hybrid power supply strategy or the use of electrically powered microdevices will facilitate the integration of different types of control components. Related techniques may also involve energy storage, power transformation, and wireless power transfer at micro- and nanometer scales.

5. POTENTIAL APPLICATIONS

5.1. Medical Applications

Minimally invasive interventions by micromachines hold the potential to revolutionize medical treatment by providing higher precision and fewer complications using miniaturization tools. In 2010, a milestone review (3) presented a clear vision and path for micromachine use in minimally invasive medicine, including precision drug delivery and interventional therapy. Since then, the field has made significant progress on increasing intelligence in terms of materials and fabrication methods as well as navigation strategies, bringing us closer to the vision of *Fantastic Voyage*.

Several important trends in the past decade have brought intelligent micromachines closer to use in medical applications. First is the increasing use of soft, biocompatible, and biodegradable materials. Early micromachines were made of rigid materials (metals and rigid polymers) that are available from established MEMS. To use the micromachines in vivo, materials must be biodegradable, and the pathway for elimination from the body should be considered when designing them. The second trend is to study the dynamics of micromachines in complex non-Newtonian fluids with biological relevance (liquids with salt, proteins, and cells). The third trend is to study locomotion in more physically relevant structured environments (e.g., vascular models and 3D fluidic channels) instead of in free open spaces. New strategies that use vessel walls to propel micromachines with greater speeds have been demonstrated (110). Most minimally invasive interventions are multiscale procedures, and it is prohibitively challenging for a machine at the micrometer scale to overcome the meters-per-second blood flow speed at the aorta; however, a combination of robotic technologies at different scales may help in overcoming this challenge. Meter-long medical catheters can be used to guide microrobots to an area near a targeted location where the local flow speed is low and then release them there.

5.2. Device Inspection and Repair

With electrostatic patches, microrobots can climb up various slopes even walk invertedly on the inner surface of a jet engine (16). Their small size and locomotion capability on various surfaces enable them to easily navigate in confined spaces that cannot be reached with traditional methods. This technology is particularly promising for the inspection and examination of expansive and complicated mechanical machines, such as jet engines. In the future, with increasing intelligence, small cameras, and miniaturized sensors, micromachines can be integrated onboard to meet different inspection requirements. At the micrometer level, mobile particles can be used to repair broken electric circuits on microchips. The broken electric wires generate strong electric field gradients at the break that can attract micromachines by electrophoretic force (139). Implementing a dynamic magnetic field also makes it possible to shape swarm micromachines to conduct electricity to the microchip (140). The swarm micromachines can function as a microswitch and constitute flexible circuits, showing potential for applications in novel electronics and circuit design.

5.3. Environmental Applications

At micrometer scales, self-propelling micromotors have unique advantages in terms of surface-to-volume ratio, catalytic activity, and surface chemistry. In the past decade, they have shown their

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potential for on-site and real-time pollution analysis, including DNA and heavy metal detection. The high motility of the micro- and nanomotors promotes mixing and mass transport and therefore improves the local reaction speed. Implementing a swarm of micromachines enables them to be used in water-cleaning applications, including degradation of organic dyes, environmental oil remediation, and oxidative detoxification of nerve agents (141). Some artificial micromotors have shown chemotactic behaviors that can actively seek and degrade pollutants. Importantly, these mobile micromachines need to be recycled after usage or degrade over time to minimize their environmental impact. On land, intelligent micromachines at centimeter scales are promising for environmental monitoring. Integrated with solar panels, wheels, cameras, and environmental sensors, the micromachines can move around and collect data on humidity, plant health, pests, and soil conditions (142). These terrestrial robots can be used together with flying drones to provide valuable data for advanced agricultural management that can help improve yields and sustainability.

5.4. Chemical Analysis and Blood Filtering

Many applications in analytical chemistry require real-time identification, transport, and separation of analytes in situ (12). Compared with conventional methods, active intelligent micromachines can seek out, migrate toward, capture, transport, and separate various analytes, enabling various applications. Magnetic nanoparticles, which can be controlled by external magnetic fields for precise locomotion, are particularly promising. The complete analytical procedures can be automated by ferrobotic systems on a chip (143), and the contactless and high-strength nature of the actuation mechanism used in these systems enables rapid, repeatable, and robust testing.

Another application is blood filtering. The surface of magnetic nanoparticles can be decorated with various groups for specific bonding with targeted pathogens (144). After mixing, a high surface-to-volume ratio enables nanomachines to quickly filter the blood and recycle it back using a strong magnet. This strategy enables novel treatments for many diseases, including sepsis, malaria, and coronavirus disease 2019 (COVID-19).

6. FUTURE ISSUES

6.1. Microfabrication and Packaging

Fabrication and integration of multiple functional elements into a single body are the core challenges in realizing intelligent micromachines. As in **Figure 5**, the complexity of microsystems is increasing with the requirement to integrate multiple functional devices, including sensors, actuators, and microprocessors. With a growing number of processes, the yield rate decreases exponentially. In some cases, the fabrication processes of different functional components are not compatible. The high temperature, etching liquid, and aggressive solvent used in the later fabrication processes may destroy the devices and structures already on the chip. Avoiding this situation requires adding protective layers and reorganizing the process flow, which complicates the fabrication process and further decreases the yield rate. For microdevices that can be directly purchased, customized microassembly equipment is required to integrate all components repeatedly with proper electrical and mechanical connections.

Packaging is another major challenge after successful microfabrication. Depending on the type of working environment, intelligent micromachines may need to have close contact with water, salt, and microbes, which could be detrimental to their internal electronic components. Insulating layers are required to protect sensitive components from harsh working environments.

The standard packaging process for integrated circuits seals the functional components into an isolated rigid body. However, packaging micromachines is quite different due to the moving components and the compliant body. The packaging of intelligent micromachines may compromise interactions with other micromachines, environments, and humans.

The recent development of novel microfabrication techniques shows promising directions for increasingly intelligent micromachines. These advances include multimaterial 3D printing (145), micromachine-assisted assembly (146), 2D-to-3D shape transformation (147), roll-up microdevices (148), and micromachines that are compatible with the standard integrated circuit fabrication process (41). Many of the methods have found immediate applications in flexible electronics and miniaturized surgical tools.

6.2. Materials and Surfaces

Many of the functional elements inside intelligent micromachines are not commercially available, which means researchers must build up complex micromachines from the material level. Synthesizing materials with stable properties is the foundation for building intelligent micromachines. Intelligent micromachines can be difficult to collect and recycle after use due to their small size. For micromachines used in environmental cleaning, the materials must be degradable over time and not generate toxic waste. For implanted medical devices, the materials must be biocompatible and biodegradable within a certain period of time. These requirements raise challenges in material selection, design, and fabrication.

The full life cycles of intelligent micromachines must be designed to be environmentally friendly and safe for humans from the beginning (149). At small scales, micromachines have a high surface-to-volume ratio, making them more sensitive to surface properties and conditions. For example, the formation of bacterial biofilm can entangle and cause dysfunction in mobile micromachines. Surface tension can also dominate microrobot motion, which necessitates the use of a surface coating to prevent unwanted wetting. However, this also creates opportunities to design micromachines that can take advantage of surface effects.

6.3. Power Autonomy

The available onboard space for miniaturized micromachines is extremely limited. Thus, it is crucial to design a power system to enable sufficiently long operating times for intelligent micromachines. A recent review showed that the cost of transport does not scale down with decreasing size for terrestrial micromachines (150), which suggests that the development of a more energy-efficient actuator and locomotion mechanism at small scales is required. Some micromachines use onboard high-density energy sources, including electrical capacitors, chemical fuel, and novel batteries. Others use wireless power transmission to continuously drive the intelligent micromachines. For these systems, an external power system is required near the workspace during operation.

There are three major types of power transmission for mobile micromachines: magnetic fields, electromagnetic waves, and acoustic waves. Technologies using these methods are being developed for biomedical applications inside the human body. Magnetic fields can apply force and torque on the magnetic object using a controlled external magnetic field. Electromagnetic waves at radio frequencies (in the megahertz range) and infrared light (in the gigahertz range) can also penetrate the human body and transform electrical power into local heating (40). Acoustic waves can also safely penetrate the human body and excite bubble-based micromachines for propulsion (31) and triboelectric microdevices for brain stimulation (151).

6.4. Localization and Communication

Tracking a small object inside a large workspace is challenging, particularly when the object is at the micrometer scale. In some cases, standard and confocal optical microscopes have sufficient resolution for on-chip manipulation. Super-resolution imaging techniques (152) further improve the precision of optical imaging. However, for many medical inspection applications, the medium is nontransparent to visible light, requiring new technologies for high-resolution imaging and localization. Clinical magnetic resonance imaging is not compatible with most magnetic micromachines, and fluoroscopic imaging exposes patients and doctors to carcinogenic X-rays. For swarms of micromachines, communications between the neighboring agents are important. For submillimeter micromachines, existing communication methods take place through physical interactions (e.g., magnetic or hydrodynamic interactions). However, it is difficult to design complex intelligent interactions based on simple physical interactions. It is also challenging to miniaturize existing wireless communication modules so that they can be used onboard for swarm coordination.

7. FRONTIERS

7.1. Large-Force Micromachines

We summarize the keywords related to intelligent micromachines and list 10 promising research directions in **Figure 7**. To begin with, force is an important measure when micromachines interact with the surrounding environment. The force output of a micromachine is intrinsically limited by its size, material properties, and actuation mechanism. For magnetic micromachines, a force can be generated by the gradient of the external magnetic field. However, the gradient scales down linearly during miniaturization, providing limited force output for micromachines (55). New methods that can break the limitations of the force output are highly desired for biomedical applications, including biopsy, drug injection, and locomotion on rough surfaces.

7.2. Tactic Micromachines

Bacteria have been a major source of inspiration in terms of designing intelligent micromachines. Tactic behaviors, where microorganisms can sense environmental stimuli and respond to it by actively moving toward or away from it, are strongly desirable for artificial systems. These tactic behaviors include, but are not limited to, aerotaxis (stimulation by oxygen), barotaxis (by pressure), chemotaxis (by chemicals), durotaxis (by stiffness), electrotaxis or galvanotaxis (by electric current), hydrotaxis (by moisture), magnetotaxis (by magnetic field), phototaxis (by light), rheotaxis (by fluid flow), thermotaxis (by changes in temperature), and thigmotaxis (by physical contact). Some pioneering works have implemented stimuli-responsive smart materials to provide micromachines with the ability to respond to light (153), heat (36), fluid fields (154), and chemical signals (155), and higher sensitivity and more functionalities are anticipated.

7.3. Nanomagnetic Intelligence

Magnetic materials are often used as the actuation mechanism to power micromachines. Recently, by processing precisely shaped single-domain nanomagnets, researchers have reprogrammed magnetization into micromachines for complex shape morphing (39). Nanomagnet systems could prove to be the ideal platform to integrate all the components shown in **Figure 5** into the ultimate intelligent micromachine. Nanomagnets can be modulated by various physical stimuli, including temperature and light, potentially functioning as sensors. Nanomagnets can also be used to perform logic computation through domain walls (128) and magnetic interactions (156) and therefore

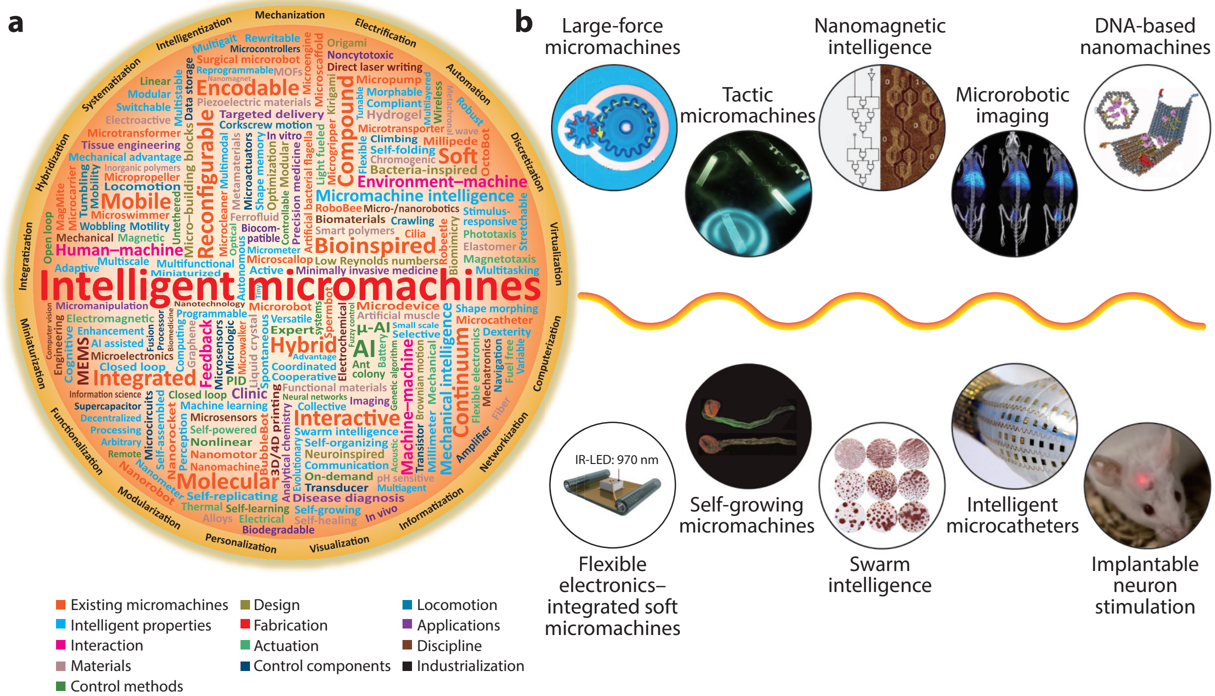

Figure 7

(*a*) Keywords related to intelligent micromachines and (*b*) 10 potential future research directions for intelligent micromachines. (*a*) The keywords related to intelligent micromachines are divided into those for existing micromachines (*orange*), intelligent properties (*light blue*), interaction (*pink*), materials (*light brown*), control methods (*dark green*), design (*olive*), fabrication (*red*), actuation (*sea green*), control components (*dark blue*), locomotion (*dark cyan*), applications (*purple*), discipline (*dark brown*), and industrialization (*black*). (*b*) The potential future research directions include large-force micromachines (173), tactic micromachines (36), nanomagnetic intelligence (128), microrobotic imaging (159), DNA-based nanomachines (103), flexible electronics–integrated soft micromachines (40), self-growing micromachines (174), swarm intelligence (43), intelligent microcatheters (137), and implantable neuron stimulation (175). Abbreviations: μ-AI, micromachine intelligence; AI, artificial intelligence; MEMS, microelectromechanical systems; MOF, metal–organic framework; PID, proportional–integral–derivative. Large-force micromachines image adapted from Reference 173 under a CC BY 4.0 license; nanomagnetic intelligence image adapted with permission from Reference 128 (copyright 2020 Springer Nature Limited); microrobotic imaging image adapted with permission from Reference 159 (copyright 2021 American Association for the Advancement of Science); DNA-based nanomachines image adapted with permission from Reference 103 (copyright 2012 American Association for the Advancement of Science); flexible electronics–integrated soft micromachines image adapted with permission from Reference 40 (copyright 2020 Springer Nature Limited); self-growing micromachines image adapted with permission from Reference 174 (copyright 2015 SAGE Publications); swarm intelligence image adapted with permission from Reference 43 (copyright 2019 American Association for the Advancement of Science); intelligent microcatheters image adapted with permission from Reference 137 (copyright 2020 Springer Nature Limited); implantable neuron stimulation image adapted with permission from Reference 175 (copyright 2018 Springer Nature Limited).

have potential as controllers. The magnetization pattern, which reflects the sensing and computing result, can be programmed to exhibit complex motions in dynamic magnetic fields.

7.4. Microrobot Imaging

Localization of micromachines is a major challenge in biomedical applications, and innovative imaging solutions with improved spatiotemporal resolution could boost their impact in the real world. Photoacoustic imaging (157), ultrasound Doppler imaging (158), and positron emission

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tomography (159) have demonstrated promising results in micromachine navigation in in vivo experiments.

7.5. DNA-Based Nanomachines

DNA not only carries genetic information but also functions as a structural material. With assistance from automatic design and simulation tools, DNA strands can fold into arbitrary shapes with functional structures, including a drug carrier controlled by logic gates (103). From the machine design point of view with this single base material, DNA origami can function as sensors, computational units, and actuators and shows potential to realize the ultimate intelligent micromachine as envisioned in **Figure 5**. DNA-based nanomachines have a natural interface with cell biology, making them extremely useful for designing smart drugs and other medical applications (160). DNA can also be used to decorate the surfaces of colloidal particles to assist in the assembly of large microscopic structures (161), thereby increasing the intelligence of existing micromachines.

7.6. Flexible Electronics–Integrated Soft Micromachines

Both flexible electronics and soft machines have low mechanical stiffness, which provides a natural interface to integrate both systems. Flexible electronics have made major progress in the past decade, establishing mass fabrication methods to integrate large arrays of sensors and other functional components. Flexible electronic systems can serve as the platform to power the soft actuators and process information. We now see a trend of increasing integration of sensors and actuators in one body. Soft micromachines integrated with flexible electronics open up new avenues for intelligent microdevices, transforming the field of robotics and medical devices (162).

7.7. Self-Growing Micromachines

Self-growing structures are ubiquitous in the plant kingdom. Among the well-known examples are vines, roots, and pollen tubes, where materials are continuously transported inside tubular structures and reorganized as structural materials. Robotic systems inspired by self-growing plants have been developed at a large scale (163, 164), but machines with smaller sizes are yet to be realized. Unlike most soft actuators, which can move between two states, self-growing requires a mechanism that can continuously deform with unlimited length. This process involves reorganizing materials from the center of the tube to the outer shell, which remains challenging to realize. Envisioned self-growing micromachines not only can continuously grow, but also can sense the environment with their tips for customized shapes and trajectories.

7.8. Swarm Intelligence

Swarm intelligent micromachines demonstrate the relationship between microscopic interacting agents and the collective behavior of the group. Inspired by nature, robotic swarms have achieved amazing emergent patterns. Compared with larger robotic swarms, where individual behaviors can be programmed through logic gates, swarm micromachines rely on the physical interactions among their neighbors. These active particles can collectively deform a lipid bilayer (165), transform between modes (43), and navigate in a maze (25). A swarm of micromachines can also become an arena to test more complicated interactions between agents to find additional methods for new collective behaviors (166).

7.9. Intelligent Microcatheters

Catheters with increasing intelligence are widely used for medical applications. As a structural platform, catheters can become highly functional by integrating different elements. Magnetic materials can provide magnetic navigation (80), and integrated sensors enable catheters to sense and map physiological signals (137). Shape memory alloys can trigger programmed actuation, and fluidic channels enable catheters to perform liquid biopsies (167). With the trend of miniaturization and functionalization, catheters are becoming more capable and autonomous in medical applications.

7.10. Implantable Neuron Stimulation

Direct neuron stimulation using medical implants can regulate aspects of human physiology and disease, including blood pressure, rheumatoid arthritis, incontinence, sexual function, and immune system function (151). Recent developments have reduced total implant size, decreased implantation risk, improved tissue interface longevity, and eliminated transcutaneous wires (168). Combined with onboard actuation, future implantable devices may be able to use integrated micropumps to precisely deliver liquid drugs at their tips (169) and use external magnetic fields to adjust their position in order to navigate inside the brain (170).

SUMMARY POINTS

1. The technical innovations of machines have led or are leading to the development of the four industrial revolutions, transitioning from mechanization through electrification and informatization to intelligentization.
2. Intelligent micromachines leverage the two most significant trends in research on machines and robotics: miniaturization and intelligentization.
3. Micromachines have become increasingly intelligent and are progressing toward micromachine intelligence.
4. Creating intelligence at small scales has unique advantages in the transduction, processing, and exchange of information because of the very short transmission distances, ultrafast response speeds, and low energy consumption as a result of microscale effects.
5. Micromachine intelligence potentially includes material intelligence, embodied intelligence, bioinspired intelligence, sensing intelligence, actuation intelligence, swarm intelligence, artificial intelligence algorithms, and more.
6. The realization of micromachine intelligence relies primarily on the establishment of interactions at small scales involving adaptive micromechanisms, feedback loops, and intelligent microsensors, microactuators, and microcontrollers.

DISCLOSURE STATEMENT

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