Nanomotors: 20 years anniversary and future roadmap

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Abstract

Since their discovery in 2004, there has been remarkable progress in research on nanomotors starting with the elucidation of different propulsion mechanisms to the study of their collective behavior, culminating in investigations into their applications in biomedicine and environmental remediation. This perspective reviews this evolution in nanomotors research and discusses the key challenges ahead, including the development of advanced characterization techniques, precise motion control, materials innovation, theory and modelling, and in vivo applications. These challenges not only highlight the current limitations of synthetic nanomotors but also point to exciting future opportunities to revolutionize theranostics, and the creation of ‘living’ hybrid systems. Thus, this perspective aims to inspire future generations of researchers in advancing both fundamental understanding and practical breakthroughs, thereby engineering a paradigm shift in nanomotors research.

1. Background

The field of self-propelled nano- and microparticles, known collectively as nanomotors, celebrated its 20th birthday following two decades of continuous growth. Its inception can be traced to an experimental paper from the Pennsylvania State University in 2004[1], followed closely by another publication from the University of Toronto[2]. Around the same time, two

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conference papers from the Swiss Federal Institute of Technology in Zürich described magnetic nanomotors[3,4]. Independently, a theoretical paper suggested the possibility of the design of nanomotors based on the asymmetric distribution of reaction products[5], Fig. 1. The first experimental nanomotors were bimetallic rods propelled by the catalytic conversion of hydrogen peroxide to products produced asymmetrically across the body of the nanomotors, leading to force-free phoretic transport[6]. Another class of chemical nanomotors achieved propulsion by the generation of gas bubbles inside micro-tubular jets, which were expelled preferentially from one end, enabling directional motion[7].

Separate from the above self-powered chemical motors, nanomotors driven by external light[8–10], magnetic[11–13], electric[14,15], and acoustic fields[16–21] were also constructed. Additionally, a theoretical proposal for a nanoscale artificial swimmer that breaks time-reversal symmetry[22], followed by experimental demonstration involving a linear chain of colloidal magnetic particles linked by DNA appeared in 2004-2005[23].

Two decades on, this rapidly growing, multidisciplinary field has evolved from the study of single-particle motion to the study of emergent behavior, from directional chemotactic motility[24–28] to dynamic assembly based on interactions amongst themselves[29–35] and with the environment[36–42]. The potential applications of these synthetic active materials are vast. They would be capable of remodeling themselves and transforming their environment, they could self-organize and evolve their structures and functions to improve their performance, accomplishing tasks collectively. Practical applications including sensing[43–46], directed cargo and drug delivery[47–54], *in vivo* imaging[55–60], theranostics[61–63], and environmental remediation[64–68] are being actively explored. From a fundamental standpoint, energy-harvesting nanomotors have emerged from scientific curiosities to powerful models for the study of complex systems[69].

Recent reviews have comprehensively covered the state of the art, focusing on materials[70], propulsion mechanisms[71,72], and applications in biomedicine[73], sensing[74], and the environment[75]. This perspective aims to spark discussion on the challenges, opportunities, and future directions in the field.

Today, two decades after the first examples, scientists have the opportunity to address fundamental questions in active, non-equilibrium systems, matter to life transition, synthetic cells, and demonstrate realistic applications that were unimaginable twenty years ago. New and scalable technological tools are available to engineer smart nanomotors from nearly any

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material and configuration, along with setups, and microfluidic devices that offer full control over the systems. Additionally, artificial intelligence (AI) and computational tools are now accessible to explore and resolve questions that were previously beyond reach. Although regulatory and ethical considerations are progressing faster than ever (albeit not as swiftly as desired), this field is nearing *in vivo* and patient-based applications. Along with remarkable opportunities, comes a myriad of challenges. Addressing these will require multidisciplinary collaborations among physicists, chemists, engineers, biologists, and medical practitioners.

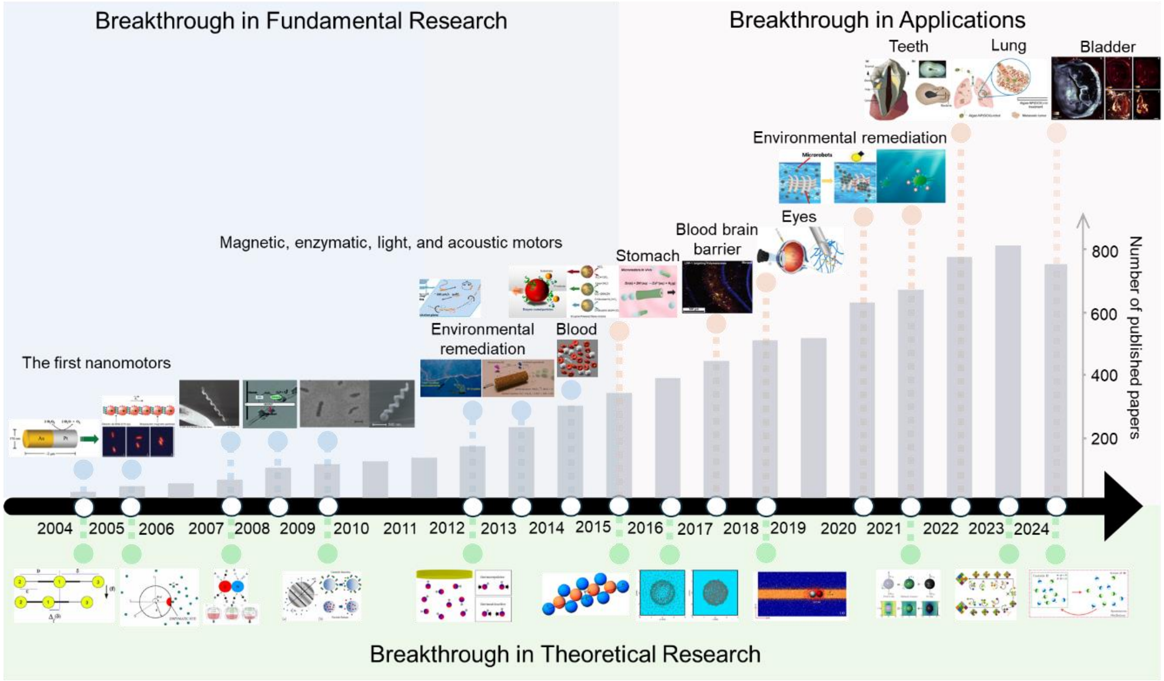

Fig. 1. Timeline of key breakthroughs in nanomotor development. The background columns represent publication data, derived from a refined search in the Web of Science Core Collection using topics "nanomotors", "micromotors", "nanobots", "nanorobots", "microrobots", "self-propelled particles", or "artificial swimmers", as indexed in the Science Citation Index Expanded (SCI-EXPANDED) from 1900 to the present. The dashed lines connect representative papers to their respective publication years.

2. Gaps and challenges

While the field of nanomotors has made significant advances since its inception 20 years ago, there remains significant gaps in our fundamental understanding of the behavior of these nano and microscale out-of-equilibrium systems both at the single particle level, as well as in the form of swarms. These are especially pressing issues as the size of the nanomotors approaches the scale of macromolecules[76]. New ways to design nanomotors and control their motility and

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dynamic assembly are critically important. Additionally, there are challenges in characterizing and tracking the motors, especially *in vivo*, Fig. 2.

The need of new and accurate characterization techniques

As we learn more about nanomotors and their motion in complex fluids and biological environments, it becomes critically important to improve the techniques used to monitor them. It is necessary to increase resolution in size and accuracy for tracking, find ways to measure the forces at play, and the means to observe chemical processes at the single nanomotor level. This is essential to gain a better understanding of the physical and chemical mechanisms that take place. New measurement techniques and cross-validation by different methods will become essential, as well as close coupling to theoretical modeling. Magnetic nanomotors provide a distinct advantage in this respect since the magnitude and direction of the forces exerted by the nanomotors can be controlled externally with high precision[77]. This can allow accurate quantitative estimates of the local environment[78] that are not possible otherwise and may also allow more accurate targeting.

Because of their anticipated significant future impact on theranostics, it is important to be able to track nanomotors *in vivo* and understand their dynamic interactions with the environment. Cells, tissues, and organoids not only exhibit spatiotemporally varying mechanical properties but also have optical characteristics that could present challenges in real-time characterization of propulsion and the accurate processing of information obtained from nanomotors. While brightfield, confocal or even super resolution microscopy enable high precision imaging *in vitro*[79,80], there are no good techniques to simultaneously monitor motion in real-time with high precision as the nanomotors swim through the body, penetrate cells, and undergo changes over time, such as the rearrangement of attached enzymes (or other catalysts), the formation of protein corona, and the nanomotors' eventual degradation.

In fact, one can also imagine applications where direct image-guided navigation of nanomotors may not be necessary. For example, the properties of the surrounding medium, possibly defined through topography[81], charge[82], surface chemistry[83], etc., can ensure fast and accurate movement by the active motors, such as to reach the region of interest without external navigation control[84].

Controlling motion: From single particles to swarms.

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Current nanomotor technology is largely limited by issues of accuracy, controllability, self-adaptiveness, and the ability to generate sufficient forces and torques. In particular, generating the desired forces and torques for operation in complex environments using untethered small robots is challenging, especially when these forces should be higher than what individual nanorobots can typically offer. Currently, most nanomotors exert forces in the range of nanoNewtons (nN) to picoNewtons (pN)[85,86], with enzymatic nanomotors operating at the pN level[79,87], similar to biological protein motors. This greatly restricts their ability to traverse biological barriers and perform effective mechanical operations. Addressing this challenge demands innovative concepts and actuation mechanisms, new materials, as well as improved structural design. If external fields are employed, auxiliary instrumentation must be developed to ensure it is compatible with existing medical technologies, and both safe and user-friendly for clinical applications.

Integrated nanorobotic systems require better controllability over several degrees of freedom. This calls for improved material combinations that enables multiple addressable propulsion mechanisms, including chemical, light, electric, magnetic, and acoustic forces[88].

Another challenge is to find ways to coordinate the motion of multiple nanoscale motors to obtain macroscale actuation and function, as seen in the biological world. The amplification may arise via the environment or via coupling of chemical processes to fluidic effects in suitable geometries[89]. However, it is challenging to endow swarms composed of simple building blocks with complex collective behaviors. Coordinating multiple different motor-motor interactions within a swarm, as well as regulating the impact of external environment on the swarm, can be difficult, yet it is an exciting phenomenon to be studied. These difficulties pose a challenge to the design of nanomotor-based swarms that exhibit hierarchical functions and even embodied intelligence, e.g. swarms capable of perceiving diverse environmental stimuli in an unstructured environment and making corresponding adaptations.

Material needs for nanomotors: From inorganic to biohybrid.

While nanomotor propulsion and navigation methods have been significantly advanced with two decades of research, better adaptability and biocompatibility are still required for the application of nanorobots. Particularly in the biomedical field, long-term performance is crucial in a complex physiological environment with its associated high ionic strength, high viscosity, and potential plasma protein biofouling. Surface coating has been extensively used to encode multiple functions and regulate propulsion efficiency for nanomotors[90]. Nevertheless,

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optimizing the material composition to balance all requirements for biomedical needs[91,92], while realizing multiple functions and keeping the composition simple for scalability, remains an unfinished task[93].

Some of the best controlled nanomotors are magnetic[13,94]. A challenge is to find magnetic materials with strong magnetic moments and high remanence and coercivity, that are also biocompatible and stable against physical agglomeration at high densities. Progress in this direction has been made with the biocompatible hard magnetic FePt system[95], and with ZnFe coating[92], which protects against physical agglomeration while allowing magnetic hyperthermia. Including Mg and Zn in the scaffold of the nanomotors allows the degradation to be tuned[96]. Ideally, one should employ hard magnetic materials that are also biodegradable. The combination of materials in hybrid nanomotors will require testing to determine safe operating conditions. As such, systematic screening and testing protocols will be helpful for the field.

Molecules, particles and even cells respond to applied electric fields, exhibiting motion under both DC voltage and high-frequency signals. As a result, electric manipulation holds significant potential for creating reconfigurable motors and diverse swarms. These unique capabilities call for an in-depth investigation of materials' electrical properties under various stimuli, including chemical functionalization, and magnetic, electric, and acoustic fields. Moreover, the discovery of new materials and the creation of hybrid structures with controlled chemistry, dimensions, and assembly could enable distinct mechanical behaviors in response to a given electric frequency, allowing for precise control within a swarm[97–99].

Externally imposed light represents particularly useful energy input for powering nanomotors, since the light source is easily moved and enables tight spatiotemporal control over nanomotor motility[100]. Ideally, these light-driven motors should exhibit strong light absorption, high energy conversion efficiency, and robust stability under operational conditions[101]. While materials, such as inorganic semiconductors, meet some of these criteria, an ideal light-driven system that satisfies all these features is still lacking. Hence, exploring materials with diverse optical properties is essential. For instance, small molecule organic semiconductors that delocalize charges through their backbone[102], or transition metal complexes with long-lived excitation states, rich redox properties, and intrinsic fluorescence[103], show promise but remain largely unexplored. Additionally, integrating these materials with those that enable energy storage and conversion, such as photochromic materials[104] and upconversion

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nanoparticles[81,105], is crucial. This integration can yield photoactive micromotors capable of navigating non-transparent media, harvesting biocompatible wavelengths with high penetration depth, and performing environmental readouts, such as temperature measurements. A significant challenge is to engineer these multicomponent micromotors with asymmetrical structures and effectively coordinate the multistep charge and energy transfer among materials to achieve precise motion control upon photoactivation.

Enzyme-powered nanomotors hold great promise for biomedical applications due to their versatility, ease of fabrication, and biocompatibility[79,87,106]. Because of the ability of enzymes to chemotax in response to substrate gradients, these motors can be moved directionally using such gradients[107–109]. Additionally, the use of enzyme cascades potentially allows populations of particles incorporating enzymes that are part of a cascade to form dynamic assemblies[110]. However, the factors that govern chemotaxis, such as reaction kinetics, variations in the diffusion of bound and unbound enzymes, effect of inhibitors, phoretic and hydrodynamic effects are not well understood. Moreover, only a handful of enzymes have been employed in the studies to date[111–113].

Moving further, bottom-up synthetic biology has developed synthetic vesicles with complex machinery for diverse tasks[114], including active motion, based on natural (e.g. proteins[115]) or synthetic molecular hardware (e.g. DNA origami[116–119]). These innovations offer new possibilities for the nanomotors field to bridge a variety of scientific disciplines, leading to powerful delivery solutions.

A major challenge is to design "self-evolving" systems and materials. In biology, the growth and evolution of materials involves constant turnover of building blocks, while they interact with the environment. Thus, adaptation (changes in composition, and function) takes place during the lifetime of the material itself. This contrasts with synthetic materials that are typically fabricated according to predesigned parameters and then put in place. Addressing this challenge and creating synthetic systems with life-like behaviors would be game-changing, enabling materials to possess features such as memory, adaptation, self-replication, and continuous evolution in response to their environment.

Theory and Modelling

For swarms, the collective dynamics of nanomotors are highly nonlinear, hard to model, and possess numerous uncertainties. The responses of collectives are time delayed, and their control requires the simultaneous modulation of multiple input variables[77]. Thus, advanced algorithms

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capable of delivering robust and adaptive control are worthy of investigation[120,121]. The possibility of making local measurements using nanomotors at sub-micron resolution can provide important information, especially in biophysics problems, that is not yet available.

A key theoretical and conceptual challenge is how to develop frameworks that allow us to predict collective behavior at the large scale using mechanistic knowledge of individual active motors. The so-called systematic coarse-graining techniques[122,123] allow us to derive effective theoretical descriptions at any given time and length scale by using input from a number of microscopic ingredients. While limited progress has been made along these lines, many important features of the experimental systems have not yet been included in such a programme, such as details of propulsion mechanism[124], the nature of stochastic fluctuations[125], the hydrodynamic flow field in the vicinity of the swimmer[126], aligning interactions with boundaries[127,128], and exact near-field interactions between particles[129], among others. Such theoretical frameworks allow us to have access to the phase behavior of the active system at the largest length and longest time scales, including their scaling behavior, though application of Renormalization Group techniques that have been developed in theoretical studies of phase transitions and critical phenomena[130]. It should be noted that both motility and motor-motor communication leading to swarming arise from the same chemical gradients, a critical observation that should be taken into account in any realistic theoretical modeling effort.

One of the natural consequences of chemo-mechanical transduction is the emergence of non-reciprocal interactions in active matter[131–134], which has far-reaching consequences as it generically prohibits systems to reach steady states and exhibit simplified equilibrium-like behavior. The origin of non-reciprocal interactions has been proposed for nanoscale enzyme systems[135]. Importantly, non-reciprocal active matter is capable of spontaneous symmetry breaking in systems where the symmetries are emergent to begin with, leading to a plethora of complex collective effects[136,137]. The consequences of these theoretical predictions remain to be experimentally tested.

In vivo applications of self-propelled active particles.

Nanomotors hold great promise as a new paradigm in drug delivery[93,138–140]. The active delivery of drugs to a specific disease site would a) greatly diminish the therapeutic dosage and b) reduce collateral cytotoxicity. However, there are several challenges to achieving this goal. In many *in vivo* applications, the nanomotors need to be powerful enough to move against fluid flow, such as in circulatory systems[141,142]. This remains to be demonstrated. However, the

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observation of rheotaxis by active nanomotors enabling them to move near walls against fluid flow is a useful development[143–145]. One alternative is to deploy the nanomotors locally, in confined spaces, where diffusion is limited, and traditional drugs cannot easily reach the target. Examples include the bladder[60,146], eyes[147], joints[41,148], lungs[149], skin[150–152], and other locations. In general, it is important to find ways that nanomotors can either locomote themselves autonomously to the region of interest or to develop ways to navigate nanomotors inside the body[153,154].

Another challenge is the generally poor ability of active articles to reach the interior of cells, although active internalization and subsequent manipulation of magnetic and acoustic nanomotors in living cells have been demonstrated[17,155]. From the blood vessels, the particles will need to go through the epithelial tissue and extracellular matrix before reaching and penetrating the cell membrane. It is not clear that the current nanomotors are powerful enough to cross these biological barriers that impede passive nanoparticles, although there has been significant progress made with magnetically, acoustically, and chemically driven micro/nanomotors to move through relatively dense biological environments[156,157]. With further engineering of the materials and geometry, coupled with more sophisticated instrumentation, we envision the "fantastic voyage" through dense organs may soon be realized.

Finally, the delivery of optimal drug dosage would require swarms of active particles. Guiding these swarms through the body presents unique difficulties, especially when navigating the tight spaces of the tissue microenvironment, managing residual motors, and mitigating the potential risk of increased cytotoxicity. These challenges require a deeper understanding and better control of swarming behaviors and the investigation of novel active degradable materials.

3. Opportunities

Many of the challenges discussed above also provide opportunities for future innovation. Free of biological constraints, it is now possible to probe the limits of self-organization in synthetic active systems operating far from equilibrium. Furthermore, the development of micro/nanorobotics as active tools with unparalleled precision, control, sensing, delivery, and operation capabilities will unlock opportunities in both basic biological research and practical biomedical applications. These tiny machines have the potential to actively control cell-cell communication, single-cell immunology, physiology, and subcellular sensing, delivery, and

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stimulation. They hold the promise of revealing the physiological permeability of blood-brain barriers at nanoscale resolution, crucial for brain disease therapies. Additionally, advancements are expected to enable intelligent, self-powered gene delivery and editing, achieving targeted autonomous transfection with significantly higher efficacy than current techniques.

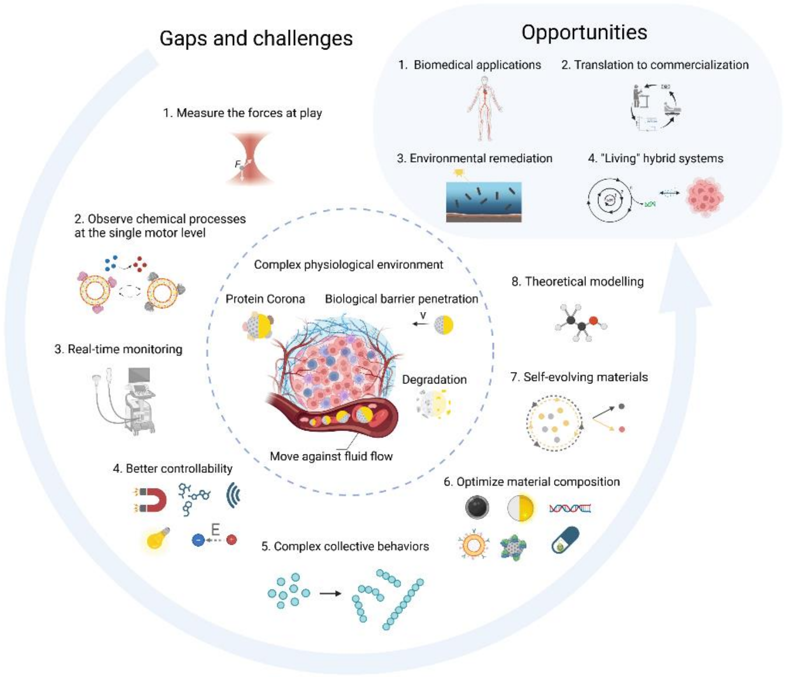

Fig. 2 Schematics illustrate that the gaps and challenges in nanomotor development provide opportunities for future innovation.

Active functional swarms.

Self-assembly and organization have been topics of considerable interest in the scientific community for their potential to create complex, functional materials. While previous efforts have primarily focused on equilibrium systems, characterized by static and predetermined structures, biological systems are known for their dynamic and diverse self-organized structures constructed from the same building blocks. As a synthetic out-of-equilibrium system, nanomotors can mimic natural self-organizing structures. Two avenues for achieving this goal are the utilization of nanomotor dissipative interactions and exploring non-reciprocal interactions. The former strategy involves replacing static interactions, such as van der Waals and Coulomb interactions, with dissipative interactions, such as hydrodynamics and chemical gradients, which can be modulated with energy input. This allows for the realization of phase transitions in nanomotor assemblies, resulting in responsive materials. The other strategy involves leveraging the non-reciprocal nature of nanomotor interactions, which mimic living

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systems. Non-reciprocal active systems have been theoretically shown to have the capacity to form a variety of self-organized structures starting with the same building blocks, participating in a choreographed sequence of assembly and dis-assembly of desired structures[158].

While the key feature of nanomotors is the generation of mechanical work, an increasing ability to acquire information about the environment, store, process it, and alter their behavior in response can potentiate their utility. In the complete absence of any information processing capability, a nanomotor can still be used to agitate a solution and accelerate mixing[159]. Making local measurements using nanomotors at sub-micron resolution can provide important biophysical information, which is not yet available. The possibilities of engineering highly advanced systems are exemplified by the ability of white blood cells to actively pursue harmful bacteria and neutralize them. Current nanomotors can successfully alter their direction of motion in response to chemical gradients and specific attachments can selectively halt their motion[160–162]. Endowing the nanomotors with internal mechanisms to acquire, store, and process information encoded in the concentrations of chemical molecules would greatly enhance their capabilities. Biochemical systems developed for the design of synthetic cells may enable transformational advances in this respect[163,164]. Macroscale systems often allow a clear delineation between the flows of energy and information, whereas in nanoscale systems, it can be a matter of individual perspective if the information has been transmitted or processed, or a physical or chemical change has occurred[165]. It would be desirable to switch from one perspective to the other seamlessly. This is of particular interest when considering swarms of nanomotors interacting with each other and the environment. To what extent can a swarm of nanomotors sense inputs and process them into complex responses by leveraging the non-linearities of the nanomotor interactions and the continuous flow of energy? The most "futuristic" scenario involves active systems that can autonomously carry out operations such as sensing, reporting, and delivery, with different populations of interacting nanomotors performing different tasks synergistically.

It should be possible to apply machine learning algorithms to swarm control. Benefiting from the strong abilities of machine learning models, impressive progress has been achieved in the design, actuation, tracking, and navigation of swarms[120]. However, the working scenarios are still limited to *ex vivo* conditions. It is now important to exploit the superiority of machine learning algorithms and realize robust and adaptive control of swarms to undertake more practical biomedical tasks in dynamic fluctuating environments.

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Biomedical applications.

As discussed in the previous section, the use of nanomotors in imaging and drug delivery is an area of great promise. For this to become reality, several roadblocks need to be overcome[166–168]. These include a) the use of biocompatible nanomotors and fuel, b) moving against fluid flow and in complex fluids, c) overcoming interstitial pressure to penetrate cells, d) the use of different propulsion mechanisms when traversing different parts of the body, e) ability to scale-up the production of nanomotors with uniformity in structure, function, and activity, and f) the challenges to "bench-to-market" transition.

It should be noted that many proof-of-concept applications currently demonstrated with nanomotors suffer from the lack of clear, quantifiable comparison with existing technologies in terms of the perceived improvement in patient care, which limits their subsequent translation toward commercialization. However, several nanomotor startups, including Nanobots Therapeutics[169], Bionaut Labs[170], and Theranautilus[171], have secured funding and are progressing toward clinical trials. The quantifiable advantages that nanomotors could bring, for example, in biomedical applications, can be in terms of enhanced diffusivity and efficacy, reduced side-effects, on-demand operation and thus speed of treatment, being able to move in spaces not accessible with existing medical techniques, moreover, they can enhance penetration through biological barriers in addition to standard advantages claimed by passive nanobiotechnology tools.

Environmental remediation.

The potential of nanomotors in environmental remediation, particularly for water purification and pollutant removal, has been extensively studied[172–177]. Recently, the conversion of pollutants into useful compounds is emerging as a promising strategy for sustainability[178,179]. Despite the abundance of research in this area, the transition of nanomotors from proof-of-concept experiments to practical, real-world applications remains a significant challenge. To make substantial advancements, efforts should focus on scalability and cost-reduction, as many of the reported nanomotors rely on complex fabrication methods and expensive materials. Additionally, it is important to demonstrate the reusability of these nanomotors over multiple cycles and examine their long-term stability under constant operation[180,181]. Likewise, the potential environmental toxicity of the motors themselves needs to be considered[182].

Integrating additive manufacturing with driven self-organization.

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When integrated with additive manufacturing, the remarkable versatility of nanomotors embedded within a frame structure, such as gels, combined with their sensitivity to chemical and biochemical signals, light, magnetic and electric stimuli, etc., could endow these static structures with lifelike senses and features. These advanced constructs will not only move but could also release electrical and chemical signals, mimicking the sensory and actuation capabilities of living beings. These structures could perceive their environment, respond dynamically to stimuli, and interact with their surroundings in ways that were previously confined to the realm of science fiction.

Matter to life

Mimicking life, a new frontier in the nanomotors field could lie in their Darwinian evolution. Rational engineering is powerful as long as structure-function relationships are fully known. As nanomotors venture into increasingly complex environments where they have to perform increasingly diverse tasks, we quickly reach the limit of known structure function relationships. Directed evolution is a possible solution to this problem. Unlike nature, we are free to choose various selection pressures and rationally engineered starting points, which broadens the evolutionary landscape. Thus, by subjecting nanomotor populations to selective performance criteria, it may be possible to optimize their locomotion, sensing, and interaction abilities. Furthermore, an evolutionary approach to nanomotor design may shed light on origins of motility, inform fundamental questions on the origins of life, and connect the nanomotors field to bottom-up synthetic biology as an adjacent field which recently started to recognize the power of evolutionary approaches. Integrating evolvability in future nanomotor designs will pose an exciting challenge. One could imagine genetically encoded locomotion, such that rounds of mutagenesis and selection of the best swimmer can be performed.

Finally, synthetic active systems are truly biomimetic when they are functionally indistinguishable from their biological counterparts. A particularly intriguing opportunity is to engineer “living” hybrid systems[183], in which communication and interaction between living and synthetic active matter lead to complex organization similar to but extend beyond morphogenesis. Synthetic active matter may communicate with living cells, secrete attractants or repellants, leading to long-range cell organization and response[184]. In addition, they may mediate cellular communication between different types of living cells which is not possible *in vivo*. Thus, synthetic active matter could initiate complex multicellular interactions across multiple length scales leading to functions and dynamics that are not observed physiologically.

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4. Conclusion and outlook

Current synthetic nanomotors fall far short in autonomy and sophistication when compared to their biological counterparts. Biological motors exhibit impressive energy conversion, self-regulation, adaptability to environmental changes, along with intricate collective behaviors like bacterial chemotaxis, properties that the artificial nanomotors aim to replicate. To advance the design of synthetic active systems, it is crucial to integrate more functionalities and establish a "division of labor" among specialized components. The ultimate goal is to create a new design paradigm for active functional materials and systems by focusing on a) precise molecular-level control to construct functional "active" building blocks, b) motility driven by locally harvested energy, c) rapid and reversible non-equilibrium self-assembly, d) intelligence and communication similar to interacting microorganisms, and e) the ability to perform specific tasks in response to signals from each other and the environment[185].

Similar to "Systems Biology," which involves interactions across various length scales from cells to tissues to entire organisms, the concept of "Systems Materials" can be applied to interacting materials, ranging from the molecular scale to the macroscale (Fig. 3). For instance, how does nanoscale motion of components lead to macroscale effects? Understanding the behavior of interacting units requires an integrated systems approach that considers the individual components, their energy sources, and the medium in which the system operates. Two key questions arise: 1) How do multiple populations of nanomotors, with their own properties, interaction rules, and missions, interact with each other? 2) How can information be efficiently stored, retrieved, and communicated to enable assembly and collective function? Answering these questions and surmounting the above-described challenges are key to further progress in nanoscale motor-driven systems.

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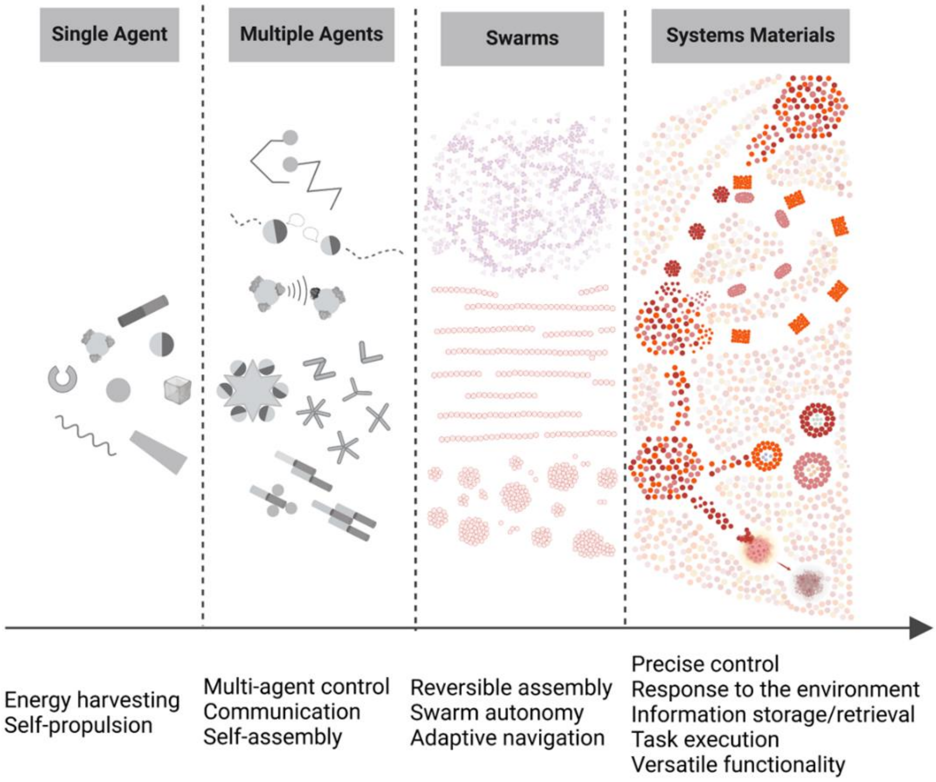

Figure 3. The evolution of nanomotors over 20 years and beyond, from single-particle motion to multi-agents, swarms and systems materials.

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