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# Nanoboat Drug Delivery Systems: From Molecular Propulsion to Precision Therapy.

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**Abstract**

Nanoboats represent a cutting-edge class of nanoscale delivery vehicles inspired by biological propulsion mechanisms and engineered for enhanced targeting, controlled release, and precision therapy. These nanosystems integrate navigation strategies derived from motor proteins, synthetic swimmers, and nano-propellers with advanced drug encapsulation techniques to traverse physiological barriers. This review synthesizes recent advances in nanoboat design, propulsion mechanisms, therapeutic payload integration, targeting strategies, and clinical translation challenges. We discuss key propulsion technologies — from catalytic and magnetic fields to biohybrid designs — and analyze their impact on delivery efficiency, tissue specificity, and biocompatibility. Finally, we assess current limitations, safety concerns, and future directions in harnessing nanoboat systems for targeted cancer therapy, neurological treatments, and personalized medicine applications.

**Keywords**

Nanoboats , Drug delivery , Molecular propulsion , Precision therapy , Targeted delivery , Biohybrid nanoswimmers

## 1. Introduction

Drug delivery is a cornerstone of modern medicine, but traditional drug administration methods face several limitations that hinder therapeutic efficacy. Oral, intravenous, and topical delivery systems often suffer from poor bioavailability, off-target distribution, and systemic side effects, which limit the therapeutic index of many drugs. For instance, chemotherapeutic agents typically affect both tumor and healthy tissues, leading to severe toxicity. Similarly, neurological drugs often fail to cross the blood–brain barrier (BBB), reducing their effectiveness in treating central nervous system disorders. These challenges have driven the development of nanoscale delivery platforms, which can improve drug solubility, stability, and controlled release. Over the past two decades, nanoparticles such as liposomes, polymeric micelles, dendrimers, and inorganic nanocarriers have demonstrated considerable promise. While these passive systems rely on diffusion or enhanced permeability and retention (EPR) effects for tumor accumulation, their limited active targeting capabilities and slow tissue penetration restrict their clinical potential.

To overcome these shortcomings, active nanoscale delivery systems have been developed. Among them, nanoboats have emerged as a novel and transformative technology. A nanoboat is a nanoscale structure engineered to navigate biological environments autonomously or under external guidance, carrying therapeutic agents precisely to the target site. The concept of nanoboats draws inspiration from natural molecular motors, such as bacterial flagella, kinesin, and dynein proteins, which demonstrate remarkable efficiency in transporting cargo across crowded cellular environments. By mimicking these propulsion mechanisms, nanoboats can actively traverse biological barriers, enhancing localization and minimizing off-target effects. Unlike conventional nanoparticles, which passively rely on blood flow and diffusion, nanoboats can be actively steered toward specific tissues or cellular microenvironments, offering unprecedented control over drug delivery kinetics.

Nanoboats integrate multiple functional components, including structural scaffolds, propulsive elements, surface modifications, and drug payloads. Structural design is critical for optimizing hydrodynamics, stability, and biocompatibility, while propulsion mechanisms determine their speed, maneuverability, and ability to overcome physiological obstacles. Current propulsion strategies include chemical self-propulsion, enzyme-mediated movement, magnetically guided locomotion, and biohybrid approaches that incorporate biological motors. These mechanisms can be combined with sophisticated surface engineering, such as ligand conjugation, PEGylation, or antibody targeting, to enhance tissue specificity and evade immune recognition.

The potential therapeutic applications of nanoboats are vast. In oncology, they offer precise tumor targeting, enhanced tissue penetration, and reduced systemic toxicity. In neurology, nanoboats capable of crossing the BBB can deliver neuroprotective agents directly to affected regions, opening new possibilities for treating Alzheimer's, Parkinson's, and stroke-related injuries. Furthermore, their stimuli-responsive drug release capabilities allow controlled and localized therapy, minimizing adverse effects while maximizing therapeutic outcomes. Despite the promise, several challenges remain, including biocompatibility, long-term stability, in vivo tracking, scalability, and regulatory approval for clinical use.

In conclusion, nanoboats represent a paradigm shift in drug delivery, merging principles of molecular propulsion with precision therapy. By combining active navigation, targeted delivery, and controlled release, these nanosystems address the limitations of conventional nanoparticles, offering new avenues for effective and personalized medicine. The subsequent sections of this review will explore the design principles, propulsion strategies, targeting mechanisms, drug loading approaches, therapeutic applications, and translational challenges of nanoboat drug delivery systems.

## 2. Design Principles of Nanoboats

The design of nanoboat drug delivery systems is a multidisciplinary challenge that integrates materials science, nanotechnology, biology, and physics. The overarching goal is to create a nanoscale vehicle that can carry therapeutic payloads, navigate complex biological environments, and release drugs precisely at the target site. Successful nanoboat design relies on three core elements: structural architecture, propulsion mechanism, and surface functionalization. Each element must be carefully optimized to achieve high biocompatibility, stability in physiological fluids, and controlled drug delivery kinetics.

Structural architectures play a crucial role in determining the hydrodynamics, stability, and cargo capacity of nanoboats. Various geometries have been explored, including core–shell, tubular, rod-like, and boat-shaped designs. Core–shell structures, typically consisting of a biodegradable polymeric core and a protective outer shell, offer high drug-loading efficiency and controlled release properties. Tubular and elongated geometries improve hydrodynamic efficiency, facilitating faster propulsion through viscous biological fluids. Boat-shaped nanostructures, which mimic macroscopic watercraft at the nanoscale, optimize surface area for functionalization and allow for directional movement when combined with propulsive forces. Material selection for these architectures is also critical; biodegradable polymers such

as poly(lactic-co-glycolic acid) (PLGA) and polyethylene glycol (PEG) are widely used due to their biocompatibility and ease of surface modification. Inorganic materials like silica, gold, and magnetic nanoparticles provide structural rigidity and enable external field-guided navigation, while hybrid organic–inorganic composites combine the advantages of both systems.

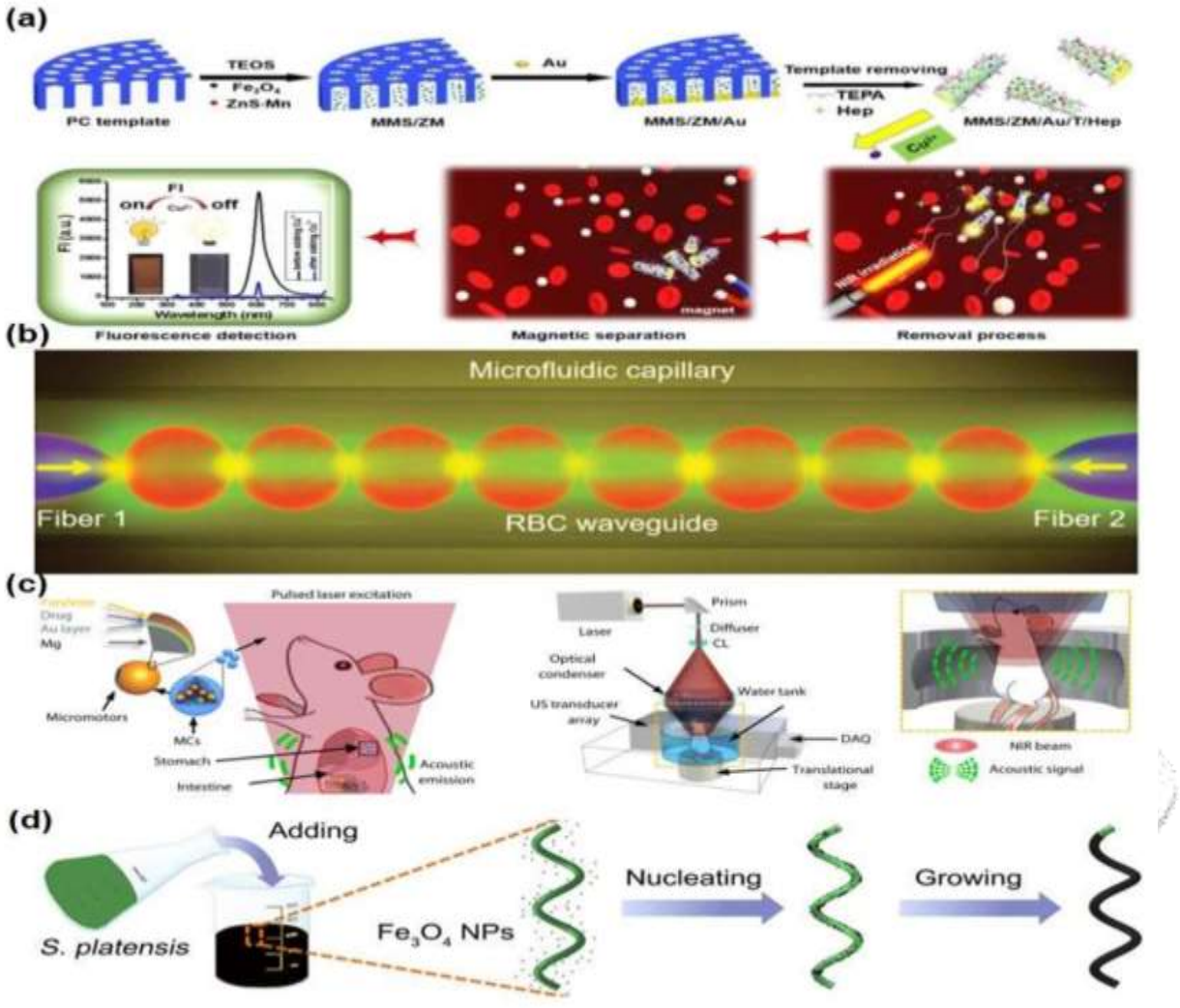



**Fig.1 Design Principles of Nanoboats**

Propulsion mechanisms are central to the functionality of nanoboats. Active movement distinguishes nanoboats from passive nanoparticles, enabling precise navigation against fluid flow, toward chemical gradients, or under external control. Chemical propulsion relies on asymmetric catalytic reactions on the nanoboat surface, generating local concentration gradients that propel the vehicle. Common catalytic materials include platinum, which decomposes hydrogen peroxide, or enzyme-based systems that convert physiological substrates into movement-inducing products. Magnetic propulsion uses external magnetic fields to steer magnetic nanoparticles or nanoboat assemblies, offering high precision without relying on chemical fuels. Biohybrid designs incorporate biological motors such as flagella or motor proteins, providing highly efficient, biocompatible movement that can navigate crowded intracellular environments. Each propulsion strategy has distinct advantages and limitations in terms of speed, biocompatibility, and in vivo applicability.

Surface functionalization enhances stability, targeting, and immune evasion. Nanoboats can be coated with hydrophilic polymers like PEG to prevent opsonization and prolong circulation time. Ligands, antibodies, and aptamers can be conjugated to target specific cell receptors, allowing selective drug delivery to diseased tissues such as tumors or inflamed regions. In addition, responsive coatings can facilitate stimuli-triggered drug release in response to pH, enzymes, or temperature changes, enhancing therapeutic precision. The combination of propulsion and functionalization is particularly powerful, allowing

nanoboats to sense and respond dynamically to their microenvironment while remaining stable in the bloodstream.

Finally, integrating these design principles requires a careful balance between performance and biocompatibility. Nanoboats must be small enough (typically 50–500 nm) to circulate freely and penetrate tissues, yet large enough to carry sufficient drug payloads and propulsion components. Stability in physiological fluids, minimal toxicity, and efficient clearance are essential for safe in vivo applications. Emerging computational models and high-throughput fabrication techniques are increasingly used to optimize nanoboat design, enabling rational engineering of propulsion, drug loading, and targeting properties.

In summary, nanoboat design integrates structural optimization, propulsion strategies, and surface functionalization to achieve precise, active drug delivery. These principles form the foundation for subsequent discussion of molecular propulsion mechanisms, targeting strategies, and therapeutic applications, highlighting how careful engineering can transform nanoboats into highly effective precision medicine tools.

### 3. Molecular Propulsion Strategies

Molecular propulsion is the defining feature of nanoboat drug delivery systems, distinguishing them from conventional passive nanoparticles. Effective propulsion enables nanoboats to navigate complex biological environments, overcome fluidic resistance, and actively reach targeted tissues or cellular compartments. Several molecular propulsion strategies have been developed, leveraging chemical, enzymatic, magnetic, and biohybrid mechanisms, each with unique advantages and challenges.

Chemical propulsion is one of the earliest and most widely studied mechanisms. It relies on asymmetric surface reactions that create localized chemical gradients, driving nanoboat movement through self-diffusiophoresis or bubble recoil. A common design involves Janus nanoparticles, which possess two chemically distinct faces, with one catalyzing a reaction (e.g., hydrogen peroxide decomposition via platinum) to generate thrust. This approach provides continuous propulsion, but careful control of fuel concentration is necessary to avoid toxicity in vivo. Recent advances have focused on biocompatible chemical fuels such as glucose or urea, enabling safer catalytic propulsion in biological fluids.

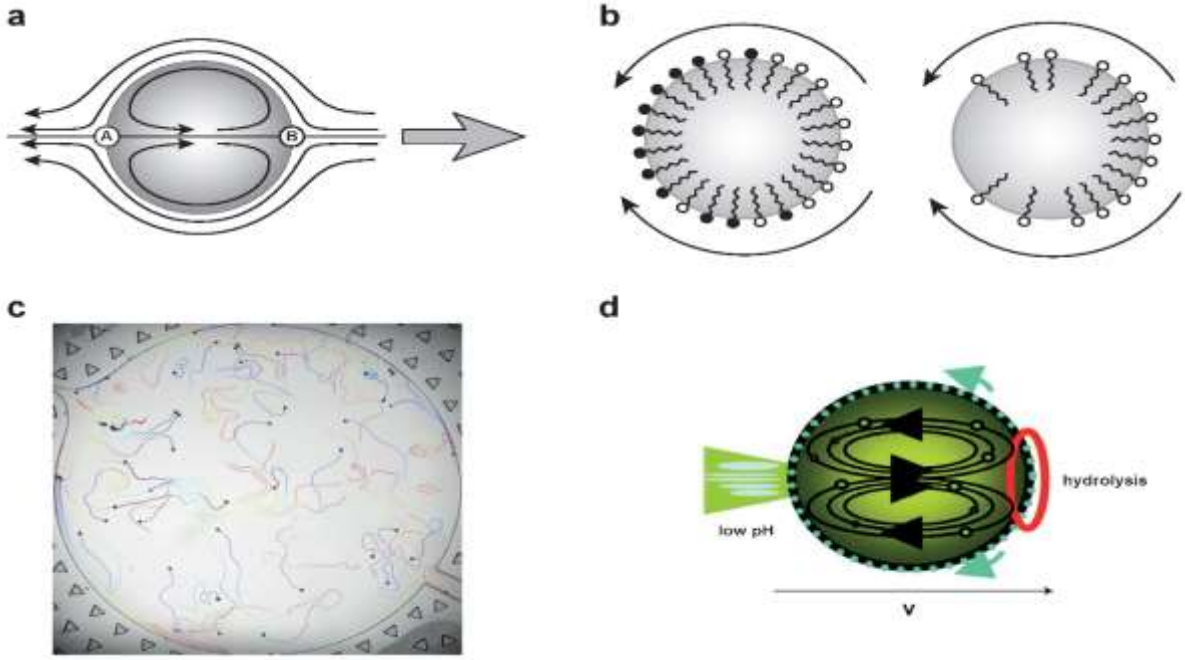



**Fig.2 Molecular Propulsion Strategies**

Enzyme-driven propulsion mimics natural biochemical processes. Specific enzymes immobilized on the nanoboat surface convert physiological substrates into chemical energy that drives motion. For example, urease-based nanoboats can hydrolyze urea to generate local gradients, producing propulsion in urine-rich environments, while catalase-based systems decompose hydrogen peroxide to release oxygen bubbles that push the nanocarrier forward. Enzyme-powered nanoboats are advantageous due to their high biocompatibility, ability to operate in physiological conditions, and potential for tissue-specific activation. Additionally, enzyme activity can be tuned by temperature, pH, or substrate availability, allowing responsive control of nanoboat movement.

External field-driven propulsion uses magnetic, acoustic, or optical forces to guide nanoboats. Magnetic propulsion incorporates magnetic nanoparticles into the nanoboat structure, enabling directional movement under an applied magnetic field. This strategy offers precise steering and control over speed without relying on chemical fuels, making it attractive for in vivo applications. Acoustic propulsion, typically using ultrasound, can induce mechanical vibrations that propel nanoboats or enhance their penetration into tissues. Light-activated propulsion utilizes photochemical reactions or photoresponsive materials to generate movement upon light exposure, allowing spatiotemporal control. These external stimuli-based methods are particularly useful for deep tissue targeting, remote navigation, and real-time control.

Biohybrid propulsion combines synthetic nanostructures with biological motile components such as flagella, cilia, or motor proteins. By harnessing the inherent efficiency of biological motors, biohybrid nanoboats can achieve high maneuverability in crowded cellular or extracellular environments. For instance, bacteria-driven nanocarriers have been engineered to transport drugs by leveraging bacterial chemotaxis toward tumor microenvironments. Similarly, sperm or cilia-based biohybrids can deliver payloads to specific mucosal tissues. Biohybrid systems are highly biocompatible, self-powered, and capable of complex navigation, though they require careful handling to prevent immune responses or premature clearance.

Comparative evaluation of propulsion strategies reveals trade-offs between speed, control, biocompatibility, and fuel availability. Chemical propulsion offers autonomous motion but may introduce toxicity, while enzyme-driven systems provide biocompatible self-propulsion with moderate speed. External field-driven nanoboats enable precise directional control but require specialized equipment, limiting portability. Biohybrids offer highly efficient, adaptive movement but face challenges in scalability and regulatory approval.

In conclusion, molecular propulsion is central to the function of nanoboat drug delivery systems, enabling active navigation and precise targeting. The choice of propulsion strategy depends on the intended therapeutic application, physiological environment, and safety considerations. Integration of chemical, enzymatic, external, and biohybrid propulsion mechanisms continues to expand the versatility of nanoboats, providing new opportunities for precision therapy, targeted drug delivery, and minimally invasive interventions.

**4. Targeting and Navigation in Biological Systems**

One of the most critical advantages of nanoboat drug delivery systems is their ability to actively target specific tissues or cellular environments, overcoming the limitations of passive nanoparticle distribution. Efficient targeting and navigation are essential for achieving high therapeutic efficacy, minimizing systemic toxicity, and ensuring precision therapy. Nanoboats utilize a combination of passive and active targeting strategies, surface functionalization, chemotactic sensing, and physiological barrier navigation to achieve controlled localization.

Passive targeting relies primarily on the enhanced permeability and retention (EPR) effect observed in tumors and inflamed tissues. The leaky vasculature in such regions allows nanoparticles to accumulate

selectively, while impaired lymphatic drainage retains them locally. However, passive targeting is limited by slow diffusion, heterogeneous vascularization, and low penetration depth. Nanoboats, while benefiting from EPR, surpass passive strategies by actively moving toward target sites using propulsion and guidance mechanisms, improving tissue penetration and drug delivery efficiency.

Active targeting involves engineering nanoboats with surface ligands, antibodies, or aptamers that recognize specific cellular receptors. These functionalizations enable selective binding to tumor cells, inflamed endothelium, or other diseased tissues. For example, nanoboats conjugated with folate or transferrin ligands target overexpressed receptors on cancer cells, while antibodies against adhesion molecules guide carriers to sites of vascular inflammation. Active targeting enhances uptake by diseased cells, reduces off-target interactions, and increases therapeutic index. Additionally, multi-ligand or dual-targeting approaches improve specificity and reduce the likelihood of immune clearance.

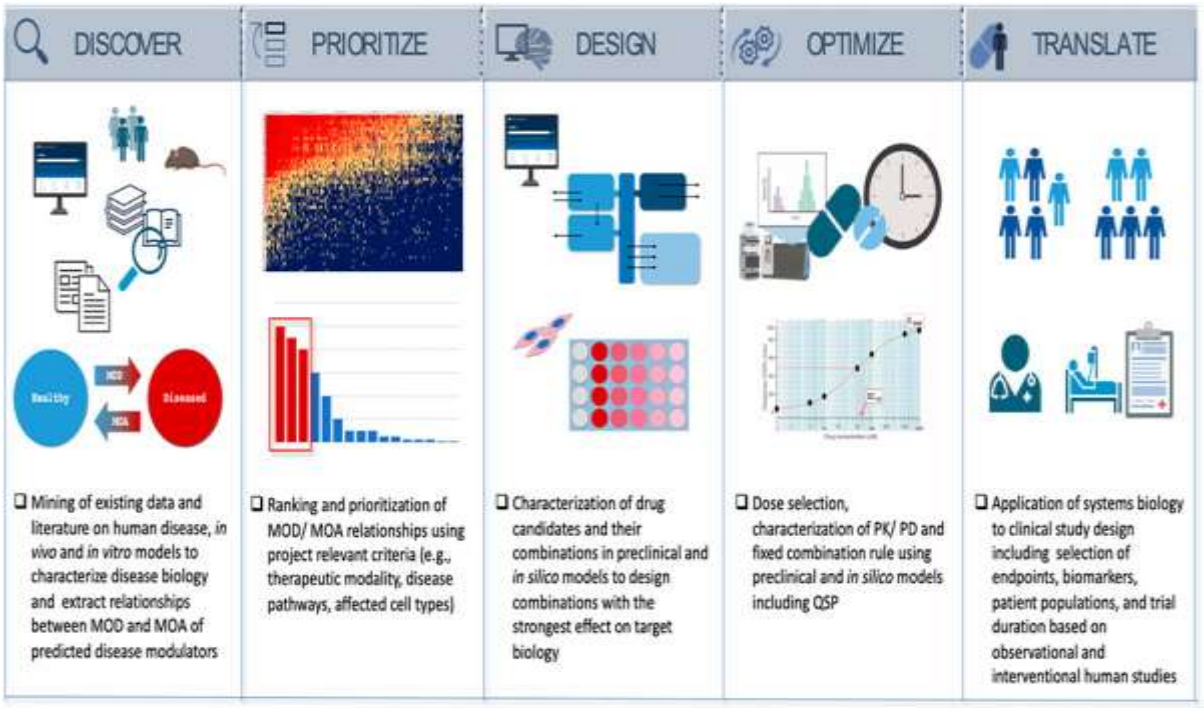



**Fig.4 Targeting and Navigation in Biological Systems**

Chemotaxis and microenvironment sensing represent sophisticated navigation strategies that exploit chemical gradients in tissues. Nanoboats can sense local concentrations of metabolites, signaling molecules, or pH variations to guide themselves toward target microenvironments. For instance, tumor tissues often exhibit hypoxia and acidic pH, which can be used to direct nanoboat movement and activate stimuli-responsive drug release. Enzyme-driven nanoboats can utilize gradients of urea or glucose to navigate specific biological compartments, while biohybrid systems incorporating bacteria or motor proteins respond to chemotactic cues for precise localization.

Overcoming physiological barriers is a key challenge in targeted drug delivery. The circulatory system, endothelial barriers, mucus layers, and the blood–brain barrier (BBB) limit passive nanoparticle access. Nanoboats utilize active propulsion to traverse viscous fluids and penetrate dense tissues. Magnetic and ultrasound-guided systems provide external control to reach deep or restricted regions. Biohybrid nanoboats, such as bacteria-driven carriers, can actively cross tight junctions, penetrate tumors, or navigate mucosal surfaces. Surface modifications, including PEGylation and hydrophilic coatings, reduce opsonization and immune clearance, extending circulation time and increasing the probability of reaching the target site.

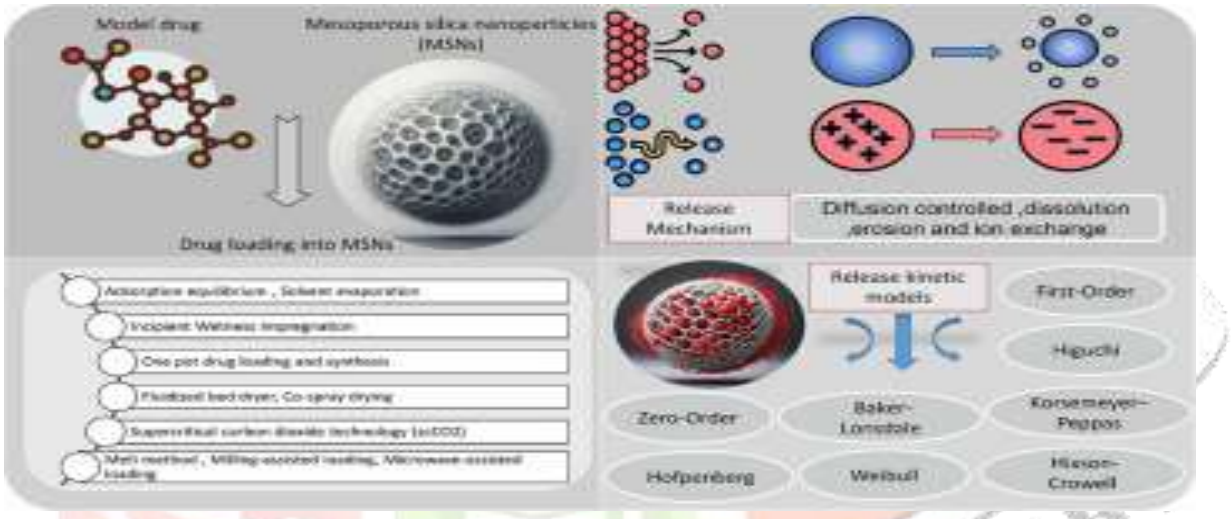
Integration of propulsion and targeting is essential for optimal nanoboat performance. The combination of chemotactic sensing, surface functionalization, and external guidance ensures that nanoboats can

dynamically respond to complex biological environments. This multi-modal approach improves tissue-specific accumulation, penetration, and retention, ultimately enhancing therapeutic outcomes.

In conclusion, targeting and navigation in biological systems are defining features that enable nanoboats to achieve precision therapy. By integrating passive accumulation, ligand-mediated active targeting, chemotactic sensing, and barrier-penetration strategies, nanoboats overcome the limitations of conventional nanoparticles. Effective navigation enhances drug localization, reduces systemic toxicity, and opens new possibilities for treating cancer, neurological disorders, infectious diseases, and other pathologies where conventional delivery methods fail.

**5. Drug Loading and Controlled Release**

Effective drug loading and controlled release are central to the therapeutic success of nanoboat systems. The primary goal is to encapsulate or attach sufficient drug molecules while maintaining nanoboat stability, ensuring that the payload is delivered precisely to the target tissue, and releasing it at the appropriate time. Nanoboats employ multiple strategies for drug incorporation, including physical encapsulation, chemical conjugation, and stimuli-responsive loading, each with distinct advantages.




**Fig, 5 Drug Loading and Controlled Release**

Encapsulation techniques are widely used for hydrophobic and hydrophilic drugs. Hydrophobic drugs can be incorporated into polymeric or lipid cores, while hydrophilic drugs are often loaded into aqueous compartments or attached to hydrophilic shells. Nanoboats can also carry multiple therapeutic agents, enabling combination therapies that synergistically improve efficacy. Core–shell architectures and tubular designs maximize drug loading capacity while maintaining hydrodynamic efficiency and stability.

Chemical conjugation methods involve covalent attachment of drugs to the nanoboat surface or scaffold. This strategy allows precise control over drug dosage and release kinetics, often through cleavable linkers responsive to specific stimuli, such as pH, enzymes, or redox conditions. Conjugation is particularly valuable for targeting sensitive molecules like proteins, peptides, or nucleic acids, which require protection during systemic circulation.

Stimuli-responsive release enhances precision therapy by ensuring that drugs are released specifically at the target site. Environmental cues, such as acidic pH in tumor microenvironments, enzymatic activity, elevated temperature, or external triggers like light and magnetic fields, can induce structural changes in the nanoboat or cleave linkers, releasing the therapeutic payload. For instance, pH-sensitive coatings swell and release drugs in acidic regions, while enzyme-sensitive linkers degrade in the presence of disease-specific enzymes.

Pharmacokinetics and bioavailability are significantly improved with nanoboat-mediated drug delivery. Active propulsion and targeted navigation reduce premature clearance and increase local drug

concentration, enhancing therapeutic effects while minimizing systemic toxicity. Controlled release ensures sustained drug availability at the target site, reducing dosing frequency and improving patient compliance. Additionally, nanoboats can be designed to release drugs sequentially, enabling combination therapy or multi-step treatment strategies.

In conclusion, advanced drug loading and controlled release mechanisms are integral to nanoboat functionality. By combining physical encapsulation, chemical conjugation, and stimuli-responsive systems, nanoboats deliver precise drug doses to specific tissues, overcoming limitations of conventional delivery platforms. These strategies maximize efficacy, minimize off-target effects, and provide a versatile platform for diverse therapeutic applications, including cancer therapy, neurological treatments, and infectious disease management.

## 6. Therapeutic Applications

1. Nanoboat drug delivery systems hold transformative potential across a wide range of therapeutic applications due to their active propulsion, targeted navigation, and controlled release capabilities. By integrating these features, nanoboats address major limitations of conventional drug delivery, including poor tissue specificity, limited penetration, and systemic toxicity.
2. Cancer therapy is the most extensively explored application. Tumors often have dense extracellular matrices and heterogeneous vasculature, which hinder passive nanoparticle accumulation. Nanoboats, with active propulsion, can penetrate deep into tumor tissues, increasing local drug concentration and improving therapeutic outcomes. Surface functionalization with ligands, antibodies, or aptamers further enhances specificity by targeting overexpressed receptors on cancer cells. Nanoboats can also carry multiple therapeutic agents for combination therapy. For instance, chemotherapy drugs combined with photothermal or photodynamic agents allow simultaneous cytotoxic and hyperthermic effects, maximizing tumor cell death while minimizing off-target toxicity. Additionally, stimuli-responsive nanoboats release drugs preferentially in acidic or hypoxic tumor microenvironments, reducing systemic side effects.
3. Neurological disorders represent another promising application, particularly due to the challenge of crossing the blood–brain barrier (BBB). Traditional therapies often fail because the BBB restricts drug entry into the central nervous system. Nanoboats can be engineered for active propulsion across this barrier, utilizing magnetic guidance, enzyme-driven propulsion, or biohybrid motile systems. Ligand functionalization targeting endothelial transporters, such as transferrin receptors, further enhances brain accumulation. Such strategies enable precise delivery of neuroprotective agents, growth factors, or nucleic acids for treating Alzheimer's disease, Parkinson's disease, stroke, and other neurological conditions.
4. Infectious diseases benefit from nanoboats' ability to penetrate biofilms and reach infection sites that are poorly accessible to conventional antibiotics. Bacteria-driven biohybrid nanoboats or enzyme-powered systems can navigate viscous mucus or infected tissues, enhancing drug delivery to resistant bacterial colonies. Controlled release mechanisms ensure sustained drug concentrations at the infection site, reducing the emergence of resistance and improving patient outcomes.
5. Personalized medicine is an emerging area where nanoboats provide unique advantages. By tailoring propulsion mechanisms, surface ligands, and drug payloads, nanoboats can be customized for individual patients based on disease type, tissue architecture, and molecular biomarkers. Theranostic nanoboats integrate diagnostic agents with therapeutic payloads, allowing real-time monitoring of drug distribution, target engagement, and treatment response. For example, nanoboats carrying fluorescent markers or contrast agents enable imaging-guided therapy, providing a closed-loop system for precision medicine.

6. In addition, other applications include targeted delivery for cardiovascular diseases, autoimmune disorders, and localized gene therapy. Nanoboats can deliver anti-inflammatory agents directly to inflamed endothelium or deliver siRNA to specific immune cell populations. Their ability to actively navigate complex physiological environments makes them suitable for minimally invasive, high-precision therapeutic interventions across diverse medical domains.

In conclusion, nanoboats offer versatile and highly effective platforms for treating cancer, neurological disorders, infectious diseases, and personalized medicine applications. By combining active propulsion, targeted navigation, and controlled release, these systems enhance therapeutic efficacy, reduce systemic toxicity, and expand the possibilities of precision medicine.

**7. Safety, Biocompatibility, and Immunogenicity**

1. While nanoboat drug delivery systems offer significant therapeutic advantages, their clinical translation depends heavily on safety, biocompatibility, and immunogenicity. Because these nanosystems often involve synthetic materials, propulsion chemicals, or biohybrid components, careful evaluation of their interactions with biological systems is essential to minimize adverse effects and ensure safe use in humans.
2. Toxicity concerns are a primary consideration. Chemical propulsion systems, for example, may rely on fuels like hydrogen peroxide or other reactive substrates, which can generate oxidative stress or cytotoxic byproducts if not carefully controlled. Similarly, inorganic components such as gold, silica, or magnetic nanoparticles, while offering structural stability and external-field responsiveness, may accumulate in organs like the liver, spleen, or kidneys if clearance is inefficient. Biodegradable polymers such as PLGA and PEG are generally safer, as they degrade into metabolizable byproducts, but dose-dependent effects and interactions with blood proteins must be considered. Comprehensive in vitro cytotoxicity studies, along with in vivo toxicity assays, are necessary to evaluate cell viability, organ function, and systemic effects.
3. Immune activation and clearance present another challenge. Nanoboats are recognized as foreign entities by the immune system, which can lead to opsonization, phagocytosis by macrophages, and rapid clearance from circulation. Such immune recognition reduces therapeutic efficiency and may provoke inflammatory responses. Surface modifications, such as PEGylation or hydrophilic polymer coatings, can provide a “stealth” effect, reducing protein adsorption and immune detection. Targeted ligands must also be designed to minimize off-target immune interactions. Biohybrid nanoboats, while highly efficient in propulsion, require careful handling to prevent immune activation, as components like bacterial flagella may trigger immune responses if not properly modified.
4. Long-term effects and degradation are critical for clinical applicability. Nanoboats must be designed to degrade or be cleared efficiently to prevent accumulation and chronic toxicity. Biodegradable polymers, enzyme-labile linkers, or metabolizable inorganic components ensure that nanoboats do not persist in tissues, avoiding potential long-term side effects. For biohybrid systems, controlled inactivation or removal strategies are essential after drug delivery to prevent unintended proliferation or interaction with host tissues.
5. Biocompatibility testing encompasses not only cytotoxicity but also hemocompatibility, genotoxicity, and inflammatory responses. Blood compatibility ensures that nanoboats do not induce hemolysis, clotting, or platelet activation. Genotoxicity studies evaluate the potential for DNA damage, while inflammatory markers indicate systemic immune responses. Such testing must be conducted in physiologically relevant models to predict in vivo outcomes accurately.
6. Regulatory considerations further underscore the importance of safety evaluation. Nanoboats intended for clinical use must meet stringent standards for biocompatibility, reproducibility, and predictable pharmacokinetics. Addressing immunogenicity, off-target toxicity, and degradation profiles early in design reduces translational hurdles.

In conclusion, safety, biocompatibility, and immunogenicity are critical determinants of nanoboat clinical success. By carefully selecting materials, controlling propulsion chemistry, optimizing surface functionalization, and ensuring efficient degradation, nanoboats can achieve high therapeutic efficacy while minimizing adverse effects. Rigorous preclinical evaluation and thoughtful design are essential to translate these advanced nanosystems into safe and effective precision medicine platforms.

## 8. Challenges and Future Directions

Despite the tremendous potential of nanoboat drug delivery systems, several challenges remain before these nanoscale vehicles can achieve widespread clinical adoption. Addressing these challenges requires interdisciplinary innovation in materials science, nanotechnology, biology, and regulatory science.

### 1. Manufacturing and Scalability:

Fabricating nanoboats with consistent size, shape, propulsion efficiency, and surface functionalization is technically challenging. Many laboratory-scale methods, such as chemical synthesis of Janus particles or biohybrid assembly with bacteria or flagella, are difficult to scale up for industrial production. Achieving high batch-to-batch reproducibility and precise control over drug loading and propulsion components is critical for clinical translation. Advanced microfabrication, 3D nanoprinting, and automated assembly techniques are being explored to overcome these limitations.

### 2. In vivo Tracking and Imaging:

Monitoring nanoboats in real time is essential for assessing biodistribution, targeting efficiency, and therapeutic outcomes. However, current imaging modalities, including fluorescence, MRI, and ultrasound, have limitations in resolution, depth, and sensitivity. Integrating diagnostic agents within nanoboats (theranostic design) allows simultaneous therapy and monitoring, but optimizing signal intensity without affecting propulsion, targeting, or biocompatibility remains a challenge. Real-time tracking is particularly critical for navigating deep tissues or crossing barriers like the blood–brain barrier.

### 3. Physiological Barriers:

Nanoboats must overcome complex physiological barriers such as vascular endothelium, dense extracellular matrices, mucus layers, and the BBB. While propulsion enhances penetration, fluid shear forces, immune clearance, and heterogeneous tissue architecture can impede navigation. Developing adaptive nanoboats capable of sensing their environment and adjusting propulsion or surface properties dynamically is an active area of research.

### 4. Biocompatibility and Safety:

Although biodegradable polymers and biohybrid systems offer promising biocompatibility, the long-term effects of inorganic nanomaterials or residual chemical fuels remain a concern. Immune recognition, off-target accumulation, and potential genotoxicity must be carefully addressed. Standardized preclinical models and comprehensive toxicity assays are required to ensure safe translation.

### 5. Regulatory and Translational Challenges:

Regulatory approval for nanoboat systems is complicated due to their multifunctional nature. They combine aspects of drugs, devices, and biologics, leading to complex classification and evaluation criteria. Demonstrating reproducibility, stability, predictable pharmacokinetics, and minimal immunogenicity is essential for regulatory acceptance.

Future directions focus on addressing these challenges while expanding therapeutic applications. Integration with artificial intelligence (AI) and machine learning can optimize propulsion, navigation, and targeting strategies. Smart nanoboats capable of autonomous decision-making based on local microenvironment cues are emerging as a next-generation solution. Combining multi-modal propulsion (chemical, magnetic, enzyme-driven) with theranostic functionality will enable precise, image-guided therapy. Additionally, advances in biodegradable, bioresorbable, and stimuli-responsive materials will enhance safety and efficacy. Researchers are also exploring personalized nanoboats, designed for individual patient pathology and molecular profiles, to enable precision medicine in oncology, neurology, and infectious disease.

## 9. Conclusion

nanoboat drug delivery systems face technical, biological, and regulatory challenges, ongoing innovations in design, propulsion, targeting, and materials are steadily overcoming these obstacles. Future developments promise to expand their applicability, improve safety, and enable fully autonomous, precise, and patient-specific drug delivery solutions.

Nanoboat drug delivery systems represent a revolutionary approach in precision medicine, combining nanoscale engineering, active propulsion, and targeted therapy to overcome the limitations of conventional drug delivery platforms. By integrating structural optimization, propulsion mechanisms, surface functionalization, and controlled drug release, nanoboats offer unprecedented control over the localization, timing, and dosage of therapeutic agents. This active, targeted approach addresses the key challenges of traditional nanoparticles, including poor tissue penetration, systemic toxicity, and lack of specificity.

Throughout this review, we have explored the multifaceted aspects of nanoboat design and application. Structural architecture, including core–shell, tubular, and boat-shaped designs, provides the foundation for stability, drug loading, and propulsion efficiency. Propulsion mechanisms, ranging from chemical and enzyme-driven to magnetic and biohybrid systems, enable nanoboats to actively navigate complex physiological environments, cross biological barriers, and reach previously inaccessible tissues such as the central nervous system or dense tumor microenvironments. Surface functionalization strategies, including ligand conjugation, PEGylation, and stimuli-responsive coatings, further enhance targeting specificity, immune evasion, and controlled drug release, maximizing therapeutic efficacy while minimizing adverse effects.

## 10. References


1. Huang Y, Peng F. Micro/nanomotors for neuromodulation. *Nanoscale*. 2024;16(11019–11027). (RSC Publishing)
2. Kagan D, Laocharoensuk R, Zimmerman M, et al. Rapid delivery of drug carriers propelled and navigated by catalytic nanoshuttles. *Small*. 2010;6(23):2741-2747. (American Chemical Society Publications)
3. Soto F, Kuralay F, et al. Design strategies for self-propelled nanoparticles. *Adv Mater*. 2019;31:e1807310.
4. Gao W, Dong R, Thamphiwatana S, et al. Artificial micromotors in vivo. *ACS Nano*. 2014;8(8):7471-7480.
5. Ebbens SJ, Howse JR. In pursuit of propulsion at the nanoscale. *Soft Matter*. 2010;6:726-38.
6. Wang J. Nanomachines: Fundamentals and Applications. Wiley-VCH; 2013.
7. Mano N, Heller A. Bioelectrochemical propulsion at the microscale. *J Am Chem Soc*. 2005;127(33):11574-11575.

8. Li J, de Ávila BE-F, Gao W, et al. Micro/nanorobots for biomedicine: Delivery, surgery, sensing, and detoxification. *Sci Robot*. 2017;2(4):eaam6431.
9. Medina-Sánchez M, Xu H, Schmidt OG. Micro- and nano-motors: The new generation of drug carriers. *J Mater Chem B*. [Review].
10. Zhang L, Abbott JJ, Dong L, et al. Artificial bacterial flagella: Fabrication and magnetic control. *Nano Lett*. 2009;9(10):3663-3667.
11. Gao W, Wang J. Synthetic micro/nanomachines in drug delivery. *Nanoscale*. 2014;6(18):10486-10494.
12. Wang W, Du X, Sen A. From static to dynamic: Progress in propulsion mechanisms of micro/nanomotors. *ACS Nano*. 2014;8(9):8378-8385.
13. Fischer P, Ghosh A. Magnetically actuated propulsion at low Reynolds numbers: Nanorobots and swarm control. *Nanoscale*. 2011;3(2):557-563.
14. Soto F, et al. Self-propelling micro/nanomotors: Review in drug delivery. *Int J Pharm*. 2021;596:120275. (ScienceDirect)
15. Dong R, et al. Enzyme-powered micro/nanomotors for drug delivery. *Chem Soc Rev*. 2021;50(7):3788-3816.
16. Hortelão AC, et al. Enzyme-powered nanomotors enhance anticancer drug delivery. *J Control Release*. 2020;317:208-216. (PMC)
17. Sánchez S, Pumera M. Bio-hybrid microbots: Recent progress and future perspectives. *Chem Soc Rev*. 2015;44:3089-3105.
18. Gao W, Garcia-Infante C, Wang J. Micro/nanomotors for targeted drug delivery. *Trends Biotechnol*. 2019;37(7):750-762.
19. Nikfar B, Musavi M, Chaichian S, et al. Nanomotor-mediated drug delivery with efficient blood–brain barrier crossing for glioblastoma therapy. *Nanoscale*. 2025;17:16592-16608. (RSC Publishing)
20. Aghakhani A, et al. Micro/nanomotor drug delivery systems propelled by endogenous power. *Sci Rep*. 2021;11:15487.
21. Li T, Ren L, Ren X, et al. Light-activated nanomotors for deep tissue drug delivery. *Adv Funct Mater*. 2020;30:1909474.
22. Sanchez S, Soler L, Katuri J. Chemically powered micro- and nanomotors. *Angew Chem Int Ed*. 2015;54(5):1414-1444.
23. Li J, de Ávila BE-F, et al. Micromotors for cargo transport in vivo. *Nat Commun*. 2017;8:15344.
24. Zhang D, et al. Magnetic nanomotors for enhanced drug delivery. *ACS Nano*. 2018;12(3):2807-2814.
25. Shi J, Li Y, Dong D, et al. Magnetic microrobots for drug delivery: Materials, design, strategies. *Molecules*. 2026;31(1):86. (MDPI)
26. Luo M, et al. Ultrasound-propelled nanomotors for drug delivery. *ACS Appl Nano Mater*. 2019;2(4):1979-1986.
27. Villarreal E, et al. Micromotors for gastrointestinal drug delivery. *Adv Mater*. 2023;35(24):e2208824.

28. Medina-Sánchez M, Schmidt OG. Biohybrid biorobots. *Annual Review of Control, Robotics*, 2017.
29. Li T, Wang H, et al. Nanorobots for drug delivery in cardiovascular diseases. *Nanomedicine*. 2021;16(4):345-356.
30. Gao W, et al. Bubble-propelled micro/nanomotors for drug delivery. *ACS Nano*. 2020;14(7):7315-7324.
31. Soto F, et al. Nanomotors for immunotherapy delivery. *Nano Today*. 2022;43:101432.
32. Ren L, et al. Stimuli-responsive nanomotors for precision delivery. *Adv Drug Deliv Rev*. 2021;176:113889.
33. Xu T, et al. Nanomotor navigation in biological fluids. *Biomaterials*. 2020;245:119962.
34. Wang W, et al. Navigation of nanomotors in tumor microenvironments. *ACS Nano*. 2021;15(8):13387-13398.
35. Kagan D, et al. Ultrasound-assisted drug delivery microtools. *Small*. 2013;9(19):3315-3321.
36. Wu Y, Yakov S, et al. Hybrid micromotors in drug delivery and sensing. *arXiv Preprint*. 2022. (arXiv)
37. Xu H, Medina-Sánchez M, et al. Sperm-hybrid micromotors for targeted drug delivery. *arXiv Preprint*. 2017. (arXiv)
38. Fadeel B, Garcia-Bueno C. Safety evaluation of nanomaterials. *Nat Nanotechnol*. 2018;13:537-542.
39. Fröhlich E. The role of surface charge on nanoparticle uptake. *Int J Nanomedicine*. 2012;7:5577-5591.
40. Chen Q, et al. Biodegradable nanomaterials for safe nanomedicine. *Adv Mater*. 2019;31(47):e1805937.
41. Park K. Facing regulatory challenges in nanomedicine. *Biomaterials*. 2014;35(25):6980-6992.
42. Conte C, Saeed AF, et al. Standardized testing of nanoscale therapeutic carriers. *Nat Rev Mater*. 2020;5(12):915-931.
43. Peer D, et al. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol*. 2007;2:751-760.
44. Saraiva C, et al. Nanoparticle-mediated brain drug delivery. *J Control Release*. 2016;235:34-47.
45. Blanco E, et al. Principles of nanoparticle design for overcoming biological barriers. *Nat Biotechnol*. 2015;33(9):941-951.
46. Decuzzi P, Ferrari M. Specific and non-specific interactions in endocytosis. *Biomaterials*. 2008;29(31):3892-3899.
47. Alexis F, et al. Factors affecting clearance and biodistribution of polymeric nanoparticles. *Mol Pharm*. 2008;5(4):505-515.
48. Yu M, Huang X, et al. pH-responsive nanocarriers for tumor targeting. *Bioconjug Chem*. 2020;31(6):1274-1292.
49. Schattling P, et al. Enzyme-driven propulsion review. *Chem Soc Rev*. 2021;50:3788-3816.
50. Sanchez S, et al. Multi-stimuli responsive nanomotors. *Adv Mater*. 2022;34(12):2106789.

51. Gao W, et al. Hybrid propulsion micromotors. *Nano Today*. 2019;27:43-65.

52. Liu X, et al. Clinical prospects of micromotors in drug delivery. *Trends Pharmacol Sci*. 2023;44(8):656-670.