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"Navigating the Future: A Comprehensive Review on Nanorobots in Therapeutic Applications"

Anushka Nadre[1], Pooja Mule[1], Priti Palkar[1], Bhakti Pagare[1], Sana Tahreem Moiez Shaikh[2], Dr. Sachidanand Angadi[3]

[1]Students, Yash Institute of Pharmacy

[2]Assistant Professor, Yash Institute of Pharmacy

[3]Principal, Yash Institute of Pharmacy

Abstract

Nanorobots represent a new field of nanomedicine, offering novel methods for targeted drug delivery, diagnostics, and minimally invasive treatment. These tiny devices can navigate complex biological environments, detect diseased tissues, and precisely and regulated by administer medication. When biohybrid designs, advanced materials, and artificial intelligence are combined, they become more precise, effective, and adaptable. This study explores the mechanics, applications, advantages, most recent advancements, and future prospects of nanorobots in drug therapy to demonstrate their potential to revolutionize modern medicine. There is discussion of possible strategies for overcoming challenges like clinical translation, biocompatibility, moral dilemmas, and manufacturing complexity. In the end, nanorobotic technology may usher in a new era of personalized, responsive, and intelligent healthcare systems.

Keywords

Nanorobots, Drug Delivery, Nanomedicine, Artificial Intelligence, Targeted Therapy, Biomedical Applications

Introduction

The Greek word "dwarf" is the root of the English term "nano." Physicist Richard Feynman, who won the Nobel Prize, introduced the idea of nanotechnology in his 1959 speech "There's plenty of room at the bottom."[1] The talk concluded with him saying, "this is a development that I believe is unavoidable. Human civilization has seen a radical transformation in the last several decades due to mechanical and robotic technology.[2] Additionally, modern micro- and nanotechnology has

significantly accelerated the reduction in size of robotic systems, bringing the idea of "swallowing a surgeon" is becoming closer to reality.[3]

Robots or robotic systems with sizes on the micron or nanometre scale are referred to as micro/nano robots.[4] These robots may carry out certain activities, such cellular processes or assembly and repair at the micro or nanoscale, and are usually made up of micro or nanoscale components molecular level The rapid development of materials science and nanotechnology has led to the use of micro/nano robots in a number of biomedical domains.[5]

Nanorobots are tiny, nanoscale devices that can effectively propel themselves by transforming external power or local energy into propulsive force.[6] These nanorobots come in different forms and usually have a diameter of less than 1 μm like a hollow, helical, spherical, rod, or other intricate formations.[7] various applications may require various material compositions, such as 3D-printed resin, biocompatible polymers, and hard metals.[8]

When properly constructed, nanorobots can contribute significantly to the creation of new instrumented platforms, making them more than merely scientific curiosity.[9] To offer an overview of the possibilities and the role that nanorobotics may play in the realm of instrumentation, some examples of innovative nanorobotic instrumented platforms under development in our research laboratory are briefly mentioned.[10]

To carry out tasks, micro/nanorobots can transform various energy sources, such as magnetic, optical, or audio, into kinetic or actuation force tasks at the micro/nanoscale with flexibility and efficiency. [11]Actuation technologies that have already been used on micro/nanorobots may be categorized into two groups based on the various actuation mechanisms.[12] External magnetic, electric, optical, and audio fields are examples of external field actuation.[13] The other is self-actuation, which encompasses a variety of techniques such as chemical and biological self-actuation.[14]

There are several ways to fuel the movement of micro and nanorobots, such as chemical catalysis (such as the production of O_2 or H_2) or chemical gradients from outside energy sources, such lights, acoustic waves, magnetic fields, electric fields and even motile organism like bacterial or sperm cells.[15] Micro/Nanorobots can be categorized as chemically (or fuels) driven, depending on the power source.[16] The terms “powered”, “actuated” or “propelled” might be used in place of driven.[17]

This perspective article's objective is to examine traditional SCS implantation methods, together with the associated drawbacks and restrictions, and to consider how magnetically to enhance the current standard, guided leads and untethered micro- and nanorobots could be used.[17]

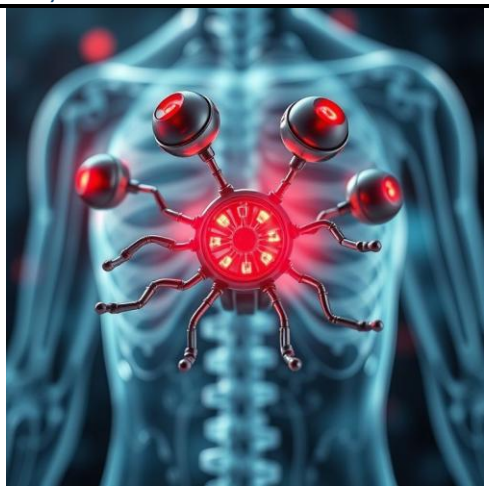

Figure 1: Nanorobot

Types of Nanorobots

1. Pharmacyte

A medical nanorobot that is 1-2 meters in size would serve as the model pharmacyte rather than a comparatively passive nanoparticle.[18] It could transport up to around 1 m3 of medication that is kept in onboard tanks. Molecular sorting pumps1a 21 installed in the hull, controlled by an onboard computer, are used to manually discharge them.[19] Since the volume of a nanorobot is just **1–10 µm³**, as opposed to **10^3–10^4 µm³** for most human tissue cells, pharmaceuticals might be directed to an intracellular organelle.[20] however in those situations, nanorobots would need to rely on nano injection because they would not have enough space to enter one (possibly with the exception of the ER and nucleus).[21]

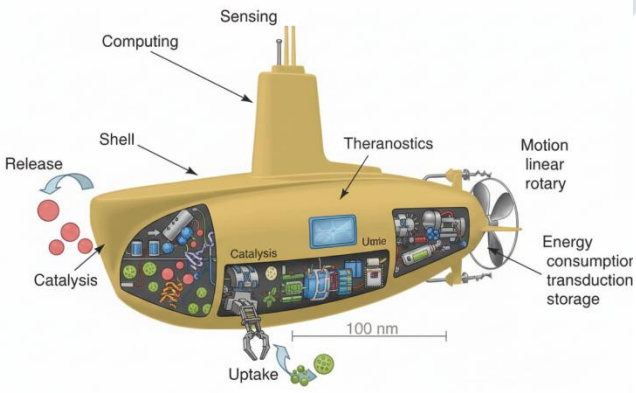

Figure 2: Pharmacyte

2.Respirocyte

Robert A. Freitas Jr. created respirocytes, which are blood-borne, 1-micron-diameter, diamondoid storage tanks used to carry breathing gasses throughout the human anatomy.[22] Up to 1000 atm of reversible pressure may be applied to these spherical nanodevice When completely filled, the current respiratory cell has 18 billion structural atoms ordered correctly and 9 billion molecules that are temporarily resident.[23] respirocytes have potential applications in treatment of various anaerobic and aerobic infections such as chronic refractory osteomyelitis, and

necrotizing soft tissue infections and can also help in recovery of burns by decreasing fluid requirements, improving microcirculation, and overcoming the need for grafting.[24]

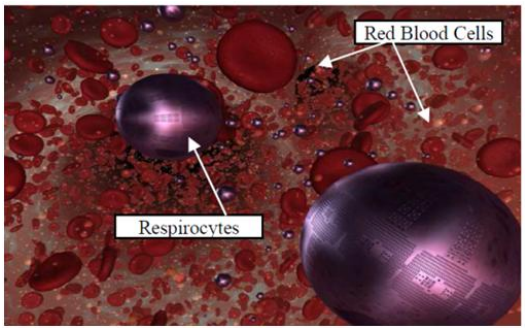

Figure 3: Respirocytes

3.Microbivore

When completely loaded, the microbivore, an oblate spheroidal nanomedical device, contains 150 billion molecules, primarily of gas or water, in addition to 610 billion carefully ordered structural atoms.[25] The nanorobot is 3.4 microns in size diameter along its main axis and 2.0 microns along its minor axis, guaranteeing that it can easily pass through even the tiniest human capillaries, which have a diameter of about 4 microns.[26]

4.Clottocytes

Twenty clottocytes, or around 1/10,000th the quantity in the bloodstream, have a clotting capability that is almost identical to that of natural platelets per blood cubic millimeter . The main danger of clottocytes is that the mechanical platelets' increased activity may cause diffused intravascular coagulation, which would produce many microthrombi.[1]

Mechanism of Drug Delivery Using Nanorobots

i.Drug loading and targeting mechanisms

Various loading techniques are used by nanorobots (micro-/nanorobots, DNA nanostructures, and hybrid biohybrids) to carry therapeutic payloads.[27] These loading techniques include covalent attachment to the robot scaffold, intercalation/encapsulation within cavities, adsorption onto functionalized surfaces, or entrapment inside polymeric coatings or liposomal shells attached to the robot. DNA-based nanorobots can precisely load proteins, nucleic acids, small molecules, or even nanoparticles by using programmable cavities and sequence-defined binding sites.[28] In other solid nanorobots (metal, silica, polymer), drugs or prodrugs are frequently anchored for later release via surface chemistry (thiol, silane, carboxyl).[29]

Targeting strategies fall into two main categories: (1) passive targeting, which uses physiological context (e.g., enhanced permeability and retention, or EPR, effect in tumours) to accumulate agents at disease sites;[30] and (2) active targeting, which functionalizes nanorobots with ligands (e.g., antibodies, peptides, or aptamers) that recognize specific cell-surface markers or guides them to the target externally (e.g., magnetic, acoustic, or optical fields).[31] Motile nanorobots provide an extra layer by enabling targeted navigation to hard-to-reach microenvironments (biofilm interiors, hypoxic tumour cores) through autonomous or externally triggered locomotion. [32]

[1] Manjunath and Kishore, *14 The Promising Future in Medicine: Nanorobots*.

Stealth and load stability: To survive circulation and avoid immune clearance, nanorobots are often coated with polyethylene glycol (PEG),[33] cell-membrane camouflaging (e.g., red-blood-cell or cancer-cell membranes), or other "stealth" coatings that prolong blood residence time and reduce protein opsonization, both of which are necessary for effective targeting.[34]

ii. Controlled release systems

Controlled release from nanorobots is achieved through the use of release kinetics design and programmable triggers.[35]

Stimulus-responsive release: Payloads are released in reaction to either internal (such as changes in the pH of the tumour microenvironment, elevated enzyme concentrations, glutathione/redox gradients, or hypoxia) or external (such as magnetic fields, light, ultrasound, or temperature) stimuli.[36] For instance, DNA nanostructures may open or change shape as a result of aptamer binding or strand displacement, providing immediate cargo exposure.[37]

Mechanical/actuation-based release: Some nanorobots use mechanical actions (opening gates, changing shape) to eject cargo only when the robot detects a combinatorial set of surface markers.[38] One example of this is the logic-gated DNA devices, which only reveal payloads when two or more target inputs are present.[39] In order to reduce off-target impacts, conditional delivery restrictions are added.[40]

Diffusion and polymeric gating: Drug release can also be controlled by hydrolytic or enzymatic breakdown of the polymer matrix, or diffusion through porous coatings with pore size and composition tailored for desired release rates.[41] The combination of timed polymer breakdown and motility results in regionally localized release patterns.[42]

Two objectives are balanced in design decisions: deliver an effective dosage quickly and with minimal systemic leakage at the target location,[43] and (ii) keep the payload sequestered and inactive during the journey.[44] Recent studies have concentrated on multi-modal triggers (e.g., pH + enzyme) to increase specificity.[45]

iii. Site-specific action (tumour targeting, infection site delivery, etc.)

a. Targeting cancer: Nanorobots enhance tumor treatment by (a) boosting intratumoral penetration through active propulsion or surface modifications that reduce extracellular matrix adhesion,[46] (b) selectively delivering chemotherapeutic agents or immune modulators to the tumor microenvironment,[47] and (c) combining localized drug delivery with in situ therapies such as phototherapy and hyperthermia.[48] Using magnetic or ultrasonic guidance, nanorobots can be directed precisely to tumor sites, thereby improving the therapeutic index and minimizing systemic toxicity.[49]

b. Targeting infections and biofilms: It has been shown that mobile micro/nanorobots can penetrate bacterial biofilms and deliver strong local antibiotic dosages.[50] Additionally, they might carry enzyme payloads that degrade extracellular polymeric substances (EPS), allowing antibiotics to reach bacteria that have become established there.[51] Biohybrid robots, like bacteria-powered microdevices, use natural chemotaxis to reach infection sites.[52] Crossing physiological

barriers: Researchers are working to create nanorobots that can mechanically pass through the blood–brain barrier (BBB) or mucosal layers using surface ligands, transient opening techniques (focused ultrasound), or active propulsion.[53] This will enable delivery to previously inaccessible areas.[54] Early preclinical models show promise, but they also emphasize how crucial safety and reversibility are.[55]

c. DNA origami-based nanorobots

One of the groundbreaking demonstrations is the DNA origami "logic-gated" nanorobot, which has molecular payloads and resembles a barrel with a locking lid.[56] Only aptamer targets-tumour cell-specific molecular cues-cause it to open. The purpose of this device was to use aptamer "locks" to detect cell-surface markers.[57] Highly selective targeted molecular delivery is made possible by structural reconfiguration and payload exposure to the cell membrane upon simultaneous recognition of the designated combination.[58] The study proved proof-of-principle targeted delivery and cellular response in vitro, and it developed the theoretical foundation for programmable, molecularly gated nanorobots.[59]

Additional research has expanded on that platform by incorporating imaging agents, cytotoxic chemicals, or immune-modulating factors; improvements include multi-input logic gates, enhanced serum stability, and integration with external guiding fields.[60] Despite the challenges that DNA origami robots face (scale-up, nuclease destruction in vivo, and immunogenicity), continuous progress in chemical modification (backbone alterations, protective coatings), clearance control, and large-scale manufacturing is closing the gap toward clinical translation.[61]

Applications in Drug Therapy

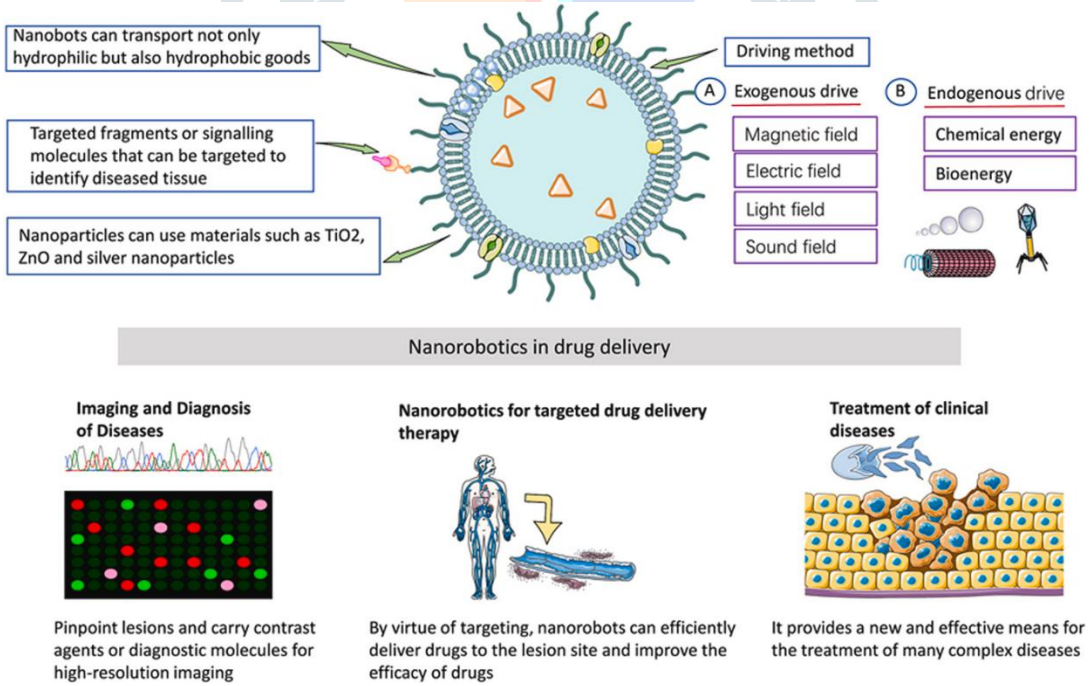

Figure 4: Nanorobots in Drug Delivery

Image adapted from: Beyond the pill: How nanorobots are transforming drug delivery https://doi.org/10.1016/j.jddst.2025.106817

1. Cancer treatment - targeted delivery and reduced side effects

Nanorobots and programmable Nano systems offer active, site-directed approaches to cancer treatment by addressing the shortcomings of passive nanoparticles (poor tumour accumulation, off-target toxicity).[62]These days, there are two main methods: (a)targeted payload delivery through molecular recognition (aptamers, antibodies) and stimuli-responsive release; and (b) mechanical/physical actions that directly damage tumour cells or the vasculature, like local energy release or vascular blockage.[63]

Additionally, autonomous or externally guided motile microrobots (magnetic, acoustic, chemical propulsion) further enhance accumulation by actively navigating complex biological fluids and penetrating tumour interstitium, enabling higher local drug concentration and dose sparing;[64] these platforms also enable combination approaches (drug + photothermal or immunomodulator) for synergistic antitumor effects.[65] In animal models, DNA-origami nanorobots have been shown to carry therapeutic cargos (e.g., thrombin) and open selectively at tumour sites using aptamer locks, resulting in localized vascular thrombosis and tumour necrosis.[66]

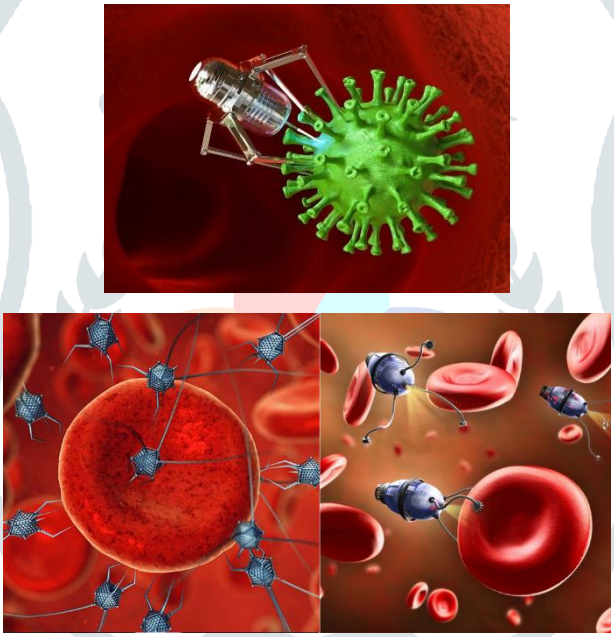

Figure 5: Nanorobots in chemotherapy

2. Infectious diseases - pathogen detection and targeted antibiotic delivery

Nanorobots and customized nano-carriers enhance antimicrobial therapy by physically disrupting biofilm matrices, releasing medication locally, and binding to pathogens or biofilms with specificity.[67] Motile micro/nanorobots can improve the elimination of drug-tolerant bacterial colonies while reducing systemic antibiotic exposure, which contributes to resistance, by penetrating biofilms and delivering high local antibiotic dosages.[68] Additionally, for point-of-care diagnostics, functionalized nanoplatforms offer rapid pathogen concentration and capture. Because of these features, nanorobotic methods hold promise for treating multidrug-resistant (MDR) infections and chronic biofilm-associated diseases.[69]

3. Neurological disorders - crossing the blood-brain barrier (BBB)

One of the most challenging barriers to CNS treatment is the BBB.[70] Advances in nanoscale carriers and nanorobot-like systems (ligand-functionalized nanoparticles, peptide-decorated polymeric carriers, and motile constructs) have shown promise in delivering small molecules,

peptides, and gene cargoes across the blood-brain barrier through receptor-mediated transcytosis, transient tight-junction modulation, or region-specific delivery.[71] Recent animal studies using dual-peptide functionalized polymeric nanocarriers and customized nanoparticles achieved targeted distribution to the hypothalamus or other brain regions, enhancing therapeutic effects in disease models.[72] Although fully autonomous human nanorobots are still in the preclinical stage, the emerging toolset suggests promising translational pathways for precision neurotherapeutics.[73]

4. Cardiovascular diseases - plaque removal and clot dissolution

Intravascular microrobots are being developed to remove atherosclerotic plaque, deliver thrombolytics locally, and mechanically break up clots with high spatial accuracy.[74] Untethered micro robots can be guided by magnetic or acoustic means to physically break up thrombi or deliver clot-dissolving enzymes to arterial blockage regions.[75] This could lower the risk of bleeding and possibly lower the systemic thrombolytic dosage.[76] Safety/embolization risk, imaging-guided control, and navigation within large-scale circulation remain major challenges despite the promising results of early preclinical and ex vivo vascular models.[77]

5. Gene and cell therapy - precision at the cellular level

Nanorobotic delivery systems supplement gene and cell therapies by improving targeting, transfection efficiency, and payload release control.[78] Functionalized nanoparticles and hybrid biohybrid microrobots (bacteria or cell-based carriers) can deliver nucleic acids or CRISPR reagents to particular cell populations while protecting cargo from degradation during transportation.[79] Furthermore, these systems reduce immune activation and off-target gene editing by facilitating local spatiotemporal control (e.g., release triggered by light or magnetic fields).[80] Combining nanorobots with cell treatment (e.g., directing cells to target tissue or providing local immunomodulation) can improve engraftment and therapeutic precision.[81]

6. Targeted Drug Delivery and Blood–Brain Barrier Penetration

One of the major obstacles in the treatment of central nervous system (CNS) disorders is the blood-brain barrier (BBB).[82] Nanorobots that are made to carry drugs can be attached with ligands or peptides that can detect the BBB transport receptors and then go through this biological barrier to deliver the neuroactive drugs with an ultra-high specificity.[83] It has been proven that using magnets to guide nanorobots has resulted in those tiny robots reaching the innermost layers of the brain and dispensing neuroprotective molecules in experiments involving Parkinson's and Alzheimer's diseases.[84]

Another application for these nano systems is that they can also carry the agents that the body needs for repair, such as, enzymes, antioxidants, or gene-editing agents like CRISPR-Cas9, which might be used to restore neuron damage by overcoming the consequence of oxidative stress .[85] Moreover, nanorobots loaded with biosensors are capable of monitoring neurotransmitter concentrations on a continuous basis and can be said to present a novel way of neurotherapeutics personalized according to the patient.[86]

7. Neural Regeneration and Repair

The utilization of nanorobots in neuroregeneration can be in the form of growth factor delivery and axon or synaptic connection rebuilding support.[87] Among the studies, biodegradable nanorobots made up of chitosan and gold nanostructures were reported to promote the extension of neurites and their functional gain after a traumatic brain injury.[88] Moreover, ultrasound-powered micro/nanorobots have also attracted attention to their high potential for the destruction of amyloid plaques in Alzheimer's models, thereby paving the way for regenerative neuro-nanomedicine.[89]

8. Nanorobots in Kidney Diseases

I. Diagnosis and Targeted Therapy

Kidney diseases such as chronic kidney disease (CKD) and acute kidney injury (AKI) are frequent cases for late diagnosis, as sensitive biomarkers are lacking.[90] Nanorobots linked with biosensing modules can spot renal biomarkers like creatinine, urea, and cystatin-C in blood, offering early diagnostic information.[91]

A breakthrough in therapeutic approaches is the use of drug-loaded nanorobots that are able to reach the renal blood system and supply the needed anti-inflammatory or anti-fibrotic agents just to the affected nephrons, thus eliminating exposure to the whole body. Moreover, "nanozymes", which are catalytic nanorobots with like-enzymes functioning, have been studied for the destruction of uremic toxins, which results in the reflux of filtration efficacy in kidney tissues.[92]

II. Regenerative and Detoxification Functions

The area of renal tissue regeneration is yet another great field for the deployment of nanorobots.[93] The implants of such nano-robots can slowly release the growth-encouraging cytokines like VEGF and FGF to speed up nephron regeneration. Also, the molecular filtering or detoxification enabled through this technology may turn out to be in the form of an artificial kidney, thereby perhaps eliminating the need for dialysis.[94]

Recent Advances

1. AI / Machine-Learning-Assisted Nanorobots

In recent years, micro/nanorobot control, sensing, and decision-making have rapidly incorporated artificial intelligence (AI) and machine learning (ML).[95] Artificial intelligence (AI) techniques are being used both offline (design optimization, materials selection, control-policy training in simulation) and online (real-time sensor fusion, adaptive navigation, closed-loop control) to enable autonomy in noisy, data-poor in-vivo scenarios.[96] It has been demonstrated that model-based reinforcement learning and visual-feedback policies are used by ultrasound-driven microrobots, allowing the systems to learn control strategies from sparse experiments and generalize across flow conditions. These AI layers reduce operator intervention and improve targeting precision in complex biological fluids.[97]

2. Magnetic and Ultrasound Propulsion - Practical Progress

Magnetic actuation is still the most well-known and widely used method for in-body steering because it offers precise remote control and deep penetration without requiring onboard power.[98]

Basic reviews demonstrate how single-particle motion can be converted into coordinated swarms for cargo delivery and highlight mechanical concepts such as helical swimmers, gradient forces, and rotating fields. Recent technological advancements that enable accumulation and triggered local payload release (e.g., embolization in aneurysm models) include hybrid torque-force magnetic fields and thermal-responsive coatings.[99] Concurrently, ultrasound propulsion has progressed: acoustic streaming and radiation forces may propel and assemble microrobots, while ultrasound imaging offers simultaneous localization, enabling closed-loop actuation and safer in-vivo imaging. Preclinical models have shown improved vision and delivery through the use of acoustically readable swarm operations and magnetic field.[100]

3. Clinical Research, Experimental Models, and Translation Pathways

Translational research is being conducted from 2019 to 2025 with realistic animal models and clinically relevant obstacles like blood flow shear, immunological interactions, mucus and biofilms, and imaging limitations.[101] Notable examples of experimental demonstrations include the use of magnetically guided cohorts of thermal-responsive nanobots for targeted embolization and intravascular navigation in aneurysm models, as well as photocatalytic/magnetically actuated swarms that penetrate sinus mucus and eliminate bacterial biofilms in pigs and rabbits. For safety and monitoring, researchers are increasingly integrating robotic actuation with real-time clinical imaging modalities (like ultrasound and X-ray/fluoroscopy) as a precondition for human trials. Numerous articles highlight regulatory and biocompatibility concerns and support the use of standardized tests for long-term retention, clearance, and immunotoxicity testing prior to first-in-human studies.[102]

4. Representative Case Studies (2019–2025)

Intracerebral aneurysm embolization with magnetic nanobots (2024): Thermally sensitive, magnetically guided nanorobots that accumulated in model aneurysms in vivo and released payloads upon focused heating to produce embolization in animal models were used to demonstrate a potent proof of concept for minimally invasive occlusion treatment.[103] The Online library at Wiley Teams demonstrated the feasibility of vascular treatments in rabbit models by demonstrating injection, magnetically driven clustering inside aneurysms, and on-site medication release using magnetically directed "nanorobot armies" for brain bleeds (2024).[104]

Using photocatalytic/magnetically actuated microrobots to remove sinus infections (2025): Swarms of light- or magnetically-activated microrobots were designed to be released after penetrating viscous pus and biofilms in pig sinuses, and they eradicated infections in rabbit models without causing obvious tissue damage. The focus of this study is on focused, non-antibiotic therapies for chronic diseases.[105]

AI-driven ultrasound control (2025): It was shown that model-based RL controllers trained in simulation could control ultrasound-driven microrobots more accurately in complex flows, indicating that acoustic propulsion could be practically autonomous.[106]

5. Synthesis - Where the Field Is Headed

Overall, multi-modal actuation (magnetic + acoustic + optical), coordinated swarms, and AI-enabled autonomy that lowers operator load and increases resilience in physiological settings are replacing single-robot demonstrations. Regulatory procedures, scalable GMP production of robot batches, standardized safety testing, and in-vivo clearance processes remain significant translational challenges.[107] However, high-impact preclinical demonstrations between 2020 and 2025 indicate that first-in-human pilot trials for targeted local treatments (like ENT and intravascular interventions) are probably going to occur in the coming years, assuming regulatory and long-term safety concerns are addressed.[108]

Advantages

Nanorobots (micro/nanorobots and DNA-based nanomachines) offer several interrelated advantages over conventional systemic therapy in the delivery of medications. These benefits work together to improve treatment effectiveness while reducing off-target toxicity, which is a key goal in precision medicine.[109]

1.High-precision targeting

Instead of passively dispersing, nanorobots can be actively driven, externally guided (magnetic, auditory, visual), or programmed to react to local biochemical signals. The therapeutic index is improved by this active, targeted administration, which raises drug concentration at problematic tissue while preserving healthy tissue. Microrobots that are magnetically guided and DNA-origami nanorobots that only open and release payloads when tumour markers are detected are two examples.[110]

2.Reduced side effects

By focusing payloads at target locations and reducing systemic exposure, nanorobots can drastically lower the dose needed for effectiveness and, consequently, systemic side effects. Preclinical studies (using animal models) have shown decreased off-target accumulation and improved safety profiles when nanorobots deliver cytotoxics or radionuclides directly to tumors.[111]

3.Minimal drug wastage (improved delivery efficiency)

Active navigation and adherence to sick tissue reduce drug loss to circulation and non-target compartments; triggered release and controlled docking further reduce premature drug release. Because of this effectiveness, more of a specific formulation gets to the diseased area, making therapies more cost-effective and reducing the accumulation of unnecessary medication in the environment and biology.[112]

4.Controlled and sustained release

In many nanorobot systems, targeting and designed release kinetics are combined. Examples include stimulus-responsive gates (pH, enzymes, light) or programmable DNA mechanisms that open in response to the detection of biomarkers. These techniques enable sustained therapeutic

levels at the site over time (less peak/trough fluctuation), which improves efficacy and lowers dosage frequency for drugs that require prolonged exposure.[113]

5.Enhanced patient compliance

By improving efficacy per dose and offering sustained or single-site administration, nanorobot systems can streamline patient regimens and potentially lower dosage frequency or enable localized depot treatment. When there are fewer doses and fewer systemic side effects, patients are more likely to continue treatment, which is crucial for chronic diseases like cancer.[114]

6.Additional practical advantages (integration & multimodality)

Many nanorobots are made to be multifunctional platforms that combine biosensing, imaging contrast, and medications in addition to the five characteristics mentioned above. This theranostic capability allows for customized dosage adjustments, real-time delivery monitoring, and immediate feedback on therapy response, all of which further improve outcomes and safety.[115]

Limitations & Challenges

Figure 6: Limitations and Challenges

1.High cost and complex manufacturing

Functional nanorobots require surface functionalization, advanced lithography, multi-step chemical synthesis, and (often) the addition of rare materials or patterned magnetic components.[116] These processes, which increase unit costs and limit access outside of research laboratories, require stringent control over the process to ensure repeatability from batch to batch, and occasionally rely on specialized equipment and clean-room facilities. This is why it is still challenging to turn laboratory prototypes into clinical medications that are profitable without investing heavily in standardized processes and scalable production systems.[117]

2.Biocompatibility and toxicity concerns

Immune recognition, inflammation, and off-target accumulation are all significantly impacted by the physicochemical properties of nanorobots, including material composition, size, shape, surface chemistry, and degradation products.[118] Additionally, nanorobots and biological systems interact closely. Non-biodegradable elements and inorganic components (like metals) are especially vulnerable to long-term tissue accumulation and chronic toxicity. Risk assessment and regulatory approval are made more challenging by the lack of thorough, lifecycle-spanning toxicology (acute, chronic, immunotoxicity, genotoxicity, and biodegradation/clearance investigations) for many nanorobot designs. There is an urgent need for standardized testing and reliable in-vivo outcomes.[119]

3.Ethical, legal and regulatory issues

Nanorobots raise new moral and legal questions due to their small size, remote control capability, and potential for prolonged bodily presence. These include liability for device failure or unintended effects, privacy concerns if data is transmitted by nanosensors, informed consent for devices whose long-term behavior is uncertain, and regulatory gaps between autonomous nanoscale machines and drugs or conventional medical devices.[120] Regulators and ethicists are still debating the best preclinical testing protocols, performance metrics, and post-market surveillance strategies for nanodevices. It will be essential to take into account the opinions of various stakeholders, such as doctors, patients, regulators, and ethicists, in order to create suitable translational pathways.[121]

4. Power source and propulsion limitations

Powering and managing nanorobots in vivo remains a major technological challenge. Even though chemical (fuel) propulsion offers independence, it frequently requires dangerous fuels (like high H_2O_2 concentrations) or produces undesirable byproducts.[122] Despite the fact that external field actuation (magnetic, acoustic, or optical) removes the need for dangerous fuels, some therapeutic objectives cannot be achieved because it requires complex external equipment, a shallow penetration depth (for light), or precisely calibrated field gradients. Currently, trade-offs between energy density, controllability, and safety limit operational longevity, precise control in physiological settings, and manoeuvrability in complex tissues. Advances in remote powering and hybrid biohybrid techniques are promising, but they have not yet been considered for routine therapeutic use.[123]

5. Difficulties in large-scale production and quality control

Scaling laboratory manufacturing to industrial levels while preserving homogeneity, sterility, and functional integrity is challenging.Many laboratory processes, such as template synthesis, microfabrication, and self-assembly, do not instantly result in high-throughput lines that meet GMP standards. Among the main challenges are managing nanoscale defects, ensuring consistent cargo loading and release patterns, and implementing reliable in-process quality control metrics for millions to billions of nanoscale units. Without scalable production plans and validated QC methods, clinical adoption will remain restricted.[124]

6. Additional practical and translational barriers

Other cross-cutting issues include the inability to image and track nanorobots in deep tissues, immune system clearance or sequestration that reduces efficacy, the difference between controlled animal models and human pathophysiology that reduces the predictive power of preclinical studies, and the interdisciplinary divide between clinicians/regulatory scientists (safety, trial design) and engineers (device design). These practical challenges emphasize the necessity of careful, incremental translational methods and comprehensive de-risking studies before human trials.[125]

Future perspectives

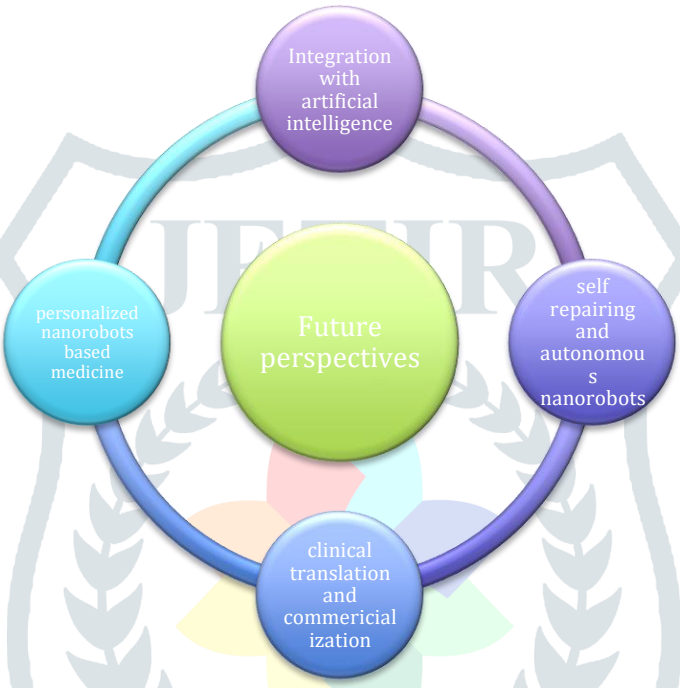

Figure 7: Future Perspective

(Adapted from Gao Z., Li H., Xu Q. et al. Injectable nanorobots for precision cancer therapy: motion-enhanced drug delivery. *Chemical Society Reviews.* 2025; 54: 10487–10530.)[126]

Conclusion

Nanorobots are a revolutionary new frontier in modern drug therapy because of their unmatched precision, control, and customization in the treatment of illness. These nanoscale devices work at the molecular and cellular levels to deliver therapeutic drugs directly to diseased locations. This maximizes therapeutic efficacy while reducing systemic exposure and adverse effects. Because they can precisely administer medication, release it under control, and monitor it in real time, they have great potential for treating diseases like cancer, infectious diseases, neurological disorders, and cardiovascular problems.

Ongoing research continues to improve their biocompatibility, propulsion efficiency, and targeting precision, and advances in material science, artificial intelligence, and nanofabrication are opening the door to more autonomous and intelligent nanorobotic systems. The concept of real-time adaptive treatment is becoming more clinically viable with the integration of biosensing, imaging, and feedback-controlled mechanisms.

Despite current challenges like challenging manufacturing, ethical and regulatory constraints, and scaling issues, the rate of interdisciplinary research suggests that clinically viable nanorobots may soon be developed as a part of customized treatment approaches. AI, biotechnology, and nanorobotics are expected to transform not only medicine delivery but also diagnostics, regenerative medicine, and minimally invasive surgery.

In conclusion, nanorobots have the potential to drastically alter therapeutic paradigms. As current research transforms laboratory success into clinical utility, it has the potential to reimagine precision medicine and usher in a new era of patient-specific, intelligent, and responsive therapies.

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