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Nano robots: The next generation of medical devices and interventions.

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Abstract: Nanorobotics represents a burgeoning discipline focused on the design, fabrication, and control of robots at the nanoscale. These diminutive machines hold the promise of transforming multiple sectors, such as healthcare, energy, and environmental management. Recent progress in nanotechnology has facilitated the creation of nanorobots capable of executing intricate tasks, including targeted drug delivery, cancer therapies, and tissue engineering. This review seeks to offer a thorough examination of the current landscape of nanorobotics, encompassing the design and production of nanorobots, their actuation and control mechanisms, as well as their prospective applications. Additionally, we address the challenges and future trajectories within the field, emphasizing the necessity for enhanced fabrication methods, more effective actuation systems, and improved control mechanisms. Moreover, we underscore the potential advantages of nanorobotics, such as advancements in disease diagnosis and treatment, increased energy efficiency, and diminished environmental impact. In summary, this review presents a comprehensive and contemporary overview of the swiftly advancing field of nanorobotics, emphasizing its significant potential to reshape various facets of our existence. This review seeks to provide a comprehensive overview of the current state of nanorobotics in the realm of cancer therapy. Through advancements in biotechnology, molecular biology, and molecular medicine, it is possible to create fully autonomous nanorobots. These nanorobots, envisioned as a remarkable advancement in future medical practices, are sophisticated submicron devices primarily composed of bio-nanocomponents. They hold significant promise in targeted drug delivery for cancer, a leading cause of mortality among individuals under 85 years of age. Nanorobots have the potential to transport and administer substantial quantities of anti-cancer medications directly to malignant cells while sparing healthy cells, thereby minimizing the adverse effects commonly associated with traditional treatments such as conventional chemotherapy. This paper explores various strategies utilized in cancer treatment through the application of nanorobots and offers insights into the future possibilities within this field.

Keywords: Nanorobotics, Cancer therapy, molecular medicine, bio- Nano components.

Introduction: Nanotechnology has emerged as a remarkable technological trend, drawing significant attention from researchers over recent decades. This field is characterized by the rapid advancement of electronics, particularly in applications related to communication, healthcare—often referred to as nanomedicine—and environmental monitoring. Current research efforts are primarily directed towards addressing the scientific challenges that affect the longevity of living organisms, with a particular emphasis on humans. Among these challenges are diseases that lack effective treatment options. A noteworthy alternative for diagnosis and treatment that has gained traction within the academic community is the Drug Delivery System (DDS). Supported by subsequent research, an interdisciplinary approach is essential to transform the promising potential of nanomedicine into a tangible reality. The collaboration of professionals from diverse fields such as medicine, pharmaceuticals, chemistry, and physics significantly enhances research in nanomedicine and the study of DDS and nanorobotics [1].

A significant challenge currently confronting this technology is the absence of efficient methods for constructing the nanoscale structures necessary for the anticipated applications. Research conducted at the University of Southern California, Los Angeles, specifically within the Laboratory for Molecular Robotics, along with other institutions, indicates that nanomanipulation utilizing Scanning Probe Microscopes (SPMs) offers a viable strategy for fabricating nanostructures through a bottom-up approach, by assembling building blocks derived from chemical synthesis, such as molecules or colloidal nanoparticles. The main limitation of this method lies in its sequential nature, which results in low throughput. Nevertheless, high throughput can be achieved through the implementation of massively parallel assembly processes utilizing SPM multichip arrays, which are developed using MEMS techniques. For instance, a team at IBM is constructing multichip systems for digital storage applications, which are anticipated to reach densities of several terabits per square inch. According to the Global Oncology Trend Report published by the Quintiles IMS Institute, global expenditures on cancer medications reached $100 billion in 2014. The need for effective cancer treatment is a significant driving force behind the advancement of nanorobotics. Traditional chemotherapeutic agents are distributed throughout the body in a nonspecific manner, affecting both cancerous and healthy cells. This indiscriminate distribution limits the achievable dosage within tumors and results in suboptimal treatment outcomes due to heightened toxicity. In response, molecularly targeted therapies have emerged as a strategy to address the lack of specificity associated with conventional therapeutic agents for cancer. By utilizing both passive and active targeting methods, nanoparticles can increase the intracellular concentration of drugs within cancer cells while minimizing toxicity to healthy cells. Consequently, this review will examine recent advancements and technological developments in nanorobotics specifically tailored for Drug Delivery Systems aimed at cancer treatment [2].

This review examines the emerging function of nanorobots in facilitating drug delivery for brain cancer, emphasizing their capabilities in active targeting, improved penetration of the blood-brain barrier (BBB), and controllable therapeutic applications. By utilizing sophisticated navigation techniques, real-time responsiveness, and localized drug release systems, nanorobots are set to transform brain cancer treatment, paving the way for more effective and safer therapeutic options. The BBB is essential for maintaining the brain's homeostasis and integrity, serving as a selectively permeable barrier that permits the passage of specific molecules while obstructing others. This protective function is vital for preserving the brain's sensitive environment and preventing the entry of harmful substances. However, this same barrier poses significant challenges in the treatment of various brain disorders. The BBB is a complex structure that restricts the passage of most macromolecules, including peptides, recombinant proteins, monoclonal antibodies, RNA interference-based drugs, and over 98% of small molecule drugs, thereby hindering effective treatment of brain tumors. The application of nanotechnology has demonstrated the potential to enhance the delivery of therapeutic agents to the brain by improving targeting, facilitating BBB penetration, controlling drug release, and minimizing toxic side effects through reduced dosages of anticancer medications. To overcome the limitations associated with conventional surgical approaches in treating brain diseases, nanoparticles smaller than 200 nm can be engineered as nanorobots using various strategies to improve their ability to traverse the BBB. The structures of different nanocarriers differ, as do their mechanisms for crossing the BBB. Drug delivery to brain cancer can occur through passive transport, carrier-mediated transport, receptor-mediated transport, and adsorption-mediated transport across the BBB [3]. This document presents a systematic review of the application of nanorobots within the medical domain, concentrating specifically on their roles and limitations in cancer therapy, invasive surgical procedures, and cell therapy. We acknowledge the dynamic nature of this field, and while our primary focus is on these three areas, the review's scope may be adapted to include emerging trends and innovations. Through this investigation, we seek to deliver a thorough overview of the current landscape of nanorobotics in medicine, chart the development of this groundbreaking technology, and identify significant challenges along with potential solutions, thereby guiding future research in this exciting and swiftly advancing area. This review is constrained by its emphasis on nanorobotics literature that explicitly addresses clinical or healthcare contexts, which may lead to selection bias, as pertinent studies that do not directly highlight clinical applications might be overlooked. Nonetheless, we recognize the limited incorporation of nanorobotics into clinical practice. This lack of integration presents a challenge in offering a complete overview of the practical implications of nanorobotics in medical environments, as the field may still be in the nascent stages of clinical implementation. Furthermore, the review notes that the term "nanorobotics" is often applied broadly within the clinical arena, with researchers using it to refer to a variety of technologies. This broad usage may create ambiguity and complicate the categorization and analysis of diverse technologies within a cohesive framework.

Objectives:

1. Targeted drug delivery: Engineer nanorobots to administer medications directly to affected cells or tissues, thereby minimizing side effects and enhancing therapeutic effectiveness.

2. Cancer treatment: Innovate nanorobots capable of specifically identifying and eliminating cancer cells, thereby preserving healthy tissues.

3. Disease diagnosis: Develop nanorobots that can identify and diagnose illnesses at an early stage, facilitating timely intervention.

4. Tissue engineering: Create nanorobots that assist in the repair or replacement of damaged tissues, including bone, muscle, or nerve tissue.

5. Environmental monitoring: Design nanorobots to assess environmental contaminants, such as hazardous chemicals or heavy metals.

6. Energy harvesting: Engineer nanorobots that can capture energy from natural sources, including sunlight or vibrations.

7. Manufacturing and assembly: Develop nanorobots capable of constructing and fabricating materials at the nanoscale, allowing for the development of novel materials and devices.

8. Space exploration: Create nanorobots designed to investigate and analyze extraterrestrial environments, such as planetary surfaces or asteroids.

9. Understanding nanoscale phenomena: Investigate the behavior of matter at the nanoscale to achieve a more profound comprehension of the fundamental physics and chemistry involved.

10. Developing new materials and technologies: Innovate new materials and technologies that facilitate the fabrication and functionality of nanorobots.

11. Advancing robotics and artificial intelligence: Create advanced robotics and artificial intelligence methodologies applicable to nanorobots, enabling them to execute intricate tasks autonomously.

Types of Nanorobots:

- Microbivore nanorobots
- Respirocyte nanorobots
- Clottocyte nanorobots
- Cellular repair nanorobots [4].

History of nanorobots:

- 1950s-1960s: The Birth of Nanotechnology

1. Physicist Richard Feynman presents a lecture entitled "There's Plenty of Room at the Bottom," igniting interest in nanotechnology.

2. Engineer Norio Taniguchi coins the term "nanotechnology."

1970s-1980s: Initial Advances in Nanotechnology

1. The invention of the scanning tunneling microscope (STM) allows for the manipulation of single atoms.

2. The ideas surrounding molecular machines and nanorobots begin to develop.

- 1990s: The Rise of Nanorobotics

1. The first nanorobots, a robotic arm constructed from individual atoms, is created.

2. Researchers start investigating the potential of nanorobots in medical fields.

2000s: Progress in Nanorobots Design and Production

1. New nanofabrication methods, including nanolithography and Nano imprint lithography, facilitate the creation of more intricate nanorobots.

2. The application of nanorobots in environmental and industrial sectors is explored.

•2010s: Significant Advances in Nanorobotics

1. The creation of autonomous nanorobots capable of navigating and interacting with their surroundings is achieved.

2. Researchers showcase the application of nanorobots in targeted drug delivery and cancer therapies.

•Current Era: Continuous Research and Innovation

1. Ongoing investigations into new materials, designs, and applications for nanorobots are being conducted.

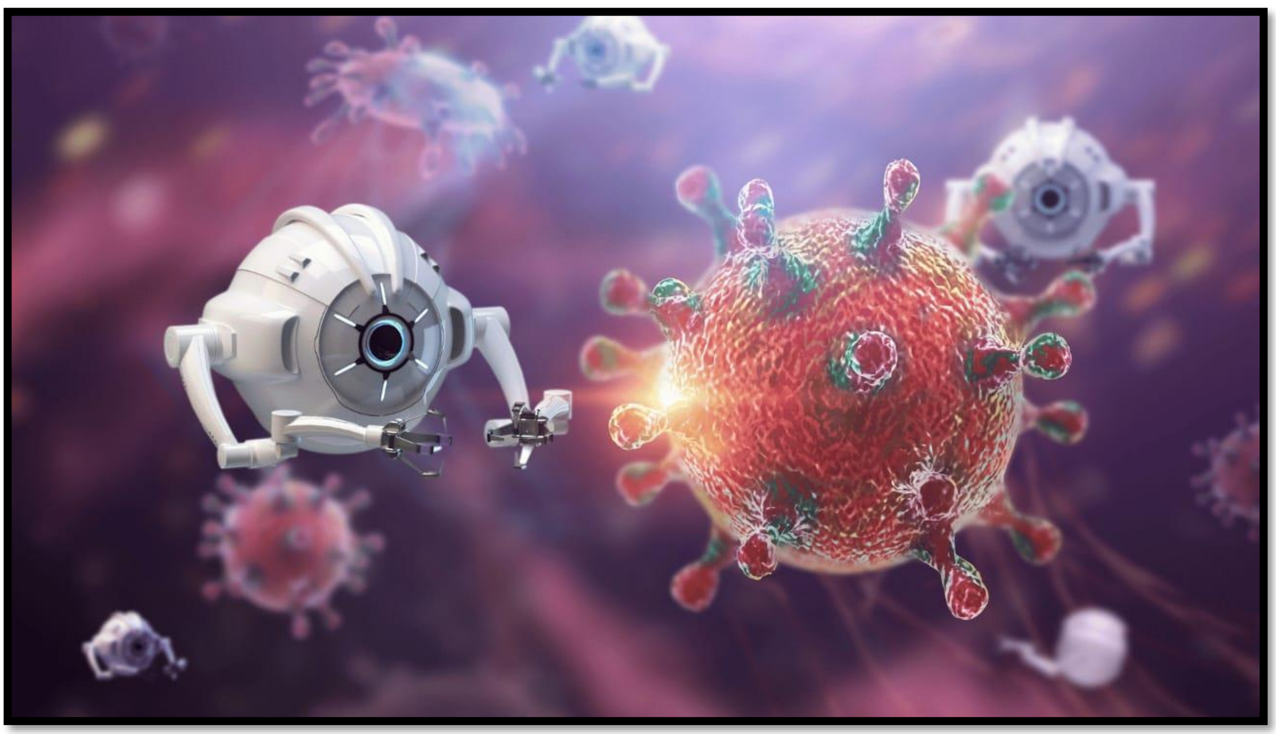
2. The advancement of sophisticated nanorobotics systems, including nanorobots swarms and sensor technologies, is underway.

Materials and fabrication techniques:

Nanorobots are miniature devices that function similarly to contemporary machines. However, the advancement of this innovative technology offers significant advantages in fields such as medicine, industry, and various other domains. These devices can be utilized to address challenges related to energy conversion through the use of catalytic nanomotors. Recent research aims to enhance the speed, strength, and longevity of synthetic nanomotors, with certain types of nanomotors demonstrating the capability to move effectively. Nanomotors are capable of operating autonomously at speeds nearing 100 body lengths per second. Enhancements in velocity, motion control, and the longevity of catalytic nanomotors are crucial for generating power in chip microsystems that utilize autonomous transport mechanisms. Furthermore, this innovative technology can be employed to develop lab-on-a-chip devices. Additionally, there are potential applications in addressing infertility issues. Engineers in Germany have designed a nanorobots that attaches to sperm tails, functioning as a propulsion system to enhance the effectiveness and accessibility of fertility treatments. Moreover, nanorobots can also contribute to environmental solutions; for example, researchers at the University of California are utilizing these devices to capture excess carbon dioxide from lakes, rivers, and oceans [5]

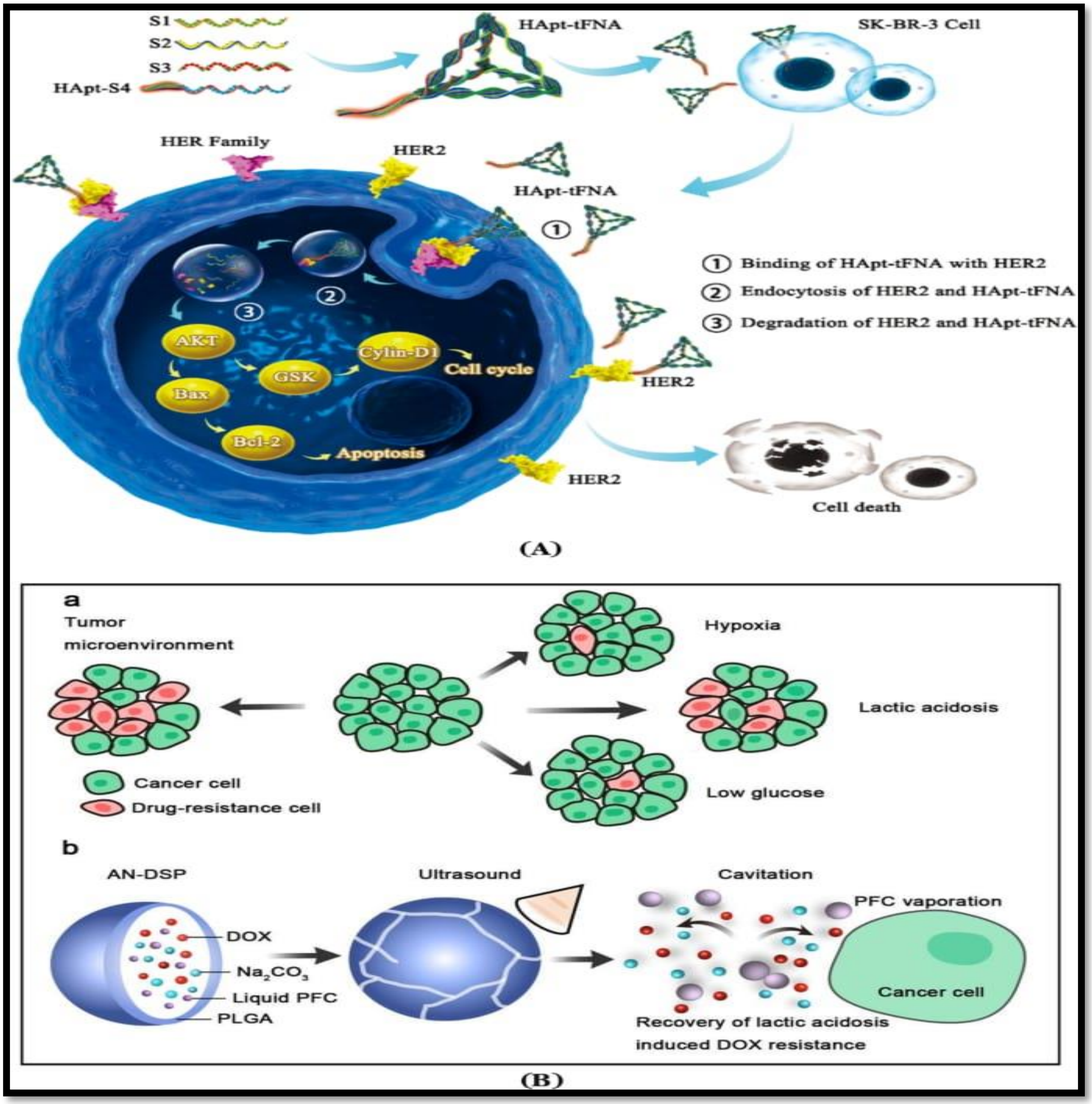
Nanorobots in treatment of Cancer:

Cancer can be described as a collection of diseases marked by the uncontrolled proliferation and dissemination of abnormal cells within the body. The incidence of cancer continues to rise annually. It occupies a prominent position in research due to its significant impact on human life and the economic burden it imposes. According to the Global Oncology Trend Report published by the IMS Institute for Healthcare Informatics, global expenditures on cancer treatments reached $100 billion in 2014. The advancement of nanorobotics is largely driven by the need for effective cancer therapies, as current medical technologies and therapeutic tools can be enhanced through the application of nanorobotics. To assess the prognosis and survival chances for a cancer patient, one must consider the duration of the disease's progression in relation to the timing of diagnosis, particularly if it is identified at an earlier stage [6] . Nanorobots, designed to function as blood borne devices, possess unique properties that can significantly enhance treatment processes for complex diseases, particularly in the realms of early diagnosis and intelligent drug delivery. These devices can facilitate the early detection of cancer and optimize chemotherapy by ensuring precise drug delivery. As drug carriers, nanorobots enable the administration of timely dosage regimens, thereby prolonging the presence of chemical compounds in the bloodstream as required. This capability allows for the prediction of pharmacokinetic parameters essential for effective chemotherapy in cancer treatment. Furthermore, they mitigate the adverse effects associated with extravasation in non-reticuloendothelial cancers, which often lead to severe side effects during chemotherapy. Additionally, nanorobots equipped with chemical Nano biosensors can be programmed to identify varying levels of E-cadherin and beta-catenin, which serve as critical medical targets in both primary and metastatic stages, thereby aiding in target identification and enhancing drug delivery [7].



<u>Nanorobots in Drug delivery across blood brain barrier:</u>

Nano carriers, which are a type of nanorobots, have established a comprehensive system platform for the in vivo delivery of pharmaceuticals and are anticipated to evolve into more advanced nanorobots in future iterations. Various methods exist to enhance transport across the blood-brain barrier (BBB) in the treatment of neurological disorders, including osmotic shock, ultrasound, and the application of cell-penetrating peptides (CPP). Additionally, magnetic gradients can significantly facilitate the movement of magnetic nanoparticles through the sieve plate into the olfactory bulb of the brain, with focused ultrasound also being a viable option. The predominant nanomaterial capable of traversing the BBB include polymers such as PLBA, PLGA, and PLA, along with gold nanoparticles, liposomes, micelles, dendrimers, exosomes, and Nano antibodies. Among these, nanorobots have emerged as particularly promising targeted drug delivery vehicles. As depicted in , these nanorobots not only serve as effective carriers for the chemotherapy agent doxorubicin in glioblastoma treatment but can also be functionalized with β-amyloid specific peptides to act as photo thermal agents for Alzheimer's disease therapy. Their ability to penetrate the BBB can be influenced by the encapsulation of insulin. Effective targeted drug delivery for brain disorders frequently necessitates overcoming the BBB. Mechanisms of drug delivery utilizing nanorobots, particularly those employing gold nanoparticles, show significant potential in this domain. For example, Huang et al. developed a traceable central nervous system delivery system that utilized neural stem cell membranes to improve BBB penetration and target neuronal cells, presenting therapeutic possibilities for Alzheimer's disease. Furthermore, Law et al. demonstrated the application of chemical exchange saturation transfer (CEST) MRI for the noninvasive tracking of liposome delivery from the nasal cavity to the brain, a technique that holds promise for drug delivery research. Employed solid lipid nanoparticles (SLN) for their studies [8].The administration of valsartan to the brain serves to alleviate the effects of stroke. A microneedle patch has been developed for the precise delivery of cannabidiol (CBD) to sites of brain tumors, demonstrating both safety and efficacy in preclinical models of glioblastoma. Additionally, nanorobots have been effective in delivering doxorubicin (DOX) to glioblastoma cells. For instance, Li et al. created a pH-sensitive dual-target carrier that facilitates the transport of DOX to glioma cells, thereby improving its passage across the blood-brain barrier and increasing drug accumulation. These nanorobots are specifically designed to release therapeutic agents in response to the acidic conditions commonly found in tumor tissues, which typically exhibit a lower pH due to their abnormal metabolic processes. The pH-sensitive nanorobots exploit this characteristic by undergoing structural modifications in the acidic microenvironment. An example of this is the pH-sensitive dual-target drug carrier G4-DOX-PEG-Tf-TAM, which employs a pH-sensitive acylhydrazone bond that disintegrates under acidic conditions, facilitating controlled drug release at the tumor site. This targeted release mechanism minimizes non-specific toxicity during circulation and enhances drug accumulation within glioma cells. Furthermore, Meng et al. developed ultrasound-responsive nanorobots that localize in tumors and release their drug payloads upon ultrasound stimulation. These nanorobots are activated by external ultrasound waves, which generate mechanical vibrations that destabilize the nanorobots shell or matrix, leading to drug release. Contain nanoparticles that vaporize into bubbles when exposed to ultrasound. This mechanism significantly improves drug release efficiency by targeting tumors through enhanced permeability and retention (EPR), allowing for specific drug accumulation in tumor tissues. Additionally, ultrasound enhances deep tissue penetration, ensuring that therapeutic agents effectively reach the tumor site, thereby overcoming the barriers presented by dense tumor tissues [9].



Mechanism of nanorobots:

The application of micro and nanorobots that can effectively utilize various energy sources for movement holds the promise of significantly transforming the pharmaceutical industry, especially in the area of targeted drug delivery. By enabling the accurate administration of medications to specific tissues or anatomical locations, along with controlled release mechanisms, these drugs can be directed to their desired sites. Targeted delivery involves a diverse array of actuation energy sources, which include self-propulsion mechanisms utilizing substances such as hydrogen peroxide and enzymes, as well as external propulsion methods powered by light, electricity, acoustics, and magnetic fields. Additionally, propulsion can be achieved through motile microorganisms, including bacteria, sperm cells, contractile cells, and immune cells. The processes of targeted and precise drug delivery are primarily facilitated through two key technologies: exogenous power-driven methods and endogenous power-driven methods [10].

Application of Nanorobots:

•Medical Applications

1. Targeted drug delivery: Nanorobots can be engineered to transport medications directly to affected cells or tissues, minimizing side effects and enhancing therapeutic effectiveness.

2. Cancer treatment: These devices can selectively identify and eliminate cancerous cells, thereby preserving healthy tissue.

3. Disease diagnosis: Nanorobots can be developed to identify and diagnose illnesses at an early stage, facilitating timely intervention.

4. Tissue engineering: They can assist in the repair or replacement of damaged tissues, including bone, muscle, or nerve structures.

5. Surgical assistance: Nanorobots can support surgeons during procedures by providing real-time data and guidance.

•Environmental Applications

1. Pollution monitoring: Nanorobots can be utilized to track environmental contaminants, including hazardous chemicals and heavy metals.

2. Water purification: They can effectively eliminate impurities and pollutants from water, ensuring its safety for consumption.

3. Soil remediation: Nanorobots can aid in the decontamination of polluted soil, extracting harmful substances and toxins.

4. Climate change mitigation: These devices can be designed to capture and convert carbon dioxide into valuable chemicals or fuels.

5. Wildlife conservation: Nanorobots can monitor and track animal populations, contributing to conservation initiatives.

•Industrial Applications

1. Manufacturing and assembly: Nanorobots can facilitate the assembly and production of materials at the nanoscale, leading to the development of innovative materials and devices.

2. Quality control and inspection: They can be programmed to examine and test materials and products at the nanoscale, enhancing quality assurance processes.

3. Energy harvesting: Nanorobots can capture energy from environmental sources, such as solar power or vibrations.

4. Construction and infrastructure: They can be employed to assess and repair infrastructure, including bridges and buildings.

5. Aerospace and defense: Nanorobots can be utilized in various applications within these sectors.

Future of nanomedicine and drug delivery system:

The field of nanomedicine stands out as one of the most intriguing domains of contemporary research. Over the past twenty years, significant advancements have resulted in the filing of approximately 1,500 patents and the completion of numerous clinical trials. As discussed in the preceding sections, cancer serves as a prime example of a disease where both diagnosis and treatment have greatly benefited from the integration of non-medical technologies. The utilization of various nanoparticles for the precise delivery of therapeutic agents to affected cells, such as cancerous or tumor cells, while preserving the integrity of normal cells, underscores the potential of nanomedicine and nano-drug delivery systems as a pivotal focus for future research and development [11].The nanoparticles referenced in this communication exhibit a range of sizes, with some truly falling within the nanometer scale, while others extend into the sub-micrometer range (exceeding 100 nm). Future research should prioritize the exploration of materials that demonstrate greater uniformity in size, as well as enhanced drug loading and release capabilities. This review also highlights significant advancements in the application of metal-based nanoparticles for diagnostic purposes. The use of metals such as gold and silver in both diagnostic and therapeutic contexts represents a promising area of research that may facilitate broader applications of nanomedicine in the future. A particularly exciting development in this field involves gold nanoparticles, which have shown a propensity to be well absorbed by soft tumor tissues, thereby enhancing the tumor's susceptibility to heat therapy induced by radiation (e.g., in the near-infrared spectrum) for targeted destruction. The potential of nanomedicine and nano-drug delivery systems is widely recognized; however, their actual influence on the healthcare system, particularly in cancer therapy and diagnosis, remains quite limited. This limitation can be attributed to the relatively recent emergence of this scientific field, which has only seen two decades of substantial research, leaving many fundamental aspects still unexplored. One significant area for future investigation involves identifying the essential markers of diseased tissues, including critical biological markers that enable precise targeting without disrupting normal cellular functions. Ultimately, advancements in nanomedicine will depend on our growing understanding of diseases at the molecular level, which will facilitate the identification of nanomaterial-subcellular size markers and pave the way for innovative diagnostic and therapeutic approaches. Therefore, a deeper comprehension of the molecular signatures associated with diseases will be crucial for the evolution of nanomedicine applications. In addition to the insights provided in this review regarding existing nanoprobes and nanotheragnostic products, further research is essential for the broader implementation of nanomedicine. The notion of controlled drug release at targeted sites, along with the technology to evaluate these processes, the drug's effects at the tissue and cellular levels, and the development of theoretical mathematical predictive models, has yet to reach maturity. Many studies in the field of nanomedicine focus on biomaterials and formulation research, which represent the preliminary stages of biomedical applications. Significant insights into the potential applications for drug therapy and diagnostic studies will emerge from animal research and interdisciplinary investigations that demand considerable time and resources. Given the increasing global emphasis on more precise medicines and diagnostics, the future of a more sophisticated and multi-faceted approach to nanomedicine and nano-drug delivery technology appears promising.

Conclusion:

The domain of nano robotics has experienced remarkable progress in recent years, particularly in the areas of design, fabrication, and control of nano-scale robots. These diminutive machines hold the promise of transforming numerous sectors, including healthcare, environmental science, and manufacturing. In the medical field, nano robots can facilitate targeted drug delivery, cancer therapies, and tissue engineering, thereby enhancing diagnostic capabilities, treatment efficacy, and patient outcomes. In environmental science, they can play a crucial role in pollution monitoring, remediation efforts, and promoting sustainability, thus alleviating the adverse effects of human activities on the ecosystem. In industrial applications, nano robots can contribute to manufacturing processes, quality assurance, and energy harvesting, leading to increased efficiency, productivity, and innovation.

However, despite these advancements, several significant challenges remain before the widespread implementation of nano robots can occur. These challenges encompass the need for improved fabrication methods, the development of more effective power sources, and the enhancement of control systems. Furthermore, there are apprehensions regarding the potential risks and unintended consequences associated with nano robots, including toxicity, environmental repercussions, and the possibility of misuse. Consequently, it is imperative to pursue research and development in nano robotics in a responsible and sustainable manner, with thorough consideration of their potential societal and environmental impacts.

As research in nano robotics progresses, we can anticipate the emergence of new and innovative applications. For instance, nano robots may be utilized to create novel medical treatments, such as personalized and regenerative medicine. They could also contribute to enhancing environmental sustainability through the development of more efficient carbon capture and utilization techniques. Additionally, nano robots may improve industrial processes by introducing more effective manufacturing and quality control methods.

In conclusion, nano robotics represents a rapidly advancing field with immense potential to revolutionize various aspects of society.

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