International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2019): 7.583

Review on Nanomotors Cancer Targeted Drug Delivery / Powder Nanomotors and Biomedical and Environmental Applications

Pallavi Prakash Jopale

M. Pharm, Department of Pharmaceutics, PES Modern College of pharmacy, Nigdi, Pune, India

Abstract: ***Nanomotors square measure rising as novel Drug delivery, providing benefits like speedy drug transport, High tissue penetration and motion construability. During this review paper we have a tendency to square measure study Nanomotors are extensively explored for economical cancer medical care and designation, as proof by important breakthrough within the style of Nanomotors. Discovery of bio-inspired, self – propelled and outwardly small-grained Nanomotors and engines' is taken into account a doubtless reappraisal paradesign in nanoscience. Among them, light-powered Nanomotors, within which motion is driven by lightweight, exhibit numerous benefits in their precise motion manipulation and there by a superior scope for application. During this we have a tendency to highlight medically familiarized Nanomotors, in notably the once created for targeted drug delivery and discus there presently limitation and prospects toward in vivo application. we have a tendency to hope to spotlight these new advances in Nanomotors within the field of cancer designation and medical care, with the last word goal of stimulating the triple-crown Exploration of intelligent Nanomotors for future clinical Applications.***

Keywords: Nanomotors, cancer targeted drug delivery, biomedical application

1. Introduction

The homeostasis of biological systems and locomotion of organisms in nature have long been an inspiring topic of research. Inspired by natural microorganisms, considerable efforts have been devoted to achieving artificial self-propelled Nanomotors, which bring about different areas of influential application, such as environmental remediation, target drug delivery, and cell manipulation and isolation. The use of Nanomotors to power nanomachines is currently a research area of tremendous activity due to a wide range of potential application. Synthetic Nanomotors, based on a multitude of propulsion mechanisms, have thus been developed over the past decade. While most of attention has been given to chemically powered catalytic Nanomotors, many applications (particularly *in vivo* biomedical ones) require the elimination of the fuel requirements toward biocompatible propulsion mechanisms. Efforts in this direction have led to the fuel free locomotion of magnetically driven nano swimmers, or acoustically propelled devices. Major advances in Nanomotors technology, including the design of powerful multifunctional machines, advanced motion control and towing capabilities, have facilitated different biomedical applications ranging from cell sorting to DNA hybridization. The substantial progress towards using functionalized Nanomotors for efficient cargo transport and release paves the way to their drug delivery applications. The targeted delivery of therapeutic cargoes represents a major future application of synthetic Nanomotors. Such nanomachines based drug delivery systems are highly attractive platform for efficient delivery of therapeutic payloads to targeted sites, and could address some of the obstacles of current drug delivery systems. Unfortunately, there is no comprehensive review published on using synthetic Nanomotors for drug delivery platforms. In this review we highlight recent research efforts aimed at developing man-made nanomachines for drug delivery application and give an outlook on current challenges and emerging trends. Cancer square measure rising in Associate in Nursing endless stream, resulting in severe threat to human health. Cancer treatment remains a worldwide drawback, nice efforts are created to fight against cancer, and enormous therapeutic variety approaches are developed for clinical treatment of cancers, like chemotherapeutical, sequence medical care, irradiation, therapy, and actinotherapy. The tremendous progresses of engineering science and nonmaterial's. That needs an affordable construction of the delivery system to avoid multiple obstacles to move to the growth web site. Self propelled Nanomotors Associate in Nursing rising and powerful agent that's capable for effectively converting numerous energy supply into actuation and autonomous movement. Self- propelled Nanomotors like high expanse and activity. Thus inefficient energy gather is crucial within the style of Nanomotors employed in biological systems. Generally, fuel – free Nanomotors, high-powered by completely different form of energy sources like magnetic, field, or acoustic endow a lot of flexibility in biological application.

Additionally to the characteristics of active motion, the Nanomotors ought to usually exhibit the subsequent options, such as:
(1) Miniaturized size and correct morphology
(2) Straight forward surface functionalization
(3) Smart biological compatibility,
(4) Low toxicity chemical composition.

Additionally, artificial Nanomotors designed with increasing ability to alter fuel-free operation have conjointly gained important attention. for instance, ultrasound-driven nanowires that hardness energy to come up with Associate in Nursing uneven pressure gradient for propulsion were able to target growth in active targeting manner. Moreover, the active portion of cell membranes by Nanomotors has conjointly been rumored. a lot of necessary, Nanomotors

may be combined with different nonmaterial's like QDs or UCNPs, that might alter the combination of cancer medical care and treatment on nanoscale platform.

This literary criticism is principally targeted on the tremendous inspiration and opportunities offered by Nanomotors for potential use in field of cancer medical care. [Fig.1]

Firstly, we have a tendency to gift the progress of Nanomotors within the field of cancer – targeting delivery, like drug delivery, meddlesome ribonucleic acid delivery. Secondly, we have a tendency to illustrate the use of Nanomotors for cancer medical care, finally, we have a tendency to investigate current issues Associate in Nursingd challenges visage by Nanomotors in growth detection and treatment and gift an outlook for the longer term development of Nanomotors toward clinical applications. All in all, the clinical application of Nanomotors on the sector on cancer medical care still includes a great distance to

2. Magnetic Nanomotors For Drug Delivery

To address the limitations of fuel-driven Nanomotors and enhance biocompatibility, several groups have been exploring fuel- free nanomachines propulsion mechanisms, including the utilization of magnetic, electrical, optical, or ultrasound fields. Magnetically driven Nanomotors, inspired by nature swimming microorganisms, are particularly promising for use in a variety of *in vivo* biomedical application. Such Nanomotors can swim under externally applied magnetic fields in various biofluids, and perform complex maneuvers while obviating fuel requirements. Magnetic actuation is suitable for *in vivo* application since the required field- strength are harmless to humans. Ghosh et al. reported recently the first successful "voyage" of magnetic Nanomotors, based on conformal ferrite coatings, in human blood. Such magnetic "nanovoyagers" were shown to be cytocompatible with mouse my oblast cell. Magnetically actuated micro machines are thus currently being explored extensively as promising platform for controlled in vivo drug delivery applications. Gao et al. reported the first example of directed delivery of drug-loaded magnetic polymeric particles using magnetic nanoswimmers. The fundamental mechanism of the cargo towing ability and the hydrodynamic features of these fexible nanowire motors have been discussed. The effect of the cargo size on the swimming performance was evaluated experimentally and compared to a theoretical model, emphasizing the interplay between hydrodynamic drag forces and boundary actuation. Potential applications of these cargo-towing nanoswimmers were demonstrated using the directed delivery of [Fig. 2]

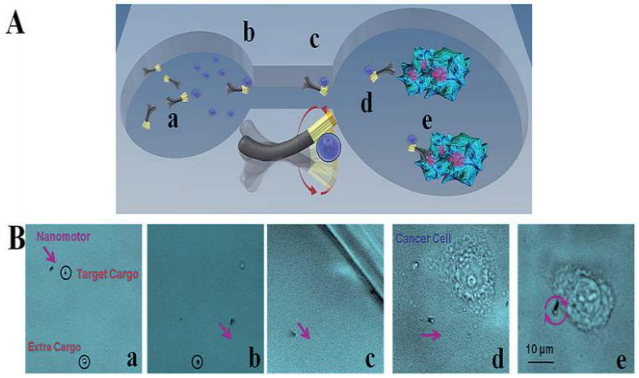


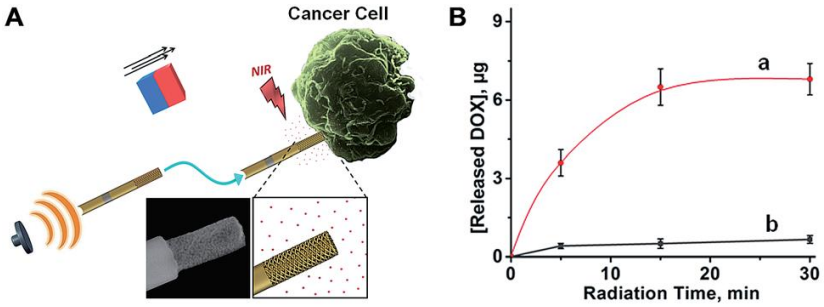
Figure 2: Drug delivery to HeLa cells using flexible magnetic nanoswimmers in cell-culture media. Scheme (A) and microscopic time lapsed images (B) depicting the process as a flexible magnetic Ni–Ag nanowire motor (a) capturing the doxorubicin-loaded magneticpoly (D,L-lactic-co-glycolic acid) (PLGA) particle in the loading reservoir (b), transporting it through the microchannel (c), approaching the target cell (d), sticking onto the target cell, and releasing the drug (e). (Reproduced from ref. 42, Wiley 2014.)

drug-loaded microparticles to HeLa cancer cells in biological media. Fig. 6 illustrates the schematic and experimental results of using the magnetic nanowire swimmers for transporting of target iron oxide/doxorubicin-encapsulated PLGA particles through a microchannel from the pick-up zone to the release microwell.

2.1 Ultrasound-powered

Nanomotors for drug delivery

Ultrasound has found in depth applications in drugs, and holds extensive promise for driving micromotors in biological fuids. Recent efforts by the groups of Mallouk's cluster and our team have illustrated the utilization of chance of mistreatment ultrasound for propulsive gold-nanowire and cannular motors in biologically relevant environments. Garcia-Gradilla et al. delineate recently the utilization of ultrasound- driven nanowire motors supported the nanoporous gold phase for increasing the drug loading capability. The new extremely porous nanomotors, ready by dealloying a Au–Ag alloy phase, provide a tunable pore size, high extent, and high capability for the drug payload. The drug antibiotic drug was loaded at intervals the nanopores via static interactions with associate degree anionic compound coating. Ultrasound-driven transport of the loaded drug toward cancer cells was followed by near-



(A) Schematic of the ultrasound-driven movement of the drugloaded nanoporous Au nanowire motors and triggered unharness of the drug around a neoplastic cell. (B) NIR-triggered antineoplastic drug DOX unharness as a perform of irradiation time mistreatment PSS-modified Pau nanomotors (a) and Au nanomotors (b). (Reproduced from referee. 45,Wiley 2014.)

infrared light (NIR) triggered unharness, as shown in Such a photothermal unharness has been expedited by the nanoporous gold structure. Directional movement was achieved by magnetic guidance. The incorporation of the nanoporous gold phase LED to an almost twenty fold increase within the active extent (compared to common gold nanowires) and to a high loading capacity of thirteen.4 mg mg_1 antibiotic drug. Recently developed ultrasound triggered cannular small bullets area unit extraordinarily promising for addressing the challenges of restricted tissue penetration of therapeutic particles, i.e., directed drug delivery into pathologic tissue thirty Such powerful small bullets, developed by Esener and Wang,30 think about Acoustic driblet Vaporization (ADV) for propulsion of peruorocarbonloaded conical-tube small bullets (MB) for penetration into targeted tissue to produce a motivating force sufficient for penetrating and deforming cellular tissue for potential targeted drug delivery and exactness nanosurgery. This extremely economical, powerful and climbable propulsion technique utilizes ultrasound to vaporize biocompatible fuels (i.e., per fluorocarbon+ greenhouse emission emulsions), confined at intervals the inside of a micromachine, for associate degree ultrahigh speed of over half-dozen m s_1 (i.e., just about a hundred times quicker than common micromachines). Such 'bullet-like 'propulsion induces sufficient thrust for deep tissue penetration and deformation for potential targeted drug delivery and exactness nanosurgery. By adjusting the extent of propulsion force, completely different depths within the tissue will be reached. Such a 'bullet-like' carrier should even have the aptitude of carrying an oversized therapeutic payload. The US-triggered microbullet propulsion strategy is predicted to own an incredible impact on numerous medical specialty applications, e.g., targeted drug delivery, current biolistics, microtissue and artery-cleaning/removal schemes, exactness nanosurgery, or cancer surgery. Mallouk's cluster additionally incontestable recently the unhearable propulsion of rod-shaped Nanomotors within living Norse deity cells. These nanomotors will attach powerfully to the external surface of the cells, and area unit pronto internalized by incubation with the cells for periods longer than twenty four h. The living thing propulsion didn't involve any chemical fuel and also the Norse deity cells remained viable. Such developments hold nice promise for future in vivo studies of the artificial Nanomotors.

2.2 Catalytically high-powered

Nanomotors for targeted drug delivery

Catalytically high-powered micro/nanoscale motors think about the chemical action decomposition of a solution-borne fuel, sometimes oxide, on a noble metal surface. Such fuel-driven motors possess a comparatively high power essential for activity completely different medical specialty tasks involving load towing. This force is mirrored by a motivating speed that may exceed one thousand body lengths s_1.47 Motion management is another necessary demand for targeted drug delivery. The directivity of chemical action micro/ nanoscale motors will be pronto controlled (commonly via magnetic guidance) and their speed will be regulated mistreatment completely different stimuli. Tremendous progress has been created on cargo-carrying chemical action nanomotors supported completely different loading and unloading mechanisms.49 These advances have expedited efforts aimed toward employing a type of chemical action Nanomotors (based on wire, sphere or open-tube configurations) for targeted drug delivery.

Wang, Zhang and coworkers incontestable the frst example of mistreatment unreal micromotors for the transport and unharness of medication.34 This pioneering study illustrated that catalytic nanowire shuttles will pronto pickup drug-loaded poly D,L-lactic-co-glycolic acid (PLGA) particles and liposomes and transport them over preset routes towards target destinations. Powerful alloy or CNT-based nanowire motors are accustomed increase the force necessary to move 'heavy' therapeutic cargos. These nickel-containing motors captured the iron-oxide encapsulated PLGA and vesicle drug nanocarriers through magnetic interactions. The Nanomotors will therefore pickup, transport and unharness variable sized drug carriers towards preset destinations. Fig. one displays theme (A) and time-lapse pictures (B) of such dynamic capture, transport and unharness of antibiotic drug (DOX)-loaded PLGA nanoparticles employing a chemical action Ni/(Au50/Ag50)/Ni/Pt nanowire motor. compared with the PLGA particles, transport of the drug-loaded vesicle is comparatively slower due to its massive size

Table 2.1: Recent progress on drug delivery using Nanomotors based on a multitude of propulsion

Types of		Type of drug/model drug	Attach/release	References

motors				
Catalytically powered nanomotors	Ni/(Au50/Ag50)/Ni/Pt LbL self-assembled PSS/PAH capsule LbL polymer multilayer CHI/ALG nanorockets Janus mesoporous silica Nanomotors LbL PSS/PAH catalase based capsules	Doxorubicin in PLGA and liposome nanoparticles FITC–dextran Doxorubicin Doxorubicin Doxorubicin	Magnetic interaction Encapsulation by varying solvent polarities LbL encapsulation/ ultrasound triggered Adsorption of porous silica/endocytosis Encapsulation/NIR laser triggered release	Kagan et al. Wu et al Wu et al Xuan et al Wu et al.
Nanomotors-powered by alternative fuels	Mg based microsphere motors Zinc based micromotors	FITC Silica and gold particles	Temperature-induced "breath-in" effect/ temperature triggered release Plating encapsulation/	Mou et al. Sattayasamitsathit et al.
Magnetic nanomotors	Flexible nanowire motors Helical swimmer	Doxorubicin loaded in PLGA nanoparticles Calcein loaded in liposome particles	Magnetic interaction/ diffusion Electrostatic interaction/ fusion of the cationic vesicles or endocytosis	Gao et al. Mhanna et al. Qiu et al.
Ultrasound nanomotors	Au/Ni/Au/PPy nanowire motor Porous Au–Au–Ni–Au nanowire	Brilliant green Doxorubicin and brilliant green	Electrostatic interaction/ pH triggered release Electrostatic interaction/ NIR triggered release	Garcia-Gradilla et al. Garcia-Gradilla et al.

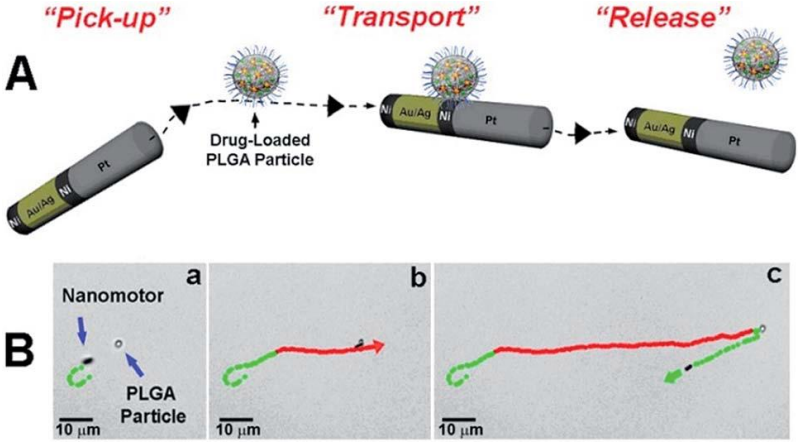


Figure 1: Transport and release of PLGA drug carriers by catalytic nanowire motors. Schematic (A) and microscopic time lapse-images (B) depicting the dynamic pick-up (a), transport (b), and release (c) of drug-loaded PLGA particles using a nanoshuttle. (Reproduced from ref. 34, Wiley 2010.)

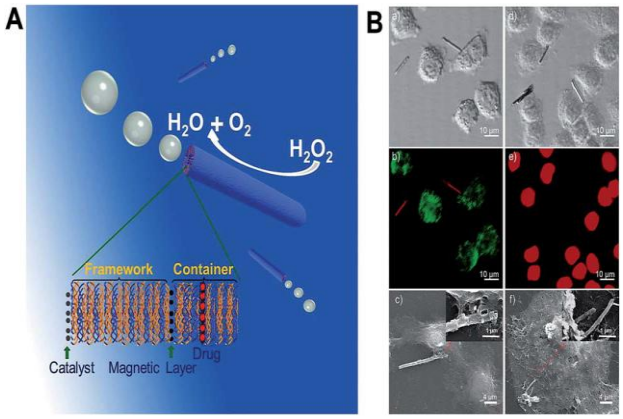


Figure 2: (A) Self-assembled polymer multilayer nanorockets based on a template-assisted layer-by-layer (LBL) technique can propel chemically in the presence of a hydrogen peroxide fuel. These motors can perform drug loading, targeted transportation, and triggered drug release by an external physical stimulus in a controlled manner. (B) The DIC (a and d), the corresponding CLSM (b and e), and SEM images (c and f) of a (CHI/ALG)4–DOX–(ALG/CHI)2–Fe3O4–(CHI/ALG)14–PtNP nanorocket before (a–c) and after (d–f) ultrasound treatment in vitro

and continuous cultivation of the HeLa cells for 3 h. (Reproduced from ref. 35, Wiley 2013.) feld was used to trigger the breakage of the outer shell of the LbL assembled polyelectrolyte multilayer microcapsules and release the encapsulated drugs. The images in Fig. 2 display (alginate (ALG)/chitosan (CHI))4–DOX–(ALG/CHI)2–Fe3O4–(CHI/ ALG)14–Pt NP nanorockets attached to the outer surface of HeLa cancer cells. Differential interference contrast (DIC), confocal laser scanning microscopy (CLSM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) images show the corresponding results before and after ultrasonic treatment. In comparison with the image before ultrasonic treatment (Fig. 2Bb), the red visible light from DOX within the CHI/ALG multilayer nearly disappeared (Fig. 2Be), indicating that almost all of DOX molecules are free through the ultrasound irradiation. Similar ideas were conjointly incontestible in LBL capsule based mostly micromotors. Wu et al. rumored conjointly the

utilization of nerve fiber Pt-nanoparticles or catalase-modified electrolyte capsules as micromotors in addition as carriers for drug delivery.36, 38 absorption indicator isothiocyanate–dextran (FITC–dextran) model medication or antibiotic are loaded onto these microcapsules by encapsulation. Another recent work from identical Chinese cluster delineated a brand new self-propelled Roman deity silicon oxide nanomotor which can conjointly function the drug carrier for living thing drug delivery.37 As illustrated in Fig. 3, this peroxide-propelled chemical process Roman deity nanomotor relies on mesoporous silicon oxide nanoparticles (MSNs) with chromium/platinum bimetal caps. MSNs provide associate degree exceptionally high area, that allows the loading of various cargoes. The DOX drug was loaded into mesoporous pore channels of Roman deity MSN motors by physical sorption, and so lined with associate degree egg phosphatidylcholine (PC) bilayer. Living thing localization and drug unleash experiments in vitro have indicated that the number of Roman deity MSN nanomotors coming into the cells is more than management MSNs with identical culture time and particle concentrations, meantime antitumour drug antibiotic complex loaded in Roman deity MSNs will be slowly free within the cells by biodegradation of the lipoid bilayers. Other recent studies hold appreciable promise for a spread of medicine applications. as an example, Sanchez et al. rumored the utilization of self-propelled rolled microtubes to drill and engraft themselves into biomaterials like cells which might be potentially wont to address the endosome escape challenge and deliver the drug or cistron within the cell. Another study by Wuet al.51 incontestible that by taking blessings of photothermal effects, PtNP-modified electrolyte multilayer microtube engines will be used for targeted recognition and subsequent killing of cancer cells.

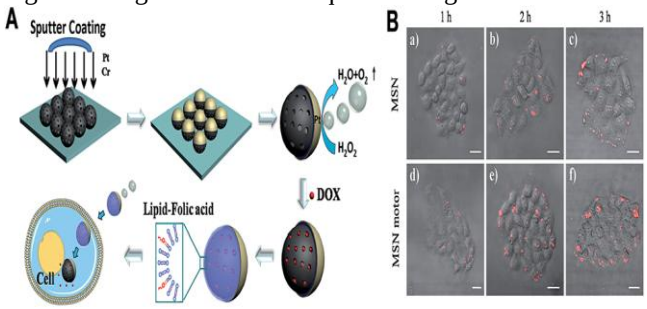


Figure 3: (A) Synthetic procedure for the preparation of Janus MSN nanomotors, as well as subsequent drug loading, lipid bilayer functionalization,transportation, and drug release. (B) DOX release from egg PC modified Janus MSN nanomotors inside HeLa cells following: (a) 0, (b) 1, (c) 2, and (d) 3 h. The images are overlays of fluorescence and DIC channels. Scale bars, 10 mm. (Reproduced from ref. 37, Wiley 2014.)

2.3 Nanomotors powered by alternative fuels for drug delivery

Although major progress has been created on drug delivery supported chemical process Nanomotors, current reliance on the common peroxide fuel greatly hinders sensible medicine applications of chemical process nanomotors. above all, in vivo drug delivery applications would need the employment of body fluids or their constituents because the powering fuel. Recent efforts are directed at increasing the scope of fuels for artificial nanomotors by exploring the employment of natural biofluids because the fuel supply, therefore preventive the requirement for external chemical fuels. for instance, Gao et al. represented Associate in Nursing acid-driven polyaniline/ metal microtube rocket that may propel autonomously and with efficiency in internal organ acid, and therefore will be operated within the abdomen surroundings. Reports of the employment of glucose-powered protein primarily based carbon swimmers are promising during this respect, though the propulsion mechanism is predicated on current flow, and was shown to diminish at high salt concentrations. Of explicit interest for sensible drug delivery applications area unit recently developed water-driven nanomotors that utilize the magnesium–water reaction for the propulsion. This eliminates the requirement for external fuels and offers economical propulsion in untreated high-salt aquatic media that is especially engaging for in vivo drug delivery applications. Another water-driven nanomotor explores Janus particles supported the Al–Ga alloy for economical atomic number 1 bubble propulsion through a method referred to as 'liquid metal enbrittlement',54 however lacks the biocompatibility of magnesium-based nanomotors. extra efforts ought to be dedicated to extending the time period of those water-powered nanomotors, at the side of correct surface functionalization, for addressing the wants of sensible drug delivery. Mou et al. represented recently a biocompatible drug-loaded magnesium-based Mg/Pt–poly(N-isopropylacrylamide) (PNIPAM) Janus nanomotor (Fig. 4).40 Such water-powered nanomotors show Associate in Nursing economical autonomous motion in simulated body substance (SBF) or plasma with none additives or fuels.It offers additionally engaging capabilities of loading, transporting and delivering drug molecules by taking blessings of the partial surface-attached ther a lot of responsive PNIPAM colloidal gel layers. The drug emotional method from the nanomotor will be controlled by the environmental temperature because of the'squeeze' result. hematolysis assay has recommended that such nanomotors and their autonomous motion have a negligible influence on the red blood cells (RBCs, extremely hemocompatible) and area unit friendly to organisms. Combination medical aid offers many distinct blessings for unwellness treatment (e.g., high potency, synergistic effects and reversal of drug resistance) compared to traditional single drug medical aid. Such combinatorial drug delivery might need new

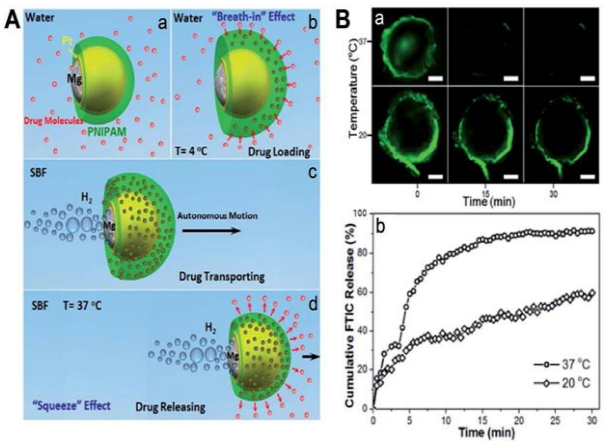


Figure 3: (A) Schematic demonstration of the drug (a and b) loading, (c) transporting, and (d) releasing behaviors of the

Mg/Pt–PNIPAM Janus nanomotors. (B) Fluorescent images representing the drug release from the Mg/Pt–PNIPAM Janus microsphere motor (a) and the normalized average cumulative drug release profiles (b) at 20 and 37 _C versus time. Scale bars: 10 mm. (Reproduced from ref. 40)American Chemical Society 2014.)

vehicles that change co-encapsulation of various medicine, active targeting, and/or temporally controlled unleash. A recent work from our laboratory illustrated a completely loaded multi-cargo Zn based nanomotor which might be doubtless used for combinatorial delivery Such associate degree acid-powered bubble-propelled nanomotor possesses many distinct functions for potential biomedical use. These embrace remarkably high loading capability, combinatorial delivery of a large number of cargoes, autonomous unleash of encapsulated payloads, and self destruction. Such multifunctional zinc-based nanomotors, ready by dual-templating nanofabrication, will move quickly in associate degree acidic surroundings and transport the absolutely loaded cargoes with a speed of one hundred ten millimetre s_1. Because the Zn body is oxidised and dissolved by the acid fuel, the various cargoes area unit discharged autonomously and also the motors area unit self-destroyed, leaving

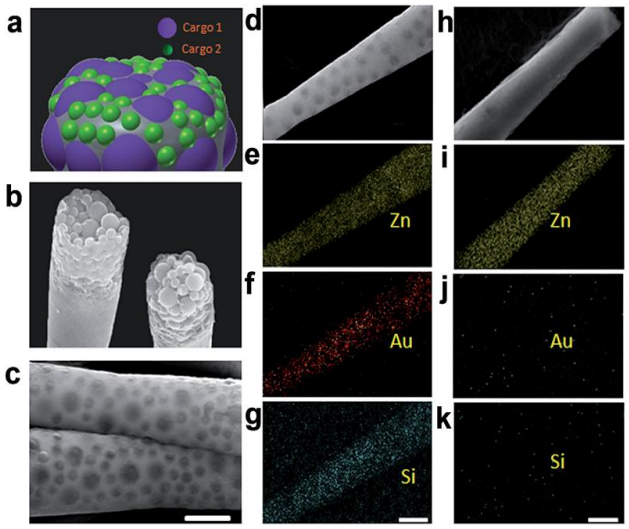


Figure 5: SEM images and energy-dispersive X-ray spectroscopy (EDX) analysis of fully loaded dual-cargo Zn nanomotors towards combinatorial therapy. (a–d) Zn nanomotors encapsulated with 500 nm SiO2 particles. (e–h) control Zn nanomotors without the SiO2 particles Scale bar, 0.5 mm (b) and (f), 1 mm (a) and (e), and 2 mm (c), (d), (g) and (h). (Reproduced from ref. 41, Wiley 2014.)

behind no harmful chemical agents. This attractive concept can be readily expanded to simultaneous encapsulation of a wide variety of payloads, possessing different biomedical functions such as therapy, diagnostics, and imaging, hence opening up new drug delivery opportunities.

2.4 Cancer Cell‑Targeted Delivery

Currently, traditional delivery systems rely solely on circulation of body fluids and lack sufficient penetration and targeting, which makes it difficult for drugs to penetrate tissue and the interior of the lesion. This seriously affects the therapeutic effect of the drug. Anticancer agents such as proteins, siRNAs, and plasmids exhibit excellent biological activity and therapeutic effects in the cytoplasm, and their emergence has brought new choices for advancing the treatment of cancer. However, effectively delivering these agents to the cytoplasm while still ensuring their activity is still very difficult. Transfection techniques can be used to deliver them to cells *via* some biological vectors such as viral vectors or liposome complexes, but the use of biological vectors could introduce an uncontrolled risk of delivery. In order to deliver the drug precisely to the target disease site, the drug carrier needs to have some unique capabilities, including propulsion, cargo and release, and penetration. Given these challenges in drug delivery systems, the advent of nanomotors offers a new and attractive option for drug delivery, thereby increasing the therapeutic effect and reducing the systemic side effects of highly toxic drugs. Here,the self-propelled nanomotors provide the carriers with continuous driving power to help them transport across biological tissues. In addition, the direction of the motor can also be adjusted to prompt cell targeting and internalization, so as to enhance the controllability and adjustability of drug delivery system. Compared to passive drug carriers, the self-propulsion abilities of these nanomotors have unique advantages in drug delivery, which may bring distinct improvements for efficient drug delivery.

2.5 Extracellular Delivery System

Numerous studies have been made in the fabrication of nanomotors that meet the requirements of ideal drug delivery vehicles and promote the development of nanomotors-based drug delivery systems. Initially, a number of synthetic nanomotors have been designed to promote cancer cell targeting and further promote drug release (extracellular delivery system). It has been found that cancer cells produce oxidative stress by producing high levels of H2O2. Therefore, a series of synthetic nanomotors have been designed to harness local H2O2 as an energy source for propulsion to demonstrate the delivery performance. For example, Villa et al. reported multifunctional superparamagnetic/catalytic microrobots (PM/ Pt microrobots) for cell manipulation and anticancer drug delivery. These micromachines contain a superparamagnetic core, allowing them to assemble as nanomotor chains and navigate by an external magnetic field. The Pt hemisphere of Janus microsphere enables catalytic self propulsion, while tosyl groups enable the motors to manipulate cells and to deliver bioactive molecules. After loading them with the anticancer water-soluble drug doxorubicin (Dox), these microrobots are able to capture breast cancer cells and simultaneously release the drug into the cancer cells by diffusion. Such versatile device simplifies the applicability of nanomotors toward diverse biomedical applications.The exploit of biocompatible enzymes to power nanomotors has opened new avenues for active delivery of specific drugs to the site of interest. Compared to other catalytic motors, enzyme-powered nanomotors possess several advantages, such as bioavailable and biocompatible, which are more suitable for biological applications. Hortelão presented enzyme-powered nanomotors for enhancing anticancer drug delivery. The nanomotors comprised of a solid silica core

which was coated with urease enzymes and a mesoporous silica shell which provided high loading capacity of Dox. Furthermore, the urease enzymes-modified nanomotors convert chemical energy into mechanical work even in ionic media (phosphate buffer saline buffer solution), which demonstrated their potential use in biomedical applications. The nanomotors-based Dox-loaded system obtained an enhanced anticancer efficiency toward HeLa cells, which arises from a synergistic effect of the enhanced drug release and the ammonia produced at high concentrations of urea substrate. Increased drug delivery efficiencies achieved by these nanomotors may have potential for use in future biomedical applications. In addition to the above applications, nanomotors have also been made into tubular structures to harness the chemical energy of H2O2.In this design, reduced nanographene oxide (n-rGO)/platinum (Pt) micromachines were fabricated for efficient drug delivery. Notably, the n-rGO/Pt micromachines showed fast speed even in very low concentration of H2O2and high loading efficiency of Dox molecules. In addition, the authors also integrated the nanocarriers with electrochemical stimulus, which lead to drug release in a specific location in only a few second. Coupling the powerful self-propulsion and high loading capacity of n-rGO/Pt micromachines with the introduced ultra-fast drug release mechanism, the self-propelled machine provides an important step toward the realization of advanced drug delivery systems.

2.6 Intracellular Delivery System

Following the initial success of nanomotor-based delivery systems, analysis within the field of intracellular delivery has advanced more. Currently, a series of nanomotors, like H2O2-powered microrobots, accelerator battery-powered nanomotors, magnetic, or ultrasound field driven nanomotors, are incontestible for economical delivery. significantly, so as to realize economical delivery toward cancer cells and extended intracellular unleash of payloads, the nanomotors should be rationally synthesized to beat multiple transport barriers. for instance, the characteristics like size, charge, shape, and surface chemistry ought to be comprehensively thought of to facilitate the economical delivery of medicine or payloads to the subcellular target in tumors. additionally, for in vivo delivery, the interaction between the nanomotors and varied tissues (e.g.,liver, kidney, spleen, brain, and tumor), the nonspecific interactions with healthy cells still because the clearance potency of the nanomotors are ought to be thought of. Some work has been reported on the employment of nanomotor to penetrate cell membranes and attain economical delivery of varied therapeutic compounds into cells. for instance, Gao et al.developed succinylated β-lactoglobulin and catalase-assembled accelerator Nanomotors for increased intracellular drug unleash. in addition, fuel-free nanomotor driven by external power, like magnetic or ultrasound fields, additionally shows nice potential for intracellular precise delivery. For a biocompatible delivery system, a magnetic-driven spermatozoan nanomotor is given as a targeted drug delivery. this method is incontestible to be Associate in Nursing economical drug delivery vehicle by initial loading a motile gamete with antibiotic coordination compound. Beneath external field of force, the sperm-driven nanomotor will be target-hunting to the neoplasm ellipsoid of revolution, free the gamete still as unleash the drug. Compared to strictly artificial nanomotors, the spermatozoan-hybrid nanomotor will encapsulate high concentrations of antibiotic coordination compound within the sperm membrane. Also, the flexibility of sperms to fuse with physical cells represents a novel property to deliver the drug domestically into cancer cells through gamete membrane fusion. These sperm-hybrid nanomotors not solely have potential relevancy for medical specialty cancer treatment, however additionally for the medical aid of alternative diseases within the feminine generative tract. Ultrasound (frequencies higher than the audible vary of humans; N20 kHz) will be targeted on terribly tiny areas thanks to its wavelength within the order of millimeters. it's been utilized for each enhancing drug delivery and up drug activity for over twenty years. for instance, the distinctive ability of ultrasound-propelled gold nanowires for cell penetration was additionally applied to siRNA delivery. During this style, nanowires were wrapped with rolling circle amplification (RCA) DNA structures hybridized with inexperienced visible light protein-targeted siRNAs. The important role compete by ultrasound propulsion was mirrored by the comparative studies between propelled and static motors. The results showed a ninety four silencing on HEK293 and MCF-7 cells when treatment for a number of minutes, or so 13-fold improvement within the silencing response as compared to the static nanomotors. Motor improvement studies understood that the nanomotors punctured the semipermeable membrane and continued to maneuver quickly within the cells, that along crystal rectifier to a high gene-silencing potency. Notably, a photoacoustic computed tomography-guided microrobotic system that permits deep imaging and precise control in vivo has been reported. The nanomotors ar wrapped in microcapsules and so protected against stomachic acid. The migration of microcapsules toward the lesion space will be determined in time period in vivo by written agreement. Near-infrared light-weight irradiation toward targeted areas induces disintegration of the capsules and triggers the propulsion of the nanomotors, which may effectively extend the continuance of the drug. Thanks to the deserves of high spatiotemporal resolution, non-invasiveness, molecular distinction, and deep penetration, the PACT-based microrobotic system provides a horny tool for targeted delivery in vivo. Considering the tremendous progress created recently within the development of nanorobots and their uses toward in vivo delivery, these nanorobots ar expected to become powerful transport vehicles that may enable a variety of therapeutic applications that are otherwise difficult to achieve through the existing passive delivery systems.

3. Applications of Nanomotors

3.1 Biomedical Applications

Conventional drug delivery systems are based on passive distribution of therapeutic agents inside the body. The blood carries drug molecules not only to the unhealthy organs but also to the health ones. These systems lack a proper drug targeting and tissue penetration ability for localized release of the therapeutics only to the unhealthy cells. Thus, self-propelling MNMs hold exciting prospects to actively deliver

drug therapeutics to target sites due to their motion, directional control, and tissue retention/penetration ability. For instance, mesoporous silica NPs with a Pt cap were loaded with a chemotherapeutic drug doxorubicin (DOX) for active intracellular drug release. Polymeric stomatocyte nanomotors made of soft self-assembled block copolymers, based on poly(ethylene glycol)-*b*-polystyrene and poly(ethylene glycol)-*b*-poly(ε-caprolactone), were loaded with Pt-NPs and DOX for active drug release to the cancer cells. An illustration of the stomatocyte nanomotor with loaded Pt-NPs and DOX is presented in Fig. Zn- and Mg-based MNMs with excellent biocompatibility and harmless byproducts hold enormous potential for drug delivery applications. PEDOT/Zn micromotors represent the first in vivo application of synthetic MNMs for gastric drug delivery. The acid-driven Zn micromotors could self-propel and penetrate the stomach tissue for prolonged retention and localized release of the cargo. Mg/Pt-pNIPAM Janus nanomotors were autonomously propelled in simulated body fluids or blood plasma without any other additives.The temperature- responsive pNIPAM underwent a swelling and squeeze effect at low and physiological temperatures to load and release the payloads, respectively. The Mg nanomotors can rapidly neutralize the acidity of the stomach fluid due to the depletion of protons by reaction with Mg.With a drug loaded, a pH-responsive polymer coated onto the Mg particles can release the payload due to a pH change. Wang and co-workers have reported Mg-microparticle-loaded PEDOT/ Au microtubes coated with an enteric polymer for precise positioning, propulsion, and retention in the mouse's gastrointestinal tract. The enteric polymer coating protected the nanomotors from reacting with the gastric acid, but dissolved in the intestinal fluid (pH 6–7) to trigger the propulsion for intestinal tissue penetration. By tailoring the thickness of the polymer coating, the dissolution time of the polymer could be tuned which in turn controlled the positioning of the motors inside the intestinal tract. Figure 8G shows the illustrated mechanism of action and preparation scheme of PEDOT/Au/Mg nanomotors coated with the enteric polymer. Due to the self consumption of the material, Zn- and Mg-based nanomotors offer unique opportunities for drug delivery due to their transient nature, which produces harmless byproducts and post delivery separation is no longer needed. Kastrup and co-workers have used self-propelled CaCO3 particles to transport therapeutics through blood.[165] The particles were synthesized by controlled precipitation of CaCl2 and Na2CO3, and mixed with protonated tranexamic acid, a drug to prevent excessive blood loss. When injected into the blood, the particles were propelled by releasing CO2 for a distance of millimeters into the vasculature of wounds. Thrombin-loaded particles worked as an efficient hemostatic agent. Catalase-based nanomotors with encapsulated DOX were prepared by layer-by-layer assembly of polyelectrolytes. The nanomotors navigated to the cancer cells and drug release was accomplished by exposure to the near-infrared light to collapse the polyelectrolyte layers. MNMs driven by biofluids, such as urea or glucose, hold a great promise for in vivo drug delivery applications, which yet remains to be demonstrated.

Synthetic MNMs with immobilized urease offer another potential benefit besides actively driving the motion. The natural defense mechanism of the gastrointestinal and urinary tract contains mucin that is responsible for the mechanical properties of the mucosal lining and restricts the penetration of foreign substances. A stomach-inhabiting bacteria *Helicobacter pylorus* manipulates the gastric mucus by releasing urease that locally neutralizes the pH by producing ammonia from urea. A change in the pH induces a sol–gel transition in the mucus to reduce its viscosity and allows the bacteria to penetrate through it.This provides a promise for synthetic MNMs to adopt a similar strategy for mucosal penetration by immobilizing urease onto their external surface. The operational mechanism of *H. pylori* and urease immobilized micropropellers is shown in. Other proof-of-concept biomedical applications include nanomotor assisted immunoassays and immunosensing for protein and biomarker detection.

3.2 Environmental Applications

A rapid increase in global industrialization has resulted in excessive disposal of toxic pollutants into the environment. This has posed a serious threat to the aquatic ecosystem, which is vital for humans. An interruption in the supply of clean water may affect millions of lives, which makes it a matter of great scientific, economic, and political interest. Some examples of the toxic pollutants that are disposed of by the industry are organic solvents, personal care or consumer products, pharmaceuticals, pesticides, heavy metal contaminants, and miscellaneous excipients/additives used in various product formulations. Nanotechnology and nanomaterials present innovative technologies for sensing and removal of pollutants due to their excellent optical and catalytic properties, high surface area, and tunable surface chemistry. The next generation of water remediation solutions aims at low-cost and energy efficient approaches to remove biological and chemical pollutants, even at remote locations where conventional methods cannot be implemented. Chemically driven MNMs hold a unique promise for environmental remediation applications due to their superior catalytic properties and autonomous propulsion that can speed up the diffusion-limited processes. The environmental applications of MNMs include sensing and removal of the pollutants. Environmental sensing refers to the changes in the motion behavior of MNMs in the presence of certain contaminants. For example, Pt/Au bimetallic nanorods show dramatic acceleration in the presence of Ag+ ions. The Ag+ ions adsorb onto the Pt surface are reduced in the presence of H2O2 into metallic Ag, which increases the electrocatalytic properties of the nanomotors for a faster motion. The motion enhancement is strongly dependent on the concentration of Ag+ ions and can be used to obtain quantitative information of the Ag+ toxicity down to the nanomolar level. In contrast, contaminants can also negatively influence the motion of MNMs by deactivating or poisoning the catalysts. Catalase-based nanomotors undergo drastic changes in their speeds in the presence of various inorganic and organic pollutants that inhibit the enzymatic activity, as illustrated in An analysis of common ecotoxicological parameters, such as the exposure concentration that causes 50% attenuation of nanomotor motion (EC50) and the lifetime expectancy, allows a direct real-time assessment of the water quality by optically tracking the motion behavior. A similar response of the

motile nanomotors to the vapor plumes of chemical warfare agents (CWAs) enables their rapid and convenient detection. The catalase-based nanomotors remain active in the absence of CWAs, but once present, the CWA vapors inhibit the catalase activity and attenuate the motion. Fluorescent MNMs can detect the presence of certain organic or inorganic pollutants that quench the fluorescence intensity in contaminated water. nanomotor-assisted fluid mixing and accelerated chemical degradation of OP threats also allow for rapid electrochemical monitoring of the decontamination processes. Rapid conversion of the non detectable paraoxon into electroactive *p*-nitro phenol can be monitored using printed electrochemical sensor strips. Guix et al. reported the first example of using synthetic MNMs for environmental remediation. The outer surface of the Au-sputtered, Pt-based microtubes was functionalized with alkanethiols for the capture and removal of oil microdroplets as a possible solution to oil spillage. However, due to a similar affinity of thiol groups for Pt and Au, the Pt catalytic surface was deactivated and the propulsion efficiency was severely reduced. We have recently proposed the use of MnO2 deposited onto the Pt surface to block the microtube opening, which protects the Pt surface from the chemisorption of thiol compounds. The resulting nanomotors maintained excellent performance after alkanethiol functionalization and were used for the capture and transport of oil droplets. The oil capture and removal by hydrophobic Mn- and Mg-based nanomotors have also been reported. Nonbiogenic organic dyestuff released by the paints, textile, and printing industry is another problem that requires innovative solutions for their degradation or recovery. Rolled-up Fe/Pt microtubes were used for Fenton-like degradation of dye molecules. The nanomotors could continuously move over 24 h and were reusable for multiple cleaning cycles over a period of several weeks. Wani et al. described a dual effect of the MnO2 microparticles which provided efficient catalytic degradation (CD) and adsorptive bubble separation of rhodamine 6G and methylene blue dyes as depicted in Figure 9E.These particles were obtained commercially and could undergo motion for a few hours, which was followed by self-degradation. The low cost, the easy availability of MnO2 in bulk quantities, and the transient nature of commercial MnO2 microparticles make them an attractive choice for practical water remediation applications. Besides dyes, other highly stable organic ingredients used in plastics, dynamically and efficiently remove polybrominated diphenyl ethers and triclosan from environmental samples. Increasing concentrations of toxic heavy metals in the soil and aquatic ecosystem also requires strict measures on their release and efficient methods for their removal. GOx nanosheets can absorb heavy metal ions due to the complexation between the oxygen moieties of the nanosheets and the metal ions. Self propelling nanomotors comprising an outer GOx layers could capture and remove lead (Pb2+) ions from the contaminated waters 10 times more efficiently than their nonmotile counterparts. Another efficient approach for the removal of heavy metal contaminations is to use metal chelating agents that can easily be functionalized on the surface of MNMs. Wang and co-workers used Au/Ti/Mg Janus particles functionalized with *meso*-2,3-dimercaptosuccinic acid for the removal of Zn2+, Cd2+, and Pb2+ ions from contaminated water. These nanomotors were driven by water and did not require any external fuel, having a lifetime of ≈3 min. A metal removal efficiency of up to 100% was observed after just 2 min of operation. Such a straightforward approach can be extended to different chelating agents to address specific cleanup needs. In the defense industry, the conversion of chemical warfare agents into nontoxic products at the remote storage locations is another big challenge that relies on peroxide-based oxidative treatment. However, the prolonged processing times and the need for mechanical mixing to enhance the mass transfer are some of the undesired conditions that are difficult to fulfill in remote locations. Bubble-propelled Pt-based nanomotors have shown a remarkable increase in the oxidative decontamination of organophosphate (OP) nerve agents by generating peroxide anions (OOH^-) in situ, without any external agitation. Water-driven Mg-based nanomotors can also photocatalytically decontaminate water samples poisoned with chemical and biological contaminants, such as OP nerve agents and anthrax stimulant *Bacillus globigii* spore.A modification of the nanomotors with bactericidal materials such as chitosan has a potential to clean water from pathogenic bacteria.The antibacterial activity of chitosan can be attributed to an electrostatic interaction with the cell membrane and its consequent damage. Besides chemical degradation, self-propelling platforms can remove organic and inorganic pollutants from contaminate water by processes based on adsorption or selective binding. Carbon dioxide (CO2) emission into the atmosphere is another major threat to the environment and a central cause for the climate change. Current CO2 capture and sequestration methods suffer either from the high cost, the high energy input, or the use of hazardous chemicals that may further pollute the environment. Uygun et al. used carbonic anhydraseim mobilized icrotubes for biocatalytic sequestration of CO2. The enzyme-catalyzed hydration of CO2 and conversion into CaCO3 by the self-propelling nanomotors is a promising development toward mobile microsystems for CO2 sequestration.

4. Conclusions

This review has discussed recent advances in man-made nanomotors towards controlled drug delivery applications. Considerable progress has been made over the past decade in designing a variety of nanomotors for diverse biomedical applications and strategies for the transport and release of therapeutic agents. As our understanding of the design and operation of nanomotors expands, it becomes feasible to utilize the new capabilities of these machines for practical biomedical applications. With increased power and functionality, future micro/nanomachines are expected to perform more demanding biomedical tasks and benefit different drug delivery applications. While key challenges remain prior to applying these nanomotors for in vivo targeted drug delivery, these recent developments advance this objective one step closer to a futuristic nanomachine suitable for improved delivery of therapeutic agents in the body. Different research teams are currently exploring several routes for realizing future nanomotor-based drug delivery. In order to improve the delivery efficiency, it is essential to explore the attachment of drug carriers to Nanomotors through chemical or biological linkers that are sensitive to the tumor microenvironment (e.g., protease

enzyme and acidity). Such a mechanism will allow for a more accurate localized drug delivery to the target site using drug-loaded particles powered by external magnetic or ultrasound fields. Improved cellular uptake could be achieved by the incorporation of an appropriate ligand. The combination of multiple functions can lead to more effective operation and this would require the assembly of multiple nano objects. In particular, incorporating therapeutic or diagnostic entities in the same nanomachine would create theranostic vehicles. Additional efforts should be devoted towards developing high-performance nanomotor locomotion based on in situ fuel sources and alternate powering schemes, offering significant thrust for overcoming the large drag (associated with the presence of the blood cells) and for improving tissue penetration. Future efforts will involve the development of intelligent logic-controlled nanomachines toward smart drug-delivery applications. Further attention should be given to the biocompatibility of drug-delivery nanomotors, and particularly to common metallic constituents such as Ni, Ag, or Pt. Lastly, the biodegradability (self destruction) or removal of nanomotors from the body after completing their delivery mission needs further consideration. For cancer-targeted delivery, the application scope of the nanomotors-based delivery systems reported is still limited at the cellular level and in vitro research. Most of the nanorobots reported are composed of inorganic materials. Although most materials are considered to be biocompatible and biodegradable, they may still be severely immunogenic and have maximum tolerance. Therefore, synthesized Nanomotors with versatility and excellent motion control in vivo are desired to provide new opportunities for efficient delivery in complex in vivo systems. At present, Nanomotors-based detection methods mainly achieved by means of the change of speed or fluorescence single, which may encounter the problem of insufficient detection signals. Therefore, more attention should be paid to design multifunctional Nanomotors for the development of versatile detection technologies.

References

[1] Synthetic in drug delivery Wei Gao and Joseph Wang*
[2] Micro- and nano-motors: the new generation of drug carriers Mariana Medina-S ´ anchez*,1, HaifengXu1 & Oliver G Schmidt1,2
[3] A. Z. Wang, R. Langer and O. C. Farokhzad, Annu. Rev. Med., 2012, 63, 185.
[4] M. E. Davis, Z. G. Chen and D. M. Shin, Nat. Rev. Drug Discovery, 2008, 7, 77
[5] K. Park, ACS Nano, 2013, 7, 7442.
[6] T. M. Allen and P. R. Cullis, Science, 2004, 303, 1818.
[7] O. M. Koo, I. Rubinstein and H. Onyuksel, Nanomedicine, 2005, 1, 193.
[8] O. C. Farokhzad and R. S. Langer, ACS Nano, 2009, 3, 16.
[9] S. K. Sahoo and V. Labhasetwar, Drug Discovery Today, 2003, 1112.
[10] W. Wang, W. Duan, S. Ahmed, T. E. Mallouk and A. Sen, Nano Today, 2013.
[11] J. Wang, Nanomachines: Fundamentals and Applications.
[12] G. A. Ozin, I. Manners, S. Fournier-Bidoz and A. Arsenault, Adv. Mater., 2005.
[13] J. Wang and W. Gao, ACS Nano, 2012, 6, 5745.
[14] B. J. Nelson, I. K. Kaliakatsos and J. J. Abbott, Annu. Rev.Biomed. Eng., 2010, 12.
[15] D. Patra, S. Sengupta, W. Duan, H. Zhang, R. Pavlick and nA. Sen, Nanoscale, 2013.