International Journal of Nanomedicine

Dovepress
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REVIEW

Micro/Nanorobots in Wound Healing: Bridging the Gap from Concept to Clinical Translation

Yukun Liu[1,*], Kang Wang[1,*], Fangli Gao[2], Zhikai Xu[3–6], Xuan Zhao[3–6], Xiangjun Bai[3–6], Zhanfei Li[3–6], Guoyun Wan[7], Jian Yang[8], Yuchang Wang[3–6]

[1]Department of Plastic and Aesthetic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [2]College of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang, Henan, People's Republic of China; [3]Division of Trauma Surgery, Emergency Surgery & Surgical Critical Care, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [4]Sino-German Research Institute of Disaster Medicine, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [5]Department of Emergency and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [6]Trauma Center, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; [7]School of Life Science and Technology, Xinxiang Medical University, Xinxiang, Henan, People's Republic of China; [8]Emergency Center, The First Affiliated Hospital of Shihezi University, Shihezi, Xinjiang, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jian Yang; Yuchang Wang, Email 125210525@qq.com; tjwangyuchang@163.com

Abstract: Chronic wounds, such as diabetic foot ulcers, venous leg ulcers, and pressure sores, pose a significant clinical challenge due to ongoing inflammation, biofilm development, and impaired tissue regeneration. Standard wound care methods often fail to address these complex barriers, highlighting the need for innovative solutions. Nanorobotics has emerged as a groundbreaking platform, enabling programmable, multifunctional systems capable of active navigation, biofilm penetration, modulation of the microenvironment, and targeted therapeutic delivery. This review systematically covers the design principles and functional components of micro-/nanorobots, including propulsion techniques, sensing and actuation mechanisms, and biomimetic surface modifications. We also examine their therapeutic potential in wound healing, focusing on drug delivery optimization, biofilm disruption, reduction of oxidative stress, immune regulation, and tissue regeneration support. The integration of nanorobotics with intelligent wound care systems offers real-time monitoring and closed-loop interventions, initiating a new era of "smart wound management." Finally, we address translational challenges such as biosafety, large-scale manufacturing, and regulatory pathways, and provide perspectives on future advancements toward clinically practical, intelligent nanorobotic wound therapies.

Keywords: micro/nanorobots, nanorobots, chronic wounds, wound, drug delivery, nano

Introduction

Skin wounds can be broadly divided into two categories based on cause and healing time: acute wounds and chronic wounds.[1,2] Acute wounds, such as surgical cuts, traumatic scrapes, and burns, usually go through four well-organized phases—hemostasis, inflammation, proliferation, and remodeling—leading to full closure within a few weeks.[3,4] Conversely, chronic wounds (eg, diabetic foot ulcers, venous leg ulcers, and pressure sores) often get stuck in the inflammatory phase due to poor local blood flow, ongoing inflammation, enzyme imbalance, and biofilm formation. These issues delay healing, cause frequent recurrence, and can lead to limb loss or serious complications.[5–7] In the US, about 10.5 million Medicare beneficiaries are affected by chronic wounds—a 2.3 million increase since 2014—and the annual treatment cost exceeds USD 25 billion.[8,9] Speeding up wound healing with high-quality treatment remains a significant clinical challenge.

Although traditional wound care methods—such as debridement, negative pressure therapy, and dressings infused with growth factors—have improved, most current products mainly serve as passive barriers to preserve the wound environment.[7,10] Conventional dressings, including cotton gauze, foam pads, hydrocolloids, and gels with silver ions or

Received: 29 July 2025
Accepted: 11 December 2025
Published: 19 December 2025

antibiotics, mainly work by absorbing fluid, keeping moisture balanced, or releasing therapeutic agents to kill surface germs and protect new tissue.[11–16] However, these materials cannot respond dynamically to real-time changes in important physical and chemical parameters like pH, reactive oxygen species (ROS), or enzyme activity. They also struggle to penetrate thick biofilms for a deep antibacterial effect and cannot monitor or adapt in real time. As a result, clinical treatments are often delayed until obvious signs of deterioration appear, missing critical early intervention opportunities.[14,15]

Recently, micro/nanorobots—programmable, controllable, tiny devices—have become a groundbreaking technology in precision medicine due to their multifunctional, modular design.[17–20] These nanosystems usually include a "propulsion engine" powered by magnetic fields, ultrasound, or chemical reactions; "sensing modules" that respond to stimuli such as pH, enzymes, or temperature; and "smart drug compartments" for delivering antimicrobial agents, growth factors, or nucleic acids.[21–24] With this modular setup, micro/nanorobots can move within the body, actively break through biofilm barriers, locate infected or dead tissues, and release therapeutics when detecting abnormal physiological signals. This introduces a new therapeutic approach combining "deep tissue targeting," "on-demand drug delivery," and "real-time feedback".[25–28] Between 2010 and Sep. 2025, a total of 7290 publications related to this field were retrieved from the PubMed database using the following search strategy: TS = (("micro/nanorobot" OR "nanorobot" OR "microrobot") AND ("wound healing" OR "chronic wound" OR "diabetic wound" OR "skin ulcer" OR "cutaneous ulcer")). As illustrated in Figure 1, the annual number of publications has shown a steady increase over the past 15 years, with a marked surge after 2019, peaking in 2024 with more than 1100 articles. In contrast, the average number of citations per publication exhibited a gradual rise from 2010 to 2018, reaching its highest point in 2018, but has since declined, particularly after 2022. This divergence between the rapid growth in publication volume and the decrease in average citations may reflect both the expansion of research activities and the increasing competitiveness of the field. Together, these trends highlight the dynamic evolution and growing attention to the topic, underlining its importance in the broader scientific community (Figure 1).

Acting as mobile drug depots, environmental sensors, and intelligent actuators, micro/nanorobots have shown unique benefits in eradicating biofilms and adjusting the microenvironment in laboratory studies and small animal models.[29,30] Despite increasing research on their potential in wound care, most studies focus on a single propulsion method or limited functional testing. A systematic review that covers their design, therapeutic mechanisms, preclinical results, and challenges in translation is still needed.

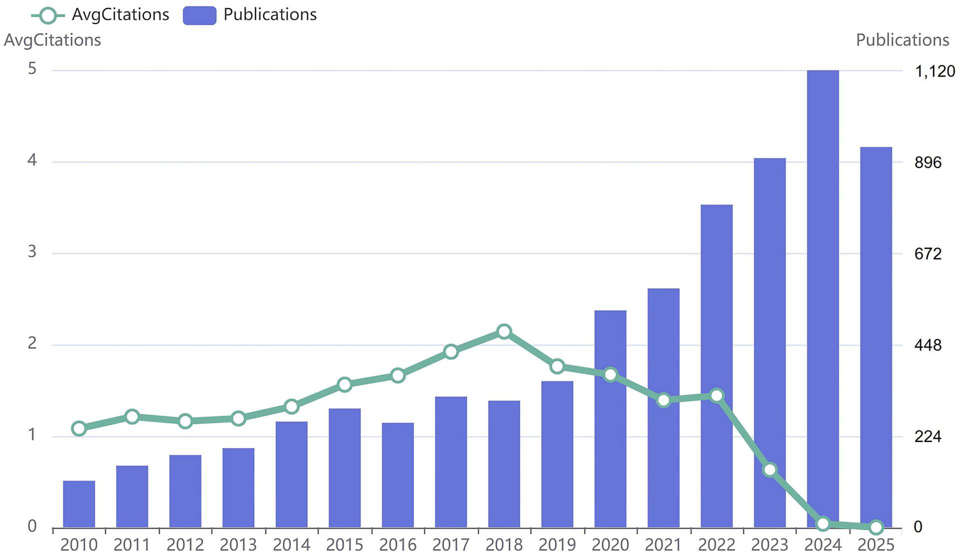

Figure 1 Annual publication volume and average annual citations. Between 2010 and Sep. 2025, a total of 7290 publications related to this field were retrieved from the PubMed database using the following search strategy: TS = (("micro/nanorobot" OR "nanorobot" OR "microrobot") AND ("wound healing" OR "chronic wound" OR "diabetic wound" OR "skin ulcer" OR "cutaneous ulcer")). X-axis represents publication year; left Y-axis indicates average citations; right Y-axis indicates number of publications.

This review aims to address this gap by providing a detailed analysis of various nanorobot platforms for wound healing. We first explain their main design principles and functional parts, including propulsion mechanisms and stimulus-triggered drug release systems. Then, we discuss their multimodal therapeutic effects, from targeted drug delivery and biofilm penetration to microenvironment regulation and promoting new blood vessel growth. Next, we highlight key findings from laboratory and animal studies, focusing on safety, biocompatibility, and overall effectiveness. Finally, we suggest future research directions and strategies for clinical translation. By identifying current gaps in research and clinical use, we hope to develop a clear scientific framework and practical guidance for future "intelligent, autonomous, and precision" wound healing solutions powered by nanorobotics.

Design Principles and Functional Architecture of Micro/Nanorobots

The application of micro/nanorobots in wound healing relies heavily on their highly customizable design principles and modular functional architecture. Broadly, Micro/nanorobots can be classified based on their propulsion mechanisms and system complexity. According to propulsion strategy, three main categories have been identified: self-propelled, externally propelled, and biohybrid microbe-propelled Micro/nanorobots.[1–3]

1) Self-propelled Micro/nanorobots generate thrust via internal chemical reactions, such as enzyme-catalyzed substrate decomposition or fuel molecule oxidation, enabling autonomous movement without external fields. For instance, active metals like magnesium (Mg) or zinc (Zn) react with H_2O to produce hydrogen gas as a driving force.[4,5] Enzyme-powered Micro/nanorobots further extend this concept by utilizing biocompatible fuels such as glucose or urea. In 2015, Ma et al reported a fully biocompatible Janus hollow mesoporous silica microrobot integrating catalase, urease, and glucose oxidase (GOx). This system achieved efficient propulsion driven by the catalytic reactions of three enzymes, demonstrating promising self-powered motion in complex biological environments.[6]
2) Externally propelled Micro/nanorobots rely on magnetic fields,[7] ultrasound,[8] or light-based stimuli[9] for controlled navigation. These systems offer precise modulation of trajectory and velocity, significantly enhancing targeting accuracy and safety. Among propulsion methods, magnetic field-actuated Micro/nanorobots are widely explored. By incorporating ferrites (eg, Fe_3O_4, $CoFe_2O_4$) into their micro/nanostructures, these devices achieve efficient propulsion and navigation under rotating or gradient magnetic fields. This approach exhibits excellent propulsion efficiency and biocompatibility and has been extensively used for biofilm disruption and targeted drug delivery.[10–12] Alternatively, ultrasound- and photo-responsive Micro/nanorobots convert acoustic or light energy into micro-vibrations or photothermal effects for locomotion, while simultaneously enabling triggered drug release. Such modalities facilitate remote control and localized energy deposition, making them suitable for deep-seated wounds or complex tissue environments.[13–15]
3) Biohybrid micro/nanorobots achieve efficient and sustainable locomotion by harnessing the natural motility of living microorganisms (such as bacteria, sperm, or other motile unicellular organisms).[16,17] Compared with purely physical or chemical propulsion strategies, such systems possess unique advantages, particularly in exhibiting remarkable adaptability and targeting capability within complex biological environments. For instance, flagellated bacteria (eg, Escherichia coli) can autonomously migrate toward inflamed or hypoxic regions via chemotactic responses, thereby providing a natural navigation mechanism for precise drug delivery to wound sites.[18,19]

Functional system complexity distinguishes single-function Micro/nanorobots, designed for specific therapeutic tasks (eg, deep drug delivery or biofilm eradication),[20] from multifunctional integrated systems. The latter combine propulsion, sensing, drug release, and immunomodulation modules within a single platform, enabling sophisticated diagnostic and therapeutic workflows.[21] Modular integration is a core strategy for endowing Micro/nanorobots with multidimensional therapeutic capabilities, typically encompassing three major components: drug-loading chambers with controlled release mechanisms, pathogen recognition/signal sensing modules, and surface modification layers. Drug chambers often utilize porous materials (eg, mesoporous silica, biodegradable polymers) or microcavity structures, coupled with smart polymers responsive to pH or ROS. This allows on–off therapeutic release triggered by the pathological microenvironment, thereby improving drug utilization and minimizing systemic toxicity.[3,21–23] The pathogen recognition and sensing modules incorporate specific receptors, antibodies, or molecular probes to detect pathogens, inflammatory factors, or physiological parameters (eg, pH, protease activity) in real time. These signals are relayed to control units, activating corresponding therapeutic responses.[20,24] Finally, surface modifications enhance biocompatibility and provide anticoagulant protection.[25,26] Bioinspired coatings, antimicrobial peptides, or immunoregulatory molecules can be integrated to actively modulate immune cell polarization and amplify antibacterial efficacy.[27] For example, Esteban-Fernández de Ávila et al developed ultrasound-driven biohybrid Micro/nanorobots by cloaking gold nanowires with red blood cell (RBC) and platelet (PL) membranes, forming hybrid shells rich in native proteins. This design endowed Micro/nanorobots with platelet-like pathogen adhesion capabilities (eg, binding Staphylococcus aureus) and the ability to neutralize pore-forming toxins (eg, α-toxin).[25] Under ultrasound propulsion, these biohybrid Micro/nanorobots achieved prolonged, efficient movement in whole blood without significant biofouling. Their biomimetic locomotion further enhanced targeted pathogen binding and detoxification, highlighting tremendous potential for infection therapy.

Through the synergistic interplay of these three modules, Micro/nanorobots can achieve a "sense–navigate–treat–feedback" closed-loop process within the wound microenvironment, positioning them as a core component of next-generation intelligent wound management systems (Figure 2).

Micro/Nanorobots for Wound Healing

As a next-generation intelligent therapeutic platform, Micro/nanorobots leverage their miniaturized architecture, active propulsion, and multifunctional modular integration to offer unprecedented advantages in the treatment of complex wounds.[28]

Unlike traditional passive drug delivery systems, Micro/nanorobots can actively navigate to pathological sites, significantly increasing local drug concentration while minimizing systemic side effects. Moreover, their programmable design allows them to respond to pathological signals within the wound microenvironment, enabling on-demand release of antimicrobial, anti-inflammatory, and pro-angiogenic agents. This makes them particularly promising for the treatment of chronic non-healing wounds, infected lesions, and diabetic ulcers.[29–31]

Targeted Drug Delivery

In treating chronic wounds such as diabetic ulcers, conventional drug delivery systems face significant challenges, including limited penetration of tissue barriers, insufficient local drug concentrations, and nonspecific distribution that often results in systemic toxicity. In contrast, micro/nanorobots, as intelligent delivery platforms, offer key advantages such as active targeting, precise control, and microenvironment-responsive release, which collectively enhance local drug bioavailability and therapeutic efficacy[2,32–34] (Figure 3A). Moreover, they can disrupt biofilms and achieve deep penetration for antimicrobial agent delivery through self-propelled systems (Figure 3B), promote cell proliferation and enable controlled release of pro-regenerative signaling molecules (Figure 3C), and improve the local microenvironment by scavenging ROS and modulating inflammatory responses (Figure 3D).

Their nanoscale dimensions, high surface modifiability, and responsiveness to external stimuli (eg, magnetic fields, acoustic waves, light) enable Micro/nanorobots to traverse complex physiological barriers and accumulate efficiently at wound sites for targeted release.[32] Structural designs such as surface functionalization, core–shell architectures, and hollow nanocapsules allow flexible loading of diverse therapeutic agents—including antimicrobials, anti-inflammatories, and pro-healing factors—to address the dynamic needs of different wound healing phases.[35–38] Notably, bioinspired Micro/nanorobots cloaked with red blood cell (RBC) or platelet membranes exhibit superior immune evasion and lesion-targeting capabilities. Such "stealth" transport properties are especially advantageous in highly inflamed and immunologically active wound microenvironments, enhancing therapeutic precision.[25,27]

Regarding drug release mechanisms, Micro/nanorobots can integrate passive and active strategies for spatiotemporal control. Passive release exploits pathological microenvironment features such as acidic pH, elevated enzymatic activity, or reductive conditions to trigger site-specific drug discharge. Active release, on the other hand, utilizes external stimuli—near-infrared (NIR) light, magnetic fields, or ultrasound—to initiate controlled drug release, improving efficiency and minimizing off-target toxicity.[39–41]

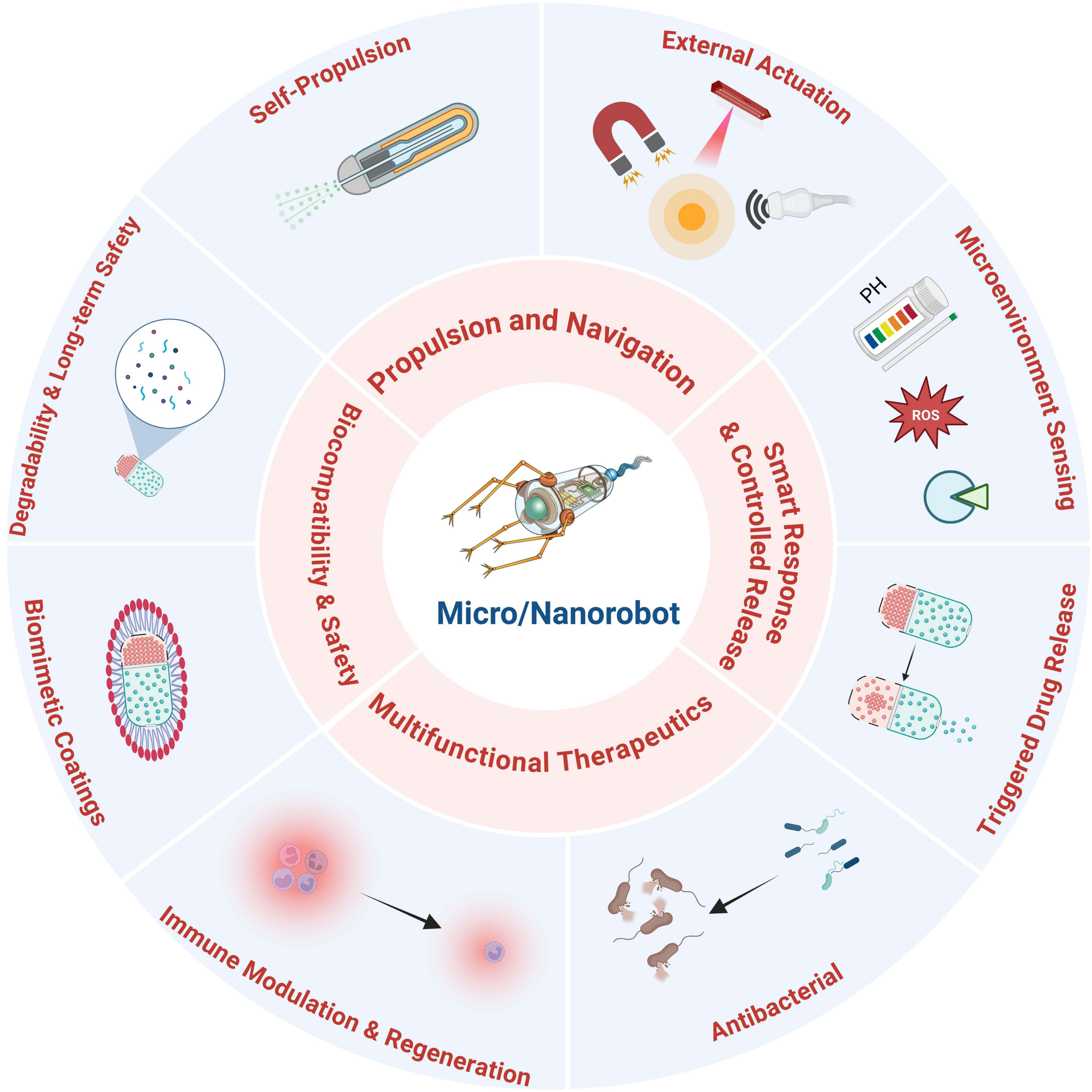

Figure 2 Design principles and functional modules of micro/nanorobots for wound healing.

Of particular interest is a recently developed biohybrid nanorobot platform combining artificial propulsion with biological recognition. The system comprises magnetically driven micro-/nanorobots functionalized with chitosan derivatives for enhanced motility and tissue penetration, coupled with engineered extracellular vesicles (EVs) loaded with mangiferin, a natural antioxidant molecule. Glycosylation of the EVs improves their uptake by fibroblasts and endothelial cells. In vivo studies demonstrated that this system significantly promotes epithelial regeneration, collagen deposition, and angiogenesis in diabetic infected wound models, offering a novel strategy that integrates active navigation, precise delivery, and microenvironment modulation for chronic wound therapy[42] (Figure 4). In summary, through structural optimization and functional integration, micro-/nanorobots overcome many limitations of conventional drug delivery methods and hold great promise for the precision treatment of chronic wounds.

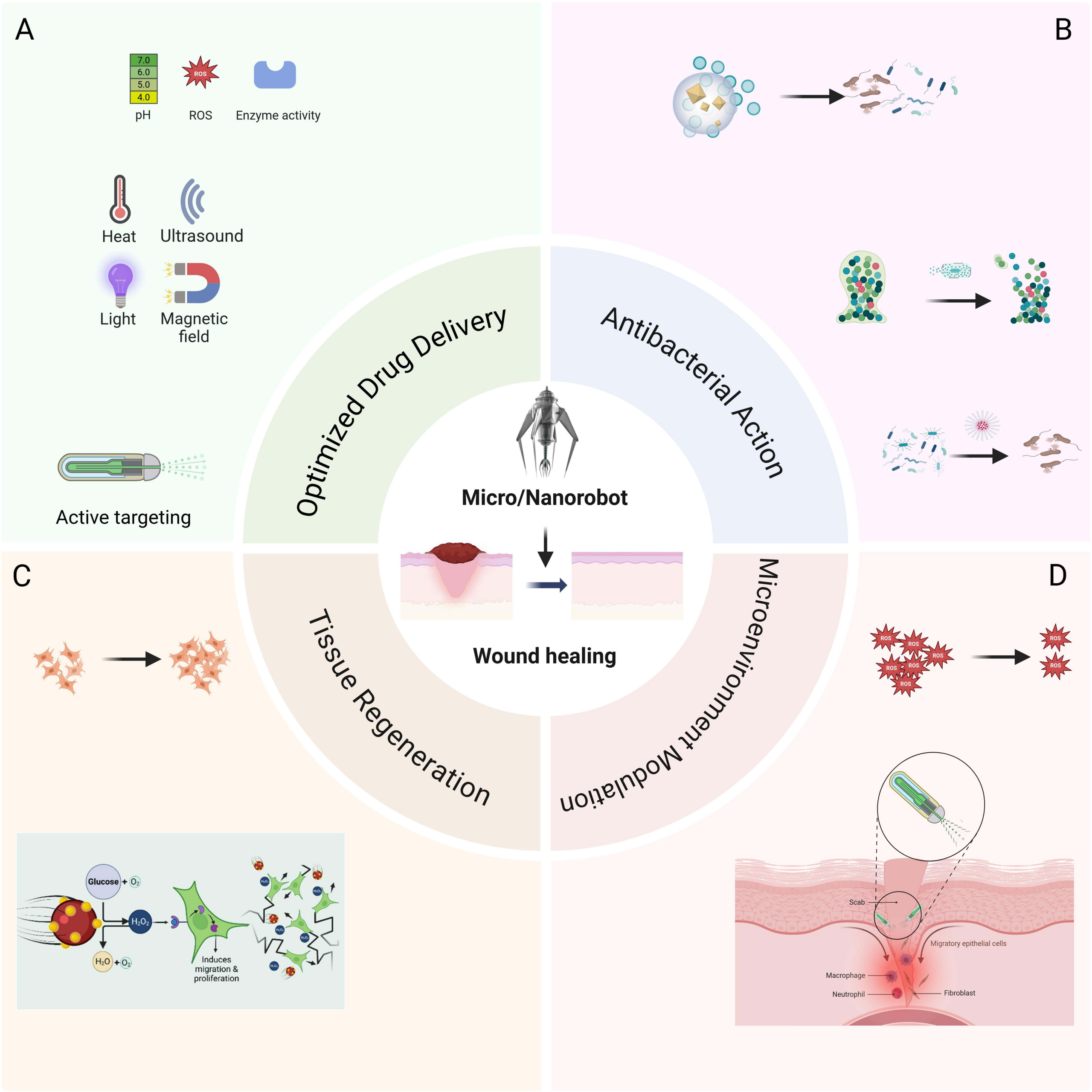

Figure 3 Multifunctional roles of micro/nanorobots in wound healing. This schematic highlights the therapeutic functions of micro/nanorobots in wound management. Key modules include: (**A**) *Optimized Drug Delivery*, enabling active targeting and external stimuli (NIR, magnetic field, ultrasound)-triggered smart release in response to pH, ROS, and enzyme activity; (**B**) *Antibacterial Action*, with self-powered systems for biofilm disruption and deep penetration for antimicrobial agent delivery; (**C**) *Tissue Regeneration*, promoting cell proliferation and controlled release of pro-regenerative signaling molecules; and (**D**) *Microenvironment Modulation*, through ROS scavenging and regulation of inflammatory responses. Together, these functions synergistically enhance chronic wound repair and functional tissue recovery.

Biofilm Penetration and Antibacterial Action

A major obstacle to chronic wound healing is the formation of bacterial biofilms.[43,44] Biofilms—three-dimensional matrices composed of bacteria and extracellular polymeric substances (EPS) such as polysaccharides, proteins, and DNA—protect pathogens from host immune responses and conventional antibiotics, enhancing resistance and contributing to persistent or recurrent infections.[44,45] Current antibacterial treatments are largely ineffective against biofilms, as they struggle to penetrate these protective structures and eradicate deeply embedded pathogens.[20,46] Micro/nanorobots, with their controllable microarchitectures and active propulsion, provide innovative solutions for overcoming biofilm barriers.[47] Their active locomotion not only allows physical disruption of biofilm matrices but also facilitates deep

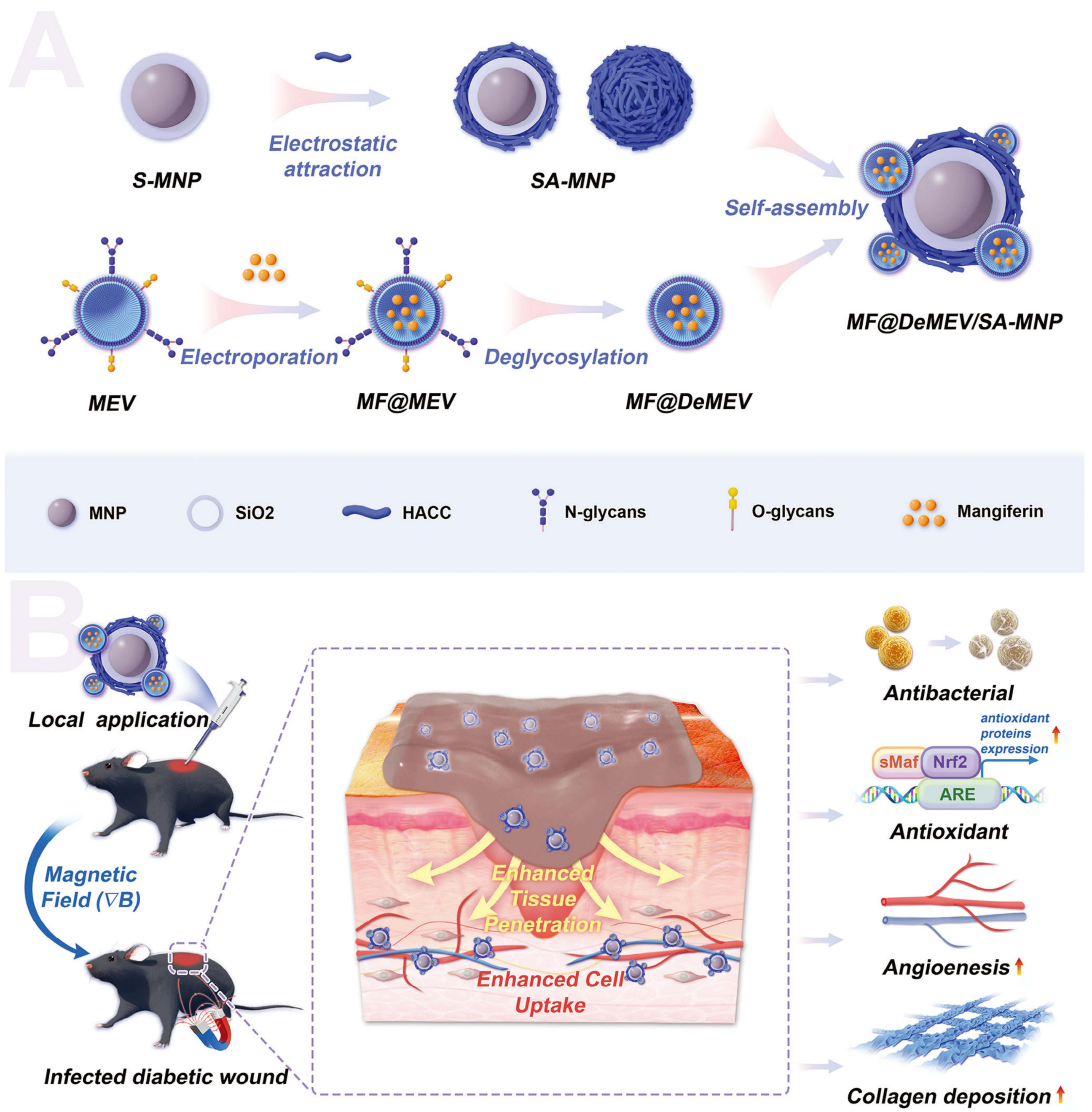

Figure 4 Schematic illustration showing (**A**) the construction process of a glycoengineered EV-based biohybrid nanorobot platform (MF@DeMEV/SA-MNP) and (**B**) its synergistic therapeutic effects on infected diabetic wounds through dual-enhanced cellular and tissue penetration and a multi-step intervention strategy. The upward arrows indicate increase, and ∇B represents the change in magnetic flux density.[42]

Note: The spelling error "Angioenesis" in the original figure have been retained from the cited source.

penetration and localized delivery of potent antibacterial agents, enabling targeted eradication of pathogens[48] (Figure 3B). For instance, a magnetic hydrogel-based microrobot system was developed using poly(acrylic acid–acrylamide) hydrogels encapsulating Fe_3O_4 nanoparticle chains, conferring excellent magnetic responsiveness. Under rotating magnetic fields, these microrobots actively aggregate at infected sites and steadily release vancomycin from their internal drug reservoirs, achieving effective clearance of Staphylococcus aureus and providing sustained, high-efficiency local antibacterial therapy.[49]

Another study introduced a "pandanus fruit–like" helical magnetic nanorobot (F@Z/C/P) fabricated by growing ZIF-8 shells on Fe_3O_4 cores, loading ciprofloxacin, and coating with polydopamine (PDA). This design endowed the system with pH responsiveness and NIR-triggered photothermal therapy capability. Under magnetic guidance, the nanorobot actively penetrates infected tissues and biofilm structures, where the acidic microenvironment significantly enhances drug release (14% higher release at low pH). Upon NIR activation, it synergistically delivers photothermal antibacterial effects, achieving >99.9% pathogen elimination within tissues. Post-treatment analyses confirmed that the Micro/nanorobots were safely cleared without notable damage to surrounding tissues, underscoring their biocompatibility and therapeutic potential[50] (Figure 5).

Furthermore, self-propelled micro/nanomotors based on metal–organic frameworks (MOFs) have been utilized for antibacterial applications. These devices exploit spontaneous degradation of MOF structures in aqueous environments to release metal ions (eg, Zn^2+, Cu^2+), which not only serve as fuels driving ionic self-diffusiophoresis but also exhibit inherent antimicrobial activity. In E. coli infection models, MOF micromotors demonstrated robust autonomous propulsion and effective bacterial growth inhibition, accelerating wound closure[51] (Figure 6).

An innovative strategy combined intelligent microneedle patches with nanomotor-mediated antibacterial therapy. The microneedles physically penetrate biofilms and deliver quorum-sensing inhibitors (luteolin) along with nanomotors co-loaded with photosensitizers (ICG) and nitric oxide (NO) donors. Upon NIR irradiation, the nanomotors are actuated by

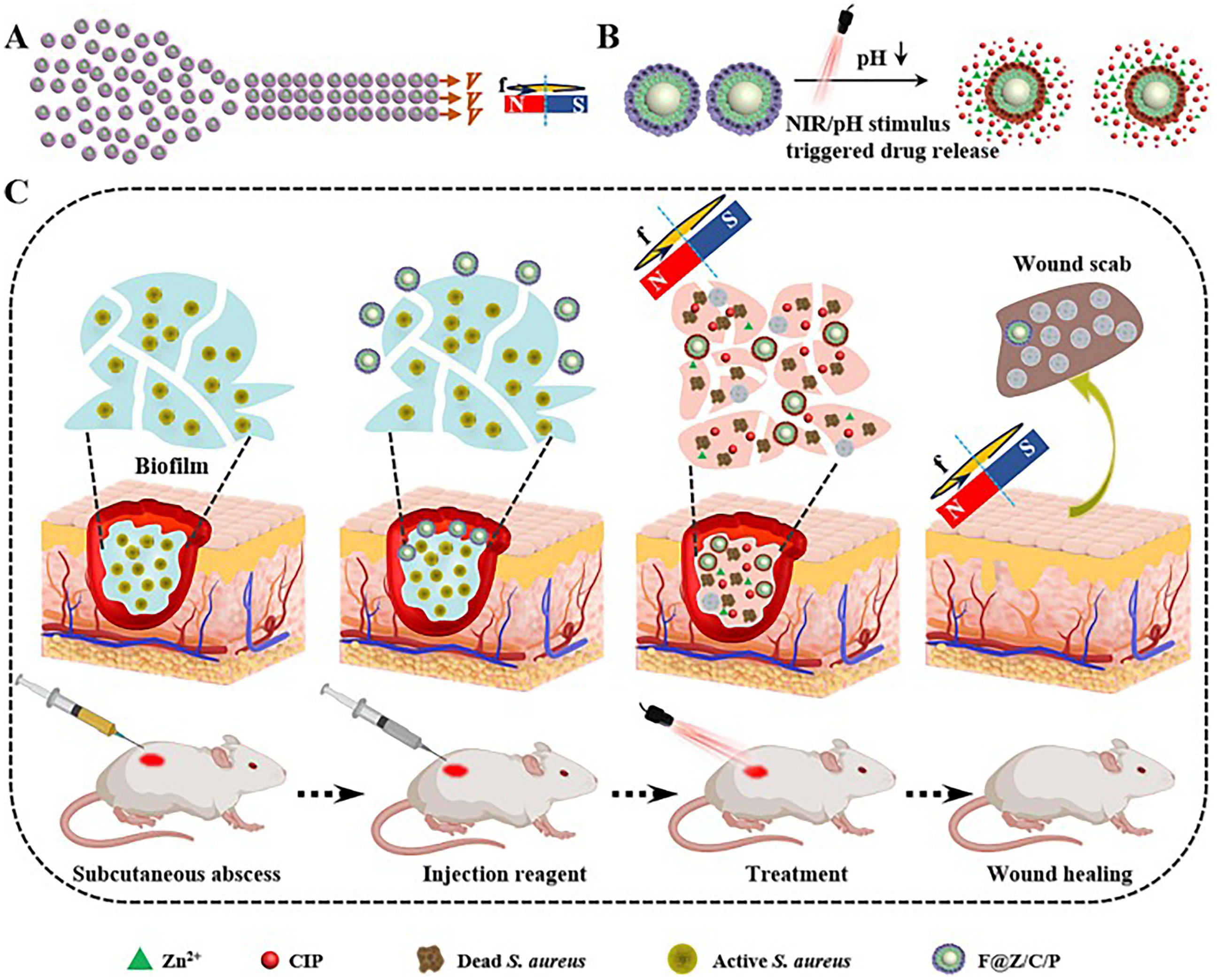

Figure 5 The schematic diagrams of the working principles of F@Z/C/P NRs. (**A**) The collective operating ability of a F@Z/C/P NR swarm. (**B**) The NIR/pH stimulated drug release. (**C**) The wound repair promoted by F@Z/C/P NRs.[50] The downward arrows indicate a decrease.

Figure 6 Schematic Illustration Showing the Fabrication Process of the MOF Micromotors and Their Antibacterial Wound Therapy.[51]
Notes: The spelling error "Antibicterial" "Coodinated" in the original figure have been retained from the cited source. The symbol "V" stands for voltage.

photothermal and NO-driven propulsion, executing combined photothermal therapy (PTT), photodynamic therapy (PDT), and NO-mediated antibacterial effects. This multifunctional platform showed excellent biocompatibility and significant antibacterial activity, efficiently disrupting biofilms and promoting wound healing, highlighting the potential of nanomotors for tackling refractory wound infections.[52]

Multifunctional antibacterial platforms based on Micro/nanorobots and micro/nanomotors enhance biofilm penetration, elevate local drug concentrations, and introduce synergistic therapies (eg, PTT, PDT, and antimicrobial ions).[53] These advances address critical limitations of conventional antibacterial strategies, paving the way for breakthrough interventions in chronic and infected wounds and offering feasible pathways for precision management of biofilm-related infections.

Microenvironment Modulation

The wound microenvironment plays a pivotal role in orchestrating tissue repair processes. In chronic wounds such as diabetic foot ulcers and pressure sores, pathological conditions—including acidic pH, excessive reactive oxygen species (ROS), persistent inflammatory cytokines, and aberrant protease activity—disrupt cellular functions and impede regeneration, significantly delaying wound closure.[54–59] Micro/nanorobots, with their miniaturized structures, intelligent response mechanisms, and multifunctional therapeutic modules, offer dynamic and precise strategies for modulating such hostile microenvironments.[60]

On one hand, Micro/nanorobots can be engineered to scavenge excess ROS by delivering antioxidant enzymes such as catalase or superoxide dismutase, or by incorporating nanozymes with intrinsic ROS-clearing capabilities. For instance, a MnO_2 nanomotor–hyaluronic acid composite smart dressing was developed that leveraged the autonomous diffusion of MnO_2 into deeper tissue layers. The system releases Mn^2+ in moist environments, enabling simultaneous antibacterial action, pro-angiogenesis, and ROS clearance. Activation of the Sirt1/Nrf2 signaling pathway further remodels the oxidative microenvironment, enhancing fibroblast migration and endothelial cell-driven angiogenesis. In animal models, this platform significantly promoted epithelial regeneration and collagen deposition, demonstrating a promising candidate for wound therapy with mechanical flexibility, facile fabrication, and microenvironment-modulating capacity[61] (Figure 7).

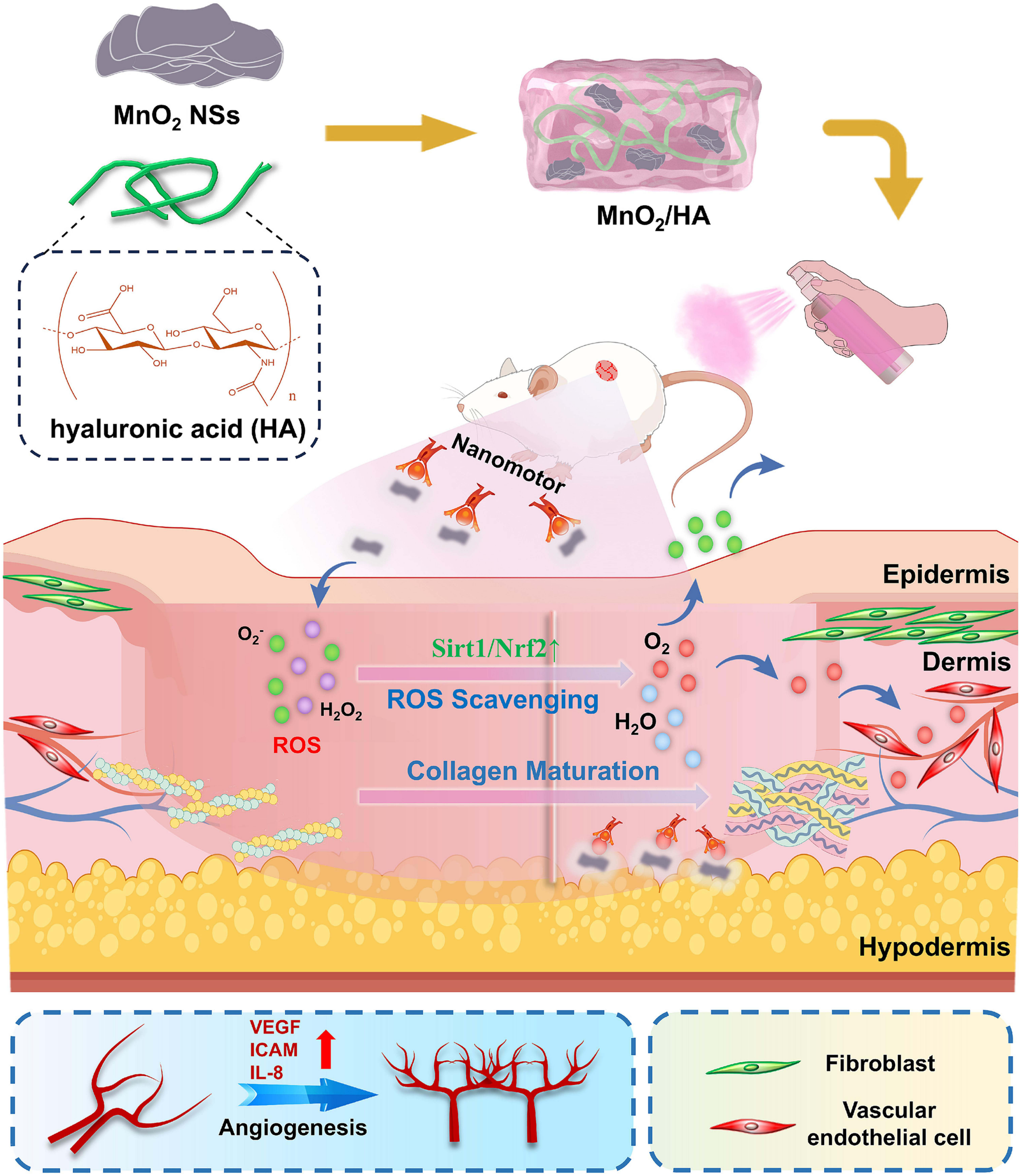

Figure 7 Illustration of the wound healing promotion mechanism of MnO_2/HA. MnO_2/HA nanomotor hybrid dressings may accelerate wound healing by addressing oxidative stress and promoting angiogenesis and re-epithelialization.[61] Red and green upward arrows indicate increase/upregulation in corresponding parameters.

For infected chronic wounds, such as MRSA-infected diabetic ulcers, a research team designed CSIL nanomotors co-loaded with indocyanine green (ICG) and lysostaphin (Ly). Under NIR irradiation, these nanomotors achieved autonomous motion and efficient biofilm penetration, enabling combined photothermal and photodynamic therapy (CPDT). By selectively clearing bacteria and modulating the local immune milieu—particularly promoting M2 macrophage polarization—the system accelerated wound healing. Compared with conventional antibiotics, this approach minimized thermal injury and ROS-related damage while achieving safer, more precise antibacterial intervention[62] (Figure 8).

Another innovation involved Janus-type Pt-MOF nanomotors integrated into smart sutures. These devices respond to endogenous H_2O_2 in the wound by generating oxygen bubbles, enabling self-propulsion for enhanced biofilm

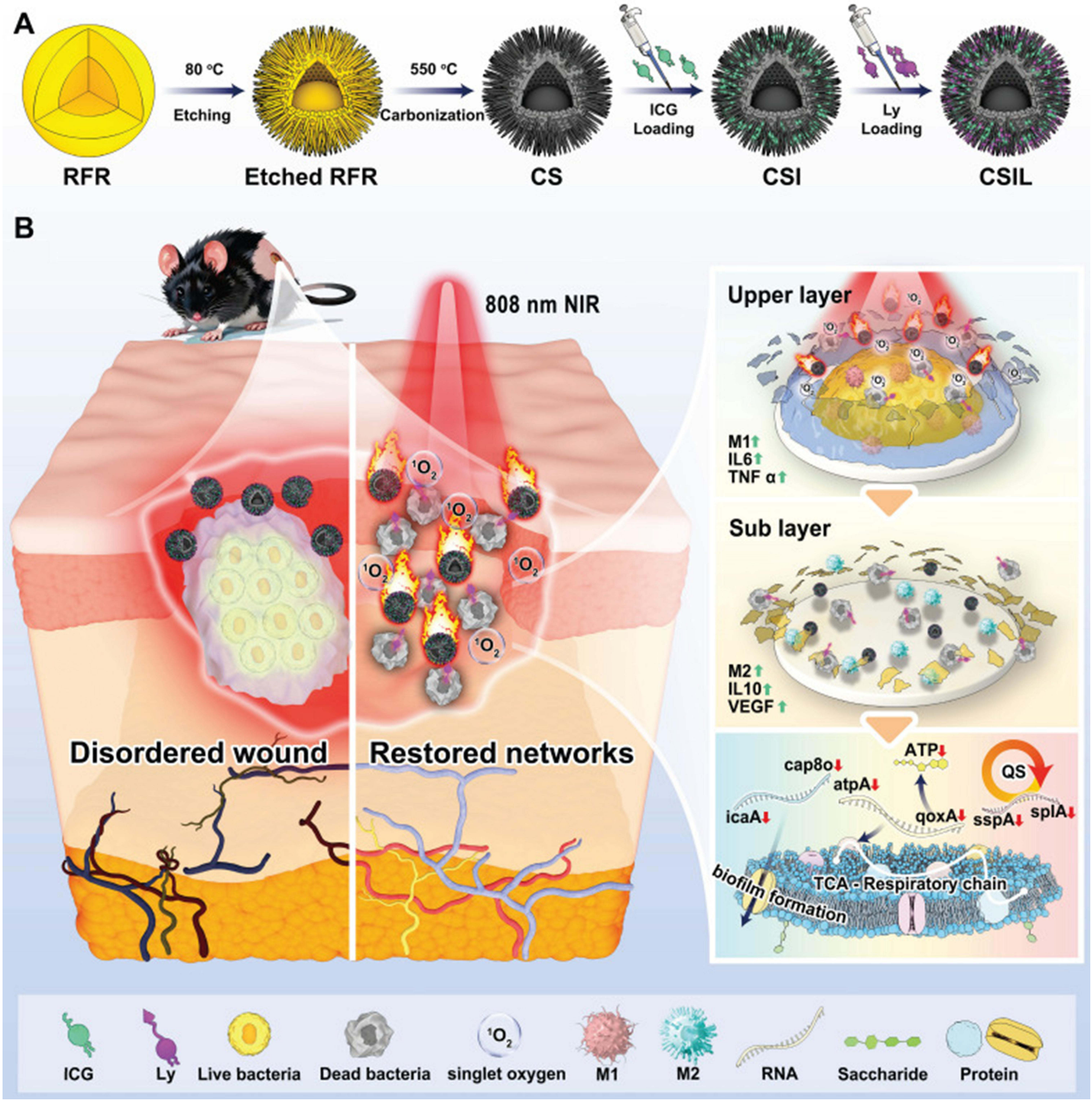

Figure 8 Schematic illustration of the formation and application of Pt-MOFs nanomotors. (**A**) Fabrication process of Pt-MOFs nanomotors coated sutures. (**B**) Infected microenvironment- activated Pt-MOFs nanomotors for bacterial monitoring and antibacterial activity. The red downward arrows indicate decrease/downregulation in corresponding parameters. The green upward arrow indicates upregulation of the parameter.[62]

penetration. Copper ions within the Pt-MOF structure participate in Fenton-like reactions, generating hydroxyl radicals for potent antibacterial effects. The system also provides imaging capabilities for real-time monitoring of infection progression. In vivo studies demonstrated that these sutures alleviated local inflammation, enhanced collagen deposition, and promoted epithelial regeneration, showing great potential for postoperative wound management[63] (Figure 9). By sensing pathological signals, clearing harmful factors, and reshaping oxidative and immune microenvironments, Micro/nanorobots achieve integrated "environment sensing–targeted intervention–multilevel modulation." This positions them as ideal carriers for next-generation intelligent wound healing platforms, accelerating their translational and clinical application.

Promotion of Tissue Regeneration

The ultimate goal of wound healing is the functional reconstruction of damaged tissue, including epithelial regeneration, angiogenesis, nerve repair, and restoration of skin appendages.[64,65] In chronic wounds such as diabetic foot ulcers, prolonged inflammation, cellular dysfunction, and impaired local microcirculation severely disrupt the regenerative process, often stalling wounds in the inflammatory or proliferative phase.[66,67] Micro/nanorobots, with their miniaturized designs, programmable intelligence, and responsive physical or chemical propulsion systems, have emerged as promising tools for promoting tissue regeneration.

Dermal fibroblasts are pivotal for skin regeneration, contributing to granulation tissue formation and extracellular matrix remodeling. However, under hyperglycemic, oxidative stress, and inflammatory conditions, fibroblast function is often markedly suppressed. To address this challenge, researchers developed a magnetically controlled gelatin–hesperidin microrobot system fabricated using microfluidics for precise structural control. Under a rotating magnetic field, these

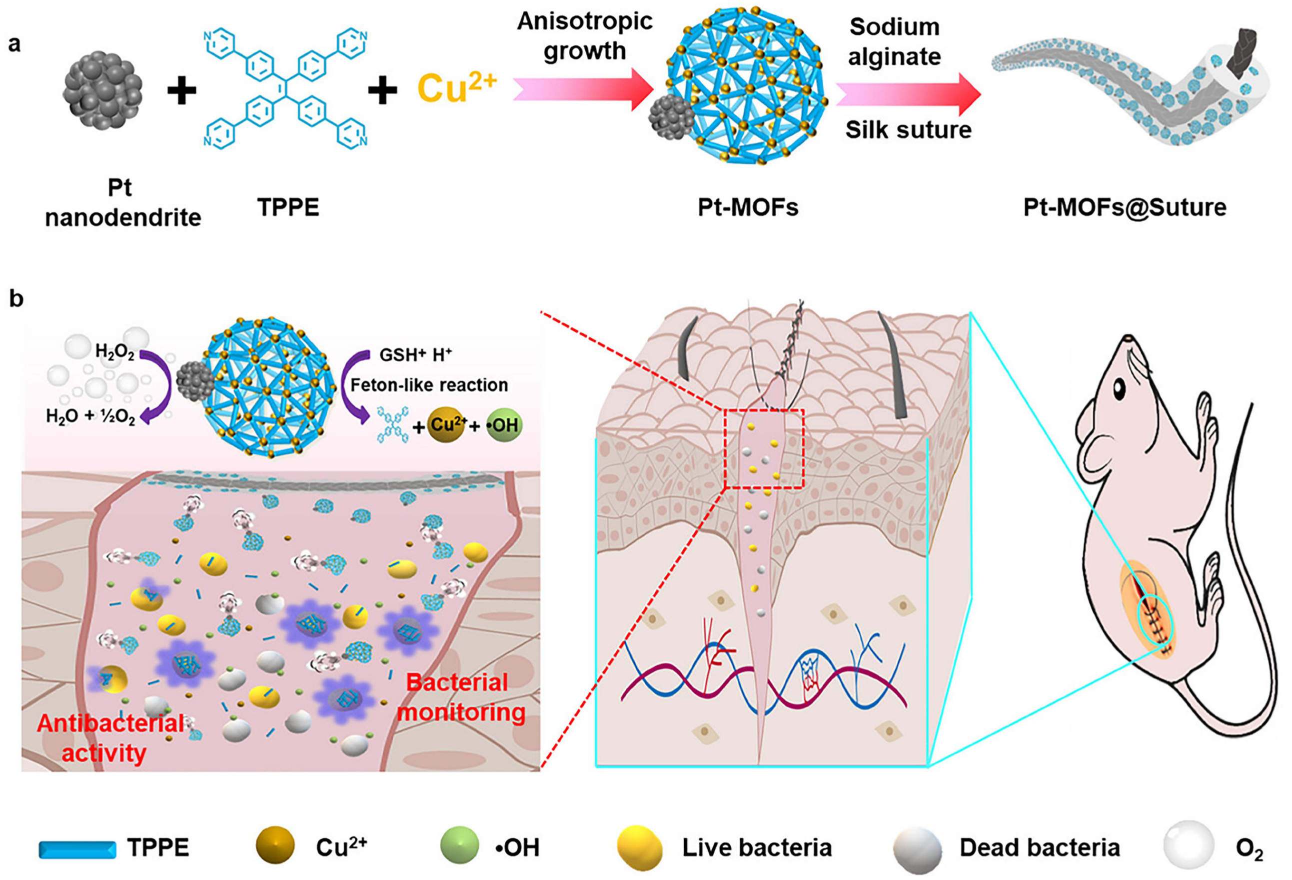

Figure 9 Schematic illustration of the formation and application of Pt-MOFs nanomotors. (**a**) Fabrication process of Pt-MOFs nanomotors coated sutures. (**b**) Infected microenvironment- activated Pt-MOFs nanomotors for bacterial monitoring and antibacterial activity.[63]

microrobots achieved controllable motion (maximum velocity of 9.237 μm/s). The system demonstrated excellent drug-loading capacity, releasing approximately 78% of hesperidin within 30 minutes. In vitro studies showed significantly enhanced migration and proliferation of human dermal fibroblasts under high-glucose conditions, coupled with outstanding biocompatibility.[68] This system provides a highly targeted and responsive intervention platform for regenerative therapy in diabetic chronic wounds, showing considerable translational potential.

Additionally, an innovative Au–SiO_2 nanorobot system powered by glucose oxidation was proposed, bypassing the need for exogenous drug release. Gold nanoparticles within the structure exhibit dual catalytic functionality, simultaneously oxidizing glucose and releasing bioactive signaling molecules such as H_2O_2. Controlled H_2O_2 release enabled "biochemical communication" within the wound microenvironment. Remarkably, low doses of H_2O_2 promoted cell migration and proliferation, whereas higher doses exerted inhibitory effects, demonstrating dose-dependent regulatory features[69] (Figure 10). This strategy marks the first realization of nanorobot-mediated precise linkage between "signaling molecule regulation" and "cellular behavior responses," opening a novel pathway for noninvasive, intelligent interventions in tissue regeneration. In summary, Micro/nanorobots not only serve as carriers for conventional therapeutic agents but also leverage motion propulsion, microenvironment sensing, and signaling molecule control to activate cellular behaviors, accelerate granulation tissue formation and angiogenesis, and drive chronic wound repair toward functional regeneration.

Smart Wound Care via Intelligent Systems

With the rapid advancement of nanotechnology, modern wound dressings are evolving from simple "passive barriers" to sophisticated "active response" platforms.[70,71] Leveraging the engineerable features of nanomaterials, nano-enabled wound dressings now allow for highly customizable functions and intelligent responsiveness to dynamic wound conditions.[70,72] These advanced dressings can modulate drug release precisely in response to variations in the wound microenvironment—such as pH, temperature, or inflammatory mediator levels—thereby effectively preventing the progression of chronic wounds. Their therapeutic mechanisms typically involve the controlled release of antibacterial agents, anti-inflammatory molecules, and multiple growth factors (eg, VEGF, EGF, FGF), synergistically promoting cell migration, proliferation, and re-epithelialization.[73,74] An ideal nano-enabled dressing should not only possess sufficient mechanical stability and a nanofiber-based architecture for strength and breathability but also offer excellent exudate absorption capacity. Moreover, it should maintain optimal wound hydration, regulate pH and oxygen supply, and provide on-demand therapeutic release tailored to individual wound healing phases.

As nanotechnology converges with frontier disciplines such as electronics, data science, and artificial intelligence (AI), wound therapy is entering an era of "intelligent care." In this paradigm, Micro/nanorobots transcend their role as mere drug carriers to become integral components of "diagnostic-therapeutic integrated systems". The concept of "smart wound care" emphasizes coupling the micromanipulation capabilities of micro/nanorobots with external intelligent platforms for data acquisition, analysis, and control. Together, these form a closed-loop therapeutic system equipped with real-time sensing, adaptive feedback, and precise intervention capabilities.[75,76] This system integrates microsensors, wireless communication modules, and responsive therapeutic carriers to dynamically monitor key wound parameters—including pH, temperature, humidity, ROS levels, and concentrations of inflammatory mediators. By processing these data through cloud-based or local AI algorithms, the system can autonomously adjust drug release timing, dosage, and delivery mode of Micro/nanorobots. This enables personalized wound treatment tailored to individual patients and specific wound types.[77,78]

To address the clinical need for continuous monitoring and closed-loop therapy in chronic refractory wounds, researchers recently developed a conformal, flexible implantable bioelectronic system. This platform integrates high-resolution amorphous silicon temperature sensor arrays and thermo-responsive drug-loaded hydrogels. With submillimeter spatial resolution and temperature sensitivity as high as 0.1°C, the system can precisely localize microthermal changes associated with local inflammation. External infrared LED irradiation then triggers targeted drug release from the hydrogel, establishing a seamless "sensing–feedback–intervention" triad. Both animal studies and preliminary human trials demonstrated excellent biocompatibility, mechanical flexibility, and practical utility, highlighting its strong translational potential for next-generation wound management[79] (Figure 11). By seamlessly integrating micro/nanorobots with

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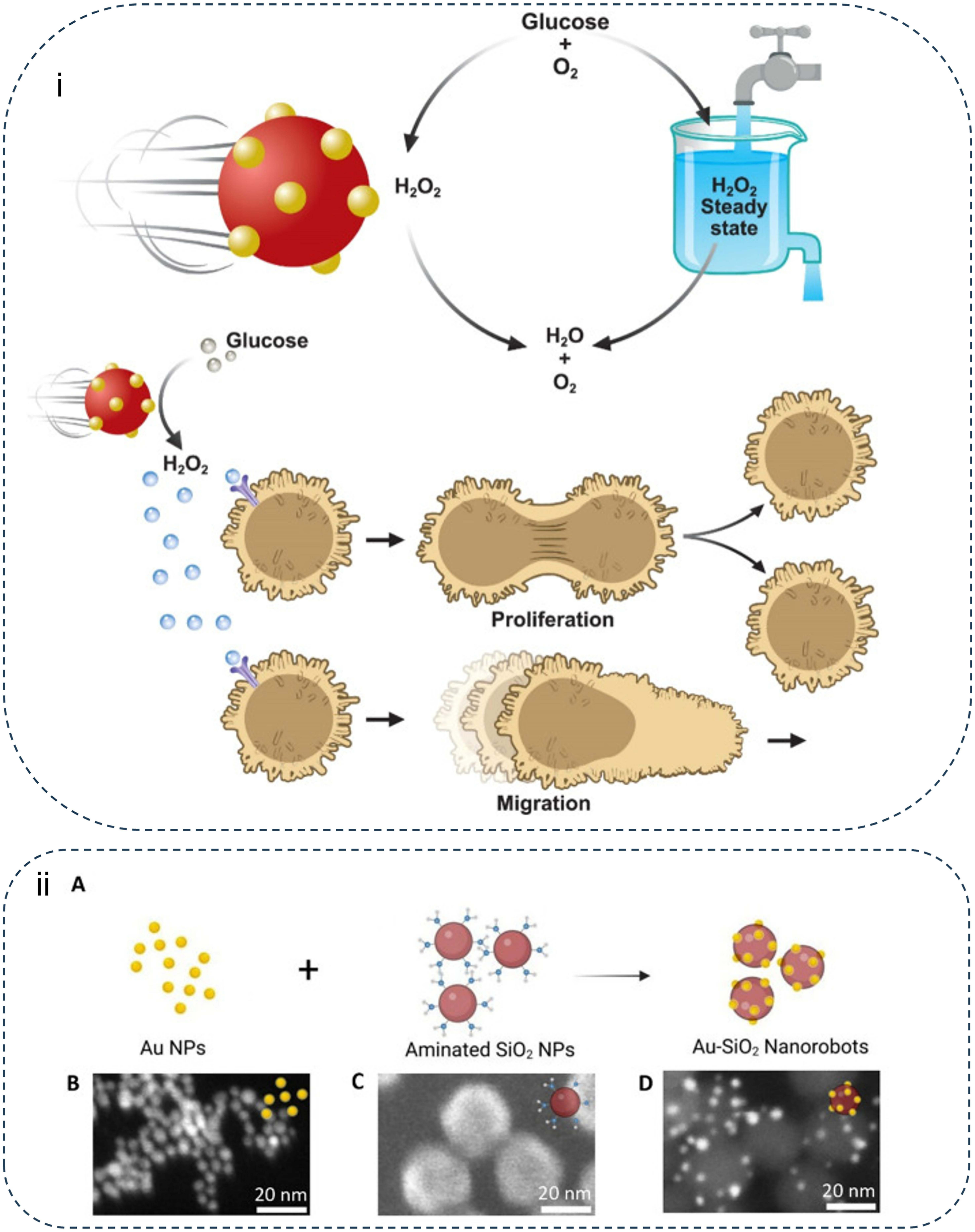

Figure 10 (i) Schematic representation of using Au-SiO_2 nanorobots to communicate with cells. Au-SiO_2 nanorobots catalytic conversion of glucose to H_2O_2, followed by its decomposition to H_2O and O_2 leading to the steady-state generation of H_2O_2. Application of nanorobots for inducing cell migration, where the self-regulated production of H_2O_2 acts as a signaling molecule to induce cell proliferation and cell migration. (ii) (A) Schematic representation of the construction steps of Au-SiO_2 nanorobots (Au-SiO_2 NRs). (B) STEM-HAADF image of Au NPs. (C) SEM image of aminated SiO_2 particles. (D) STEM-HAADF image of Au-SiO_2 nanorobots.[69]

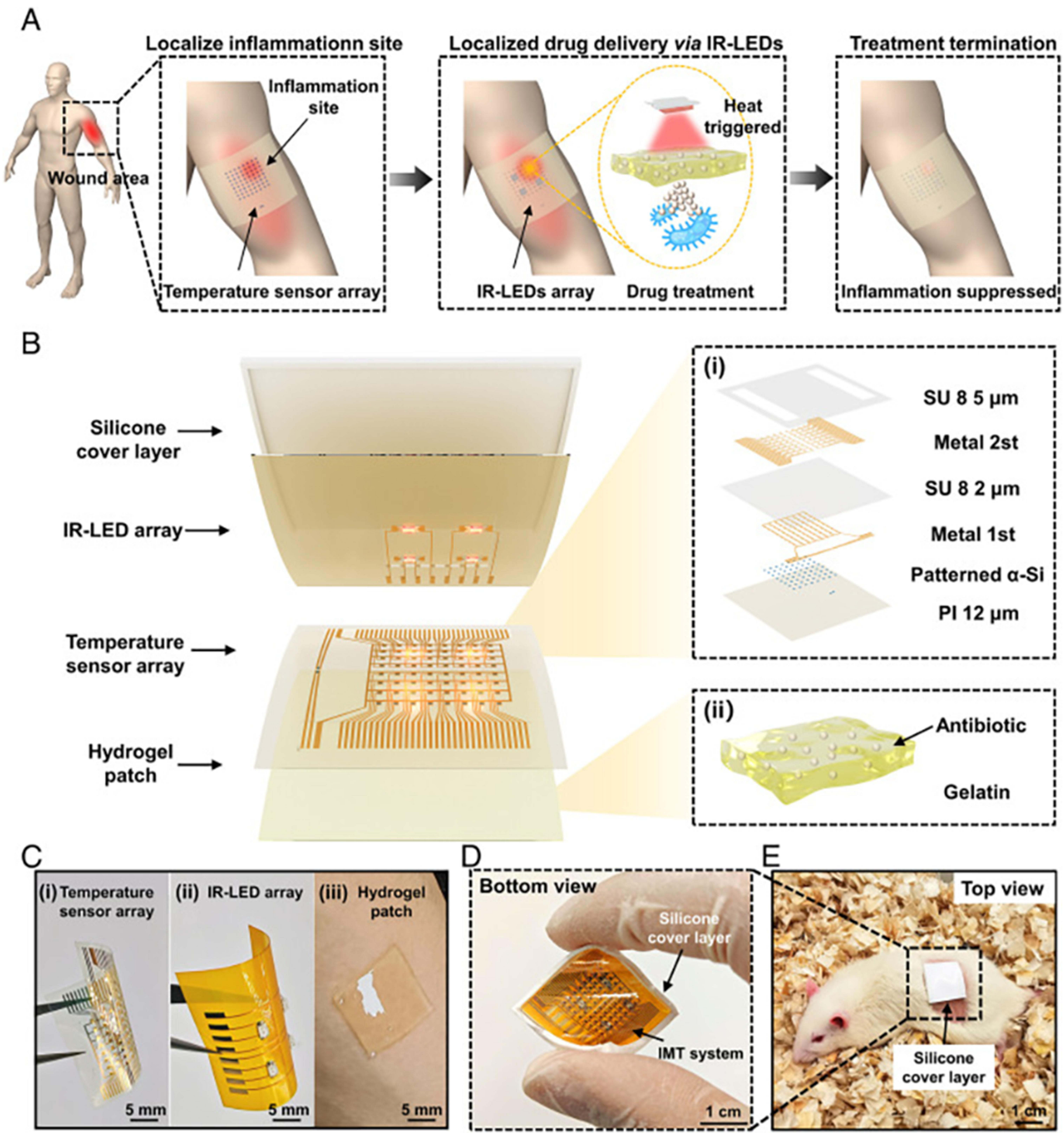

Figure 11 Design, structure, and functional schematic of IMT systems for inflammation monitoring and treatment. (**A**) Schematic diagram of the operation of IMT systems: The temperature sensor array detects a local temperature increase in the inflamed area, activating the IR-LED for in situ heat-triggered drug release from the hydrogel until inflammation is suppressed. (**B**) Exploded view illustration of the IMT systems: (i) exploded view illustration of the temperature sensor layer and (ii) enlarged view of the drug-loaded hydrogel. (**C**) Optical images of the three functional sections: (i) temperature sensor array, (ii) IR-LED array, and (iii) hydrogel patch, all without encapsulation of silicone cover layer. (**D**) Optical image of the fully assembled IMT system by the silicone cover layer from Bottom view. (**E**) Photograph of the IMT system with silicone cover layer seamlessly attached on the skin of the rat, as for a Top view.[79]

biosensing systems, responsive biomaterials, and AI-driven platforms, smart wound care offers an intelligent, personalized, and adaptive approach to wound monitoring and treatment. This innovative paradigm represents a major leap forward toward precision wound therapy, paving the way for clinical systems capable of real-time decision-making and autonomous intervention.

Translational Challenges and Clinical Pathways

Despite the promising laboratory advances of micro/nanorobots in wound healing, their clinical translation remains fraught with significant challenges. The foremost concern lies in biocompatibility and long-term safety. Micro/nanorobots are constructed from diverse materials—including metals, synthetic polymers, and bioinspired coatings such as cell membranes—each of which may degrade into byproducts with potential cytotoxicity or immunogenicity within the human body.[80] Moreover, the pharmacokinetics of micro-/nanorobots, including their biodistribution, metabolism, and clearance pathways, remain incompletely understood. Unintended accumulation in non-target tissues and potential chronic toxicity represent critical safety issues that must be rigorously addressed.[81] Future research should prioritize the design of Micro/nanorobots from naturally degradable and bioinspired materials, with optimized size, surface chemistry, and dynamic behaviors to enhance their biocompatibility and minimize adverse immune responses.[82]

A second major hurdle involves scalable manufacturing and standardization. The fabrication of Micro/nanorobots entails sophisticated micro/nano-architectures and multi-functional module integration, making the production process technically complex and cost-prohibitive. To date, there is a lack of mature industrial-scale production technologies and no unified standards for quality control and performance evaluation, which hampers the consistency and reproducibility of the final products. Future directions must focus on developing high-throughput, cost-effective fabrication techniques and establishing robust safety assessment protocols and standardized testing frameworks to enable regulatory compliance and clinical deployment. Regulatory uncertainty further compounds the translational barrier. As a novel class of "micro-scale medical devices," Micro/nanorobots do not fit neatly into existing categories of pharmaceuticals or medical devices. Defining their regulatory status, risk assessment criteria, and approval pathways within current healthcare frameworks requires careful deliberation and global consensus-building.

Despite these challenges, the clinical outlook for Micro/nanorobots in wound care remains highly promising. In recent years, nano-enabled materials and microdevices have successfully entered clinical trials, such as virtual reality and AI-based wound monitoring systems (eg, NCT06367179), offering valuable precedents for nanorobot translation. Moving forward, interdisciplinary collaboration—spanning nanoscience, materials engineering, biomedical sciences, and clinical medicine—will be pivotal to accelerating progress. Building effective translational bridges between preclinical animal studies and human clinical trials, while ensuring ethical and regulatory compliance, may ultimately enable micro/nanorobots to transition from laboratory innovation to real-world wound management. This paradigm shift holds the potential to inaugurate a new era of intelligent, precision-guided wound therapy.

Future Perspectives and Challenges

Although nanorobotics has made remarkable strides in the field of wound healing, technology remains in a stage of rapid evolution and innovation.[35] As breakthroughs continue in materials science, micro/nanofabrication, and intelligent algorithms, Micro/nanorobots are poised to achieve higher levels of autonomy, intelligence, and multifunctional integration shortly.[21,83] One key direction is the development of intelligent micro/nanorobots with autonomous navigation and decision-making capabilities. Leveraging advances in sensor technology and artificial intelligence (AI), such systems could perform real-time sensing of complex wound microenvironments, process multidimensional data streams, and dynamically adapt therapeutic strategies. This would enable truly personalized and responsive wound management.[19] Moreover, bioinspired Micro/nanorobots—engineered from natural biological templates—offer the combined advantages of inherent biocompatibility and functional versatility, presenting significant potential for applications in both biomedicine and environmental remediation.[84]

A second emerging trend is the design of multimodal therapeutic platforms. Future Micro/nanorobots will extend beyond drug delivery to integrate diverse treatment modalities such as photothermal therapy, ultrasound stimulation, electrical signaling, and immunomodulation. By harnessing synergistic effects, these systems can address the multifactorial nature of chronic wounds and accelerate healing. The incorporation of biodegradable and smart-responsive materials will further enhance their biocompatibility and therapeutic efficacy while minimizing residual risk within the body.[85] Coupled with cutting-edge technologies such as gene editing and stem cell therapy, Micro/nanorobots hold promise as precision tools for modulating cellular behavior and facilitating tissue regeneration.

Finally, the convergence of nanorobotics with digital health technologies could herald a new era of "smart wound care." Integration with human–machine interfaces, machine learning, neural networks, and 3D/4D printing technologies will enable seamless, personalized healthcare solutions.[86,87] Future smart wound management systems may transcend traditional hospital-based models, extending care into the community and home settings. This shift could dramatically improve patient quality of life and optimize the allocation of healthcare resources. In summary, as interdisciplinary collaboration deepens, nanorobotics is set to become a pivotal technology in wound healing and regenerative medicine, unlocking expansive possibilities for clinical translation and ushering in an era of intelligent, precision-guided wound therapy.

Despite rapid advances in micro/nanorobot technologies, several fundamental challenges hinder their clinical translation. Biocompatibility and toxicity remain major concerns, as immune recognition, oxidative stress from chemical fuels, and long-term accumulation risks are poorly characterized in chronic exposure studies. Manufacturing scalability poses another bottleneck, as current fabrication methods are complex, costly, and lack reproducibility for large-scale production. Navigation and localization in dynamic and heterogeneous biological environments remain unresolved due to limited real-time imaging integration and disturbance from physiological flows. In vivo stability is compromised by enzymatic degradation, protein adsorption, and premature drug release, reducing functional lifespan. Furthermore, regulatory and ethical hurdles—including the absence of standardized safety frameworks, unclear classification between device and drug, and the lack of completed clinical trials—continue to delay clinical adoption. Addressing these challenges will require interdisciplinary innovations, standardized evaluation protocols, scalable manufacturing strategies, and early regulatory engagement to accelerate safe and effective translation into clinical practice.

Conclusion

Nanorobotics offers significant advantages in wound healing, including targeted drug delivery, biofilm penetration, antibacterial action, immune modulation, and tissue regeneration, enabling multidimensional and personalized therapies. Integration with smart systems allows real-time monitoring and adaptive interventions, paving the way for "smart wound care." However, challenges remain, such as biosafety concerns, limited manufacturing scalability, navigation and stability in complex biological environments, and regulatory hurdles, which hinder clinical translation. With ongoing interdisciplinary innovation and technological optimization, micro/nanorobots hold great potential to transform wound management, offering precise, efficient, and individualized treatment strategies.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article and its references.

Consent Statement

No individual personal data is included in the study.

Funding

This study was supported by grants from Hubei Provincial Natural Science Foundation of China (No. 2023AFB825) and Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (No. 2023A15).

Disclosure

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest. Yukun Liu and Kang Wang are co-first authors.

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