

LETTER

Polymeric Microneedles as Analytical Interfaces for Biosensing and Controlled Drug Release: Achievements and Future Challenges

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Microneedle technology has emerged as one of the most dynamic and interdisciplinary frontiers in biomedical science, enabling a unique convergence between analytical chemistry, materials engineering, and clinical diagnostics.¹ Originally developed to overcome the mechanical and diffusional barriers imposed by the stratum corneum, microneedles (MNs) allow precise and minimally invasive access to the epidermal and dermal layers of the skin. This access enables controlled transport of drugs, biomolecules, or diagnostic reagents while avoiding the pain, fear, and infection risks associated with conventional hypodermic needles.²

Over the past decade, advances in polymer chemistry, microfabrication, and electrochemical detection have transformed MNs from passive drug delivery tools into multifunctional analytical interfaces capable of both monitoring and treating physiological conditions in real time.

Among the different materials explored, polymeric microneedles have demonstrated remarkable versatility, owing to their biocompatibility, chemical tunability, and mechanical resilience. Natural and synthetic polymers, such as polylactic acid (PLA), polycaprolactone (PCL), hyaluronic acid (HA), and conductive polymers like polypyrrole (PPy) and poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS), have enabled the design of devices that combine flexibility, biodegradability, and electrical conductivity within the same platform.¹

These features have not only enhanced safety and patient compliance but also expanded the range of applications, particularly in biosensing and controlled drug release.^{3,4} Recent approaches have integrated electrochemical transducers and responsive materials into microneedle arrays, enabling continuous monitoring of metabolites or biomarkers in interstitial fluid (ISF) while simultaneously allowing on-demand release of therapeutic agents.⁵ In this context, polymeric microneedles have evolved into active analytical–therapeutic systems that function as both sensors and actuators within a single miniaturized interface.

The analytical potential of these devices lies in their ability to access ISF, a complex biological matrix that mirrors systemic biochemical changes. Electrochemical detection of glucose, lactate, uric acid, or inflammatory cytokines using polymeric microneedle electrodes exemplifies a new generation of wearable sensors capable of continuous, non-invasive operation.⁶

The integration of nanostructured conductive polymers and metal nanoparticles has enabled high electroactive surface areas, improved charge-transfer kinetics, and selective immobilization of biorecognition elements, such as enzymes, antibodies, or aptamers.^{1,7,8} These characteristics are essential for achieving the sensitivity, reproducibility, and temporal resolution required for real-time clinical analysis.

Although substantial progress has been made, ensuring long-term reliability remains a major challenge. Stable electrical performance in hydrated environments, resistance to biofouling, and mechanical robustness under repeated use are essential prerequisites for successful clinical translation.

From a therapeutic perspective, polymeric microneedles have demonstrated significant potential as platforms for controlled, localized drug delivery. The intrinsic versatility of polymeric matrices allows modulation of degradation, permeability, and responsiveness, enabling precise control over release kinetics.^{9,10}

When combined with electroactive or stimuli-responsive polymers, these systems can respond dynamically to environmental or external factors such as pH, temperature, electric potential, or mechanical pressure. This behavior enables tailoring the temporal and spatial profiles of drug administration, ensuring efficient and patient-friendly delivery.

Additionally, the inherent biocompatibility and degradability of polymers minimizes residual waste and eliminates the need for device removal, an important advantage for chronic or long-term therapeutic applications.

The multifunctional nature of these materials also facilitates the coupling of sensing and release mechanisms within a single structure, laying the foundation for self-regulated systems.⁴ In these configurations, microneedles can operate as closed-loop devices, where local biochemical variations detected at the skin interface can trigger or modulate the release of therapeutic agents. This integration of analytical and therapeutic functionalities highlights the transformative role of polymeric microneedles in advancing personalized medicine and point-of-care technologies.

Despite this progress, translating polymeric microneedles into clinical practice requires overcoming critical technological and analytical limitations.¹ Optimizing geometry, tip sharpness, and mechanical robustness is essential to ensure consistent skin penetration without fracture or deformation. Additionally, the surface chemistry of polymer surfaces must be tailored to enable covalent or electrostatic immobilization of biomolecules while preventing nonspecific adsorption that can impair analytical signals.

Advanced fabrication techniques, including micromolding, laser micromachining, and high-resolution 3D printing, have expanded design possibilities, enabling precise control over microneedle dimensions, porosity, and functional gradients. However, large-scale reproducibility and regulatory validation remain major barriers for commercialization. From an analytical standpoint, coupling microneedle sensors with portable potentiostats, flexible electronics, and wireless data transmission modules is essential for transforming laboratory prototypes into reliable wearable devices.

The future of polymeric microneedles lies in the development of integrated analytical and therapeutic platforms that can operate autonomously and safely for prolonged periods. The convergence of conductive polymers, nanocomposites, and biocompatible hydrogels with emerging technologies, such as microfluidics, data analytics, and artificial intelligence, will enable real-time interpretation of biochemical signals and dynamic therapeutic adjustments.

In parallel, the analytical chemistry community plays a central role in ensuring metrological traceability, calibration accuracy, and long-term stability of microneedle-based biosensors, thereby consolidating their reliability in clinical diagnostics.

Ultimately, polymeric microneedles represent a paradigm shift in analytical science applied to health. They embody a fusion of analytical precision, material innovation, and biomedical functionality, transforming the skin into an accessible, information-rich analytical interface. By bridging biosensing and controlled drug release, these systems hold the promise of revolutionizing point-of-care testing, personalized medicine, and minimally invasive therapies. As new challenges emerge—from scalable fabrication to regulatory compliance—the integration of analytical chemistry principles will remain fundamental to unlocking the full potential of this technology, ensuring that microneedles continue to evolve as versatile tools at the intersection of diagnosis, monitoring, and therapy.

REFERENCES

- (1) Alves, W. A.; Rojas, J. E. U.; Castro, A. C. H.; Kochi, L. T.; Reis, A. C. D. L. V.; Esteves, F. A. N.; Ferreira, P. S.; Castro, F. L.; Otoni, R. C.; Barreto, J. B.; et al. Polymeric Microneedles for Biomedical Applications: Innovations in Transdermal Drug Delivery and Biosensing Technologies. *Biomed. Mater. Devices* **2025**, 1-38. <https://doi.org/10.1007/s44174-025-00330-4>

- (2) Rojas, J. E. U.; Oliveira, V. L.; Araújo, D. R.; Tofoli, G. R.; Oliveira, M. M.; Carastan, D. J.; Palaci, M.; Giuntini, F.; Alves, W. A. Silk fibroin/poly(vinyl alcohol) microneedles as carriers for the delivery of singlet oxygen photosensitizers. *ACS Biomater. Sci. Eng.* **2022**, *8*, 128-139. <https://doi.org/10.1021/acsbiomaterials.1c00913>
- (3) GhavamiNejad, P.; GhavamiNejad, A.; Zheng, H.; Dhingra, K.; Samarikhajaj, M.; Poudineh, M. A Conductive Hydrogel Microneedle-Based Assay Integrating PEDOT:PSS and Ag-Pt Nanoparticles for Real-Time, Enzyme-Less, and Electrochemical Sensing of Glucose. *Adv. Healthcare Mater.* **2023**, *12* (1), 2202362. <https://doi.org/10.1002/adhm.202202362>
- (4) Yang, Y.; Xu, L.; Jiang, D.; Chen, B. Z.; Luo, R.; Liu, Z.; Qu, X.; Wang, C.; Shan, Y.; Cui, Y.; Zheng, H.; Wang, Z.; Wang, Z. L.; Guo, X. D.; Li, Z. Self-Powered Controllable Transdermal Drug Delivery System. *Adv. Funct. Mater.* **2021**, *31* (36), 2104092. <https://doi.org/10.1002/adfm.202104092>
- (5) Yang, J.; Zheng, S.; Ma, D.; Zhang, T.; Huang, X.; Huang, S.; Chen, H.-J.; Wang, J.; Jiang, L.; Xie, X. Masticatory system-inspired microneedle theranostic platform for intelligent and precise diabetic management. *Sci. Adv.* **2022**, *8*, eabo6900. <https://doi.org/10.1126/sciadv.abo6900>
- (6) Tehrani, F.; Teymourian, H.; Wuerstle, B.; Kavner, J.; Patel, R.; Furnidge, A.; Aghavali, R.; Hosseini-Toudeshki, H.; Brown, C.; Zhang, F.; et al. An integrated wearable microneedle array for the continuous monitoring of multiple biomarkers in interstitial fluid. *Nat. Biomed. Eng.* **2022**, *6*, 1214-1224. <https://doi.org/10.1038/s41551-022-00887-1>
- (7) Reis, A. C. D. L. V.; Castro-Kochi, A. C. H.; Rojas, J. E. U.; Chiaro, D.; Guha, S.; King, G. M.; Oliveira, V. L.; Araújo, D. R.; Tofoli, G. R.; Romero, M.; et al. Polypyrrole-Coated Microneedle Platform for Offline Electrochemical Detection of Interferon-Alpha in Interstitial Fluid. *ACS Appl. Bio Mater.* **2025**, submitted.
- (8) Sabaine, A. E.; Castro, A. C. H.; Mancini, R. S. N.; Araujo-Silva, M. R.; Sepulveda, A. F.; Oliveira, J. R.; Remuzgo, C.; Santos, K. S.; Oliveira, V. L.; Kochi, L. T.; et al. Peptide-Based Biosensors for Variant-Specific Detection of SARS-CoV-2 Antibodies. *Mater. Adv.* **2025**, *6*, 7090-7103. <https://doi.org/10.1039/D5MA00485C>
- (9) Yang, Y.; Xu, L.; Jiang, D.; Chen, B. Z.; Luo, R.; Liu, Z.; Qu, X.; Wang, C.; Shan, Y.; Cui, Y.; et al. Self-Powered Controllable Transdermal Drug Delivery System. *Adv. Funct. Mater.* **2021**, *31*, 2104092. <https://doi.org/10.1002/adfm.202104092>
- (10) Rojas, J. E. U.; Andrade, L. M.; Giuntini, F.; Alves, W. A. Development and Characterization of Silk Fibroin-Enriched 3D Printed Hydrogels for Photosensitizer Delivery. *Materialia* **2025**, *40*, 102402. <https://doi.org/10.1016/j.mtla.2025.102402>



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