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Introduction to MXene chemistries in biology, medicine and sensing

Maksym Pogorielov, *[a,b] Açelya Yilmazer, *[c,d] Lucia Gemma Delogu *[e,f] and Yury Gogotsi *[g]

Maksym Pogorielov

Maksym Pogorielov is the Head of the Advanced Biomaterials and Biophysics Laboratory at the University of Latvia (Latvia) and leads the Biomedical Research Centre at Sumy State University (Ukraine). His research focuses on tissue engineering and regenerative medicine; antibacterial and anticancer strategies; and the development of advanced materials for medical implants. A key aspect of his work involves the exploration of MXenes and other two-dimensional (2D) materials for biomedical applications, including their interactions with biological systems.

Açelya Yilmazer

Açelya Yilmazer is an associate professor at the Biomedical Engineering Department of Ankara University, Turkey. Her research group works on the preclinical evaluation of nanomaterials with specific focus on anti-cancer and anti-viral development. She has pioneered the use of various novel 2D nanomaterials for photodynamic and photothermal therapy for cancer. She has received the Best Young Investigator Award by the Turkish Society of Medical Biology and Genetics (2013), Young Investigator Award by the Turkish Academy of Sciences (2018), the Scientific Encouragement Award by Ankara University (2019) and the Young Women Scientist Award in 2023 by L'Oréal Turkey and the UNESCO National Commission.

Lucia Gemma Delogu

Lucia Gemma Delogu is an associate professor at the Khalifa University of Science and Technology, United Arab Emirates, and the University of Padua, Italy, where she is head of the ImmuneNanolab at the Department of Biomedical Science. She has coordinated several multidisciplinary consortia funded by the European Commission involving over 60 research groups worldwide. She pioneered the use of single-cell mass cytometry in nanotechnology and in the context of MXenes. Her work focuses on their interaction with the immune system and their development for biomedical applications, from immunotherapy to tissue engineering and space biology.

[a]*Sumy State University, 116 Kharkivska Street, Sumy, 40007, Ukraine. E-mail: maksym.pogorielov@lu.lv*
[b]*University of Latvia, 3 Jelgavas Street, Riga, LV-1004, Latvia*
[c]*Department of Biomedical Engineering, Ankara University, Golbasi, Ankara, 06830, Turkey. E-mail: acelya.yilmazer.aktuna@ankara.edu.tr*
[d]*Stem Cell Institute, Ankara University, Balgat, Ankara, 06520, Turkey*
[e]*Khalifa University of Science & Technology, Abu Dhabi, United Arab Emirates. E-mail: luciagemma.delogu@unipd.it*
[f]*ImmuneNano-Lab, Department of Biomedical Sciences, University of Padua, Padua, Italy*
[g]*A.J. Drexel Nanomaterials Institute and Department of Materials Science and Engineering, Drexel University, 3141 Chestnut St, Philadelphia, PA 19104, USA. E-mail: yg36@drexel.edu*

MXenes, a family of two-dimensional transition metal carbides and nitrides (general formula $M_{n+1}X_nT_x$), have rapidly risen to prominence as materials for applications in life sciences. First discovered just over a decade ago,[1] MXenes have been described as transformative in the realm of healthcare materials, stimulating intense interest for their biomedical applications.[2] Their unique combination of properties – including excellent electrical conductivity, large surface area, rich surface chemistry, and strong photothermal conversion – makes them highly attractive for a broad range of uses. Initially explored for energy storage and catalysis, MXenes now enable new possibilities in biology and medicine, from biosensors and bioelectronics to drug delivery and regenerative therapy.[3] Just as importantly, researchers have found MXenes to be broadly biocompatible in preliminary studies, with generally low cytotoxicity observed *in vitro* and *in vivo* (though some effects vary with dose, cell type, and MXene composition).[4] This favorable early safety profile further underscores their potential for clinical translation. In this themed issue on "MXene Chemistries in biology, medicine, and sensing", we introduce the state-of-the-art developments that highlight how MXene chemistry can be leveraged for cutting-edge biomedical and sensing technologies (Fig. 1). Below, we discuss the major aspects covered – from bioactive surface functionalization and therapeutic applications to sensing technologies and scale-up challenges – maintaining a balance of technical depth and accessibility for a broad readership.

A defining feature of MXenes is their tunable surface chemistry. Synthesis by selective etching of MAX-phase precursors leaves MXene sheets terminated with functional groups T_x (such as =O, –OH, –F, –Cl, *etc.*), which can be further modified or exchanged.[5] This chemistry leads to hydrophilicity and easy dispersion of MXenes in aqueous solutions. It is also responsible for good contact and low contact impedance of MXene films/electrodes with skin and tissue. Therefore, epidermal and implantable MXene electrodes outperform noble metals and graphene in the signal-to-noise ratio. It is also a powerful handle to impart bioactive functionality. By grafting polymers, biomolecules, or inorganic coatings onto MXene surfaces, researchers can tailor properties like dispersion stability, biocompatibility, targeting ability, and reactivity, to suit specific biological and sensing applications. Indeed, MXenes have already been employed in an array of biomedical contexts – including biosensing, bioimaging, cancer therapy, infection control, bone regeneration, and wound repair – owing to their favorable physicochemical properties and inherent bioactivity.[6] As highlighted in one of the key reviews of this issue by Li *et al.*, surface modification strategies enable the design of multifunctional MXene-based nanomaterials that achieve enhanced therapeutic effects and biological performance (**https://doi.org/10.1039/D4NR04260C**). For example, coating MXene flakes with bioactive polymers or peptides can promote cell adhesion and tissue integration, while also allowing the conjugation of drugs or growth factors. Such engineered MXenes have shown promise in tissue regeneration scaffolds and in tumor therapies, where they can combine structural support with on-demand therapeutic release or stimuli-responsive behavior. The ability to fine-tune MXenes' surface chemistry will undoubtedly remain central to expanding their biomedical utility, as it allows integration of MXenes with the complex biological environments in a controlled and targeted manner.

MXenes' exceptional electrical conductivity and chemical versatility have catalyzed their rapid adoption in sensing technologies. In particular, MXene-based electrochemical sensors and biosensors have attracted considerable attention for health monitoring and diagnostic applications.[7] Their 2D morphology offers a high active surface area, and the abundant surface functional groups facilitate the immobilization of biomolecular probes (such as antibodies, DNA aptamers, or enzymes) for selective analyte recognition. These attributes enable MXene sensors to achieve high sensitivity and fast response times in detecting biomarkers, pathogens, and metabolites relevant to human health, as indicated in several articles of this themed issue (**https://doi.org/10.1039/D4NR04060K**, **https://doi.org/10.1039/D4NR04388J**, **https://doi.org/10.1039/D4NR04333B**, **https://doi.org/10.1039/D4NR03008G**, **https://doi.org/10.1039/D4NR03984J**). Recent advances have demonstrated MXene-enhanced detection of cancer biomarkers, glucose, neurochemicals, and even viral antigens, often with performance rivaling or surpassing traditional nanomaterials. Notably, MXenes can be integrated into microfluidic platforms and flexible electronics, supporting the development of portable point-of-care devices. Their conductive networks improve signal transduction, while their chemistry allows tuning sensor surfaces to minimize fouling in complex biofluids. For example, MXene-based electrodes in wearable patches can continuously monitor physiological signals or bio-

Yury Gogotsi

Yury Gogotsi is Director of the A.J. Drexel Nanomaterials Institute, Distinguished University Professor and Charles T. and Ruth M. Bach Professor of Materials Science and Engineering at Drexel University. He received his BS/MS (1984, metallurgy) and PhD (1986, physical chemistry) from Kyiv Polytechnic and a DSc degree from the Ukrainian Academy of Sciences in 1995. He works on 2D carbides and nitrides (MXenes), which he discovered with his students and collaborators, and their applications in energy, optoelectronics, communication, and medicine.

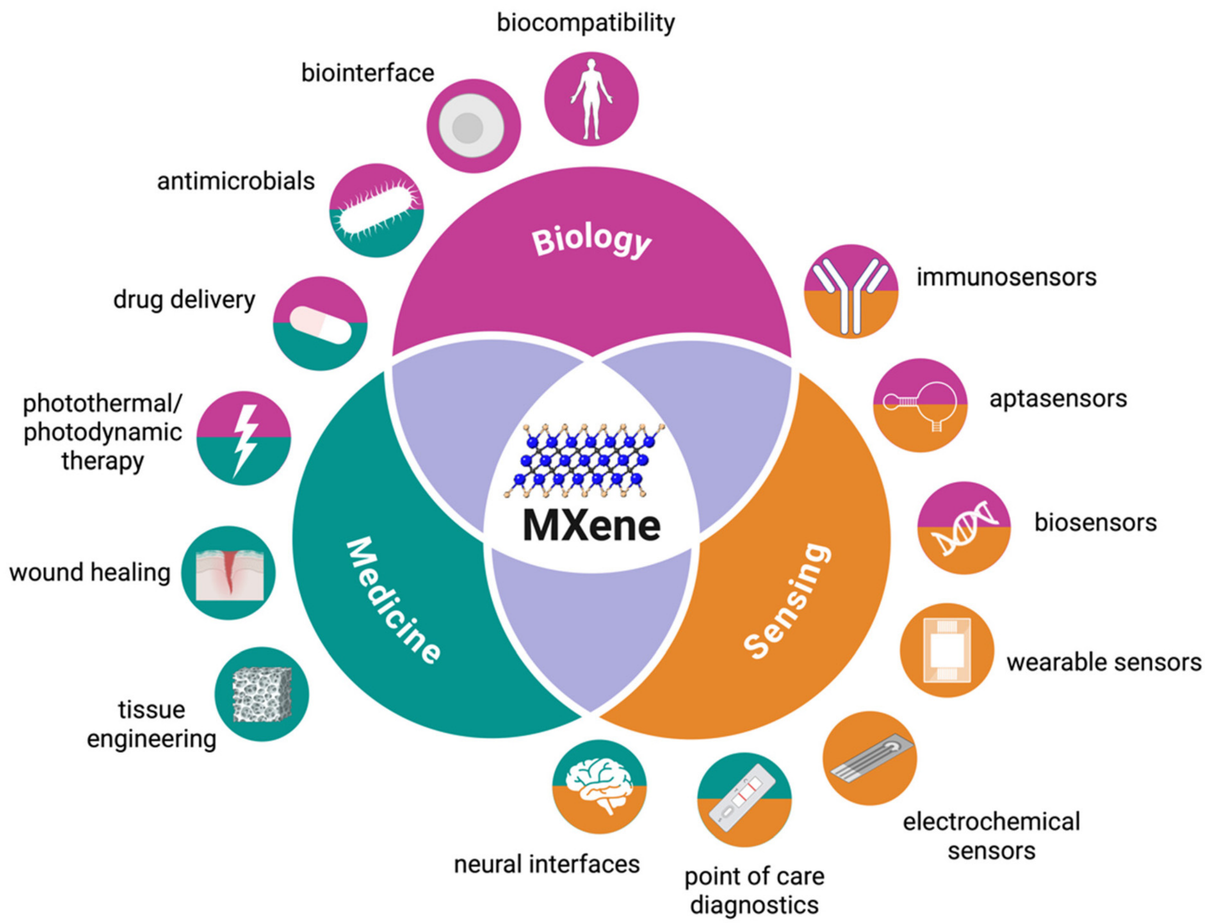

Fig. 1 MXene chemistries addressing the current challenges in biology, medicine and sensing. Created in BioRender.

chemical markers in sweat and interstitial fluid. More broadly MXene biosensors are poised to address critical needs in disease diagnostics and personalized medicine through multiplexed and real-time detection capabilities. Continued innovation in MXene sensor design – including composite formation with polymers or other 2D materials – is expected to further enhance stability, selectivity, and biocompatibility, paving the way for the next generation of biomedical diagnostic tools.

One particularly compelling application that bridges MXenes' therapeutic and sensing capacities is skin wound healing. Chronic and complex wounds benefit from materials that can not only promote tissue repair and prevent infection, but also monitor the wound environment in real time. MXenes are emerging as key ingredients in advanced wound dressings – such as antimicrobial hydrogel coatings, electrically conductive bandages, and wearable healing patches – that fulfil these multifunctional requirements. Thanks to their excellent photothermal effects, conductivity, and biocompatibility, MXenes can serve as antibacterial agents by photothermally destroying bacteria or generating heat to release antimicrobial compounds, and as stimulatory scaffolds conducting electrical signals that encourage cell proliferation and tissue growth.[8–10] At the same time, the MXene-based components can function as sensors for wound conditions. Smart bandages incorporating MXenes have demonstrated real-time monitoring of parameters like wound temperature, pH, and moisture – all of which are crucial for early detection of infection and inflammation. By coupling therapy with sensing, such MXene-enabled devices offer a closed-loop approach to wound management: they can deliver a therapeutic effect and immediately report on healing progress, allowing timely medical intervention if needed. The review by Ferrara *et al.* in this issue surveys MXenes' roles in these innovative skin repair strategies, summarizing their synthesis, chemical features, and biological effects in wound healing contexts (**https://doi.org/10.1039/D4NR02843K**). Integrating MXenes into wearable biomedical devices exemplifies the broader theme of MXenes as multifunctional platforms – materials that unify the capabilities of a drug, a scaffold, and a sensor. As research in this area progresses, we anticipate MXene-based wound dressings and other wearables will move closer to clinical use, offering improved outcomes and quality of life for patients with difficult-to-heal wounds.

As the scope of MXene applications in biology, medicine, and sensing continues to expand, researchers are also addressing the practical challenges that stand between laboratory discoveries and real-world implementation. A critical concern is the scalable and safe production of MXenes. Traditional MXene synthesis relies on harsh etching reagents (such as concentrated hydrofluoric acid) and multi-step exfoliation processes, which pose safety hazards and are not easily scalable for industrial manufacturing. In their comprehensive contribution to this issue, Bao *et al.* outline the key obstacles impeding large-scale MXene deployment – including high production costs, toxic etchants, susceptibility of MXene flakes to oxidation, and variability in quality – and survey emerging strategies to overcome them (**https://doi.org/10.1039/D4NR04560B**). Promising approaches such as fluoride-free etching methods, electrochemical or molten salt exfoliation, and improved MXene stabilization techniques, are highlighted as pathways to produce MXenes in bulk while mitigating hazards. Tackling these issues is crucial not only for energy storage applications but equally for producing medical-grade MXenes with consistent properties. In addition to synthesis scale-up, attention must be given to long-term stability and biocompatibility of MXenes under physiological conditions. For instance, surface coatings or encapsulation may be necessary to prevent oxidative degradation of MXene-based implants or sensors over time. Regulatory and manufacturing challenges also loom on the horizon – any MXene intended for clinical or consumer use must pass stringent safety evaluations and meet reproducibility standards. As noted by Vitale *et al.*, developing MXene-based biomedical technologies will require coordinated efforts to address materials processing and regulatory hurdles for successful clinical translation.[3]

Despite these challenges, the outlook for MXenes in the life sciences is exceedingly bright. Ongoing interdisciplinary research is rapidly advancing our understanding of how to optimize MXene structure–property relationships for specific bioapplications. Innovative studies have already demonstrated the power of combining MXene functionalities: for example, MXenes have been used as potent photothermal agents for cancer therapy that can be co-delivered with chemotherapeutic drugs or even magnetically actuated, creating synergistic multi-modal treatment regimes. Comparisons with other 2D materials (graphene, MoS_2, *etc.*) suggest that MXenes often offer superior performance in biomedical contexts, thanks to their unique and highly tunable surface termination chemistry and metallic conductivity. Looking ahead, we expect to see MXenes playing a pivotal role in next-generation medical devices and sensors – from nanocarriers for targeted drug/gene delivery to flexible bioelectronic interfaces for neural recording or cardiac monitoring. The contributions in this themed issue underscore both the remarkable progress to date and provide the roadmap for future developments. By coupling fundamental MXene chemistry with creative engineering in biology and medicine, researchers are charting a path for MXenes to move from the lab to the clinic. We hope this collection of articles inspires further breakthroughs in MXene research and fosters the interdisciplinary collaborations needed to fully realize the potential of MXenes in biology, medicine, and sensing.

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