

architect customized medicine. In biomedicine as well as nanobiotechnology, numerous unique nanoscience-based techniques have been developed, allowing theragnostic modalities like synergistic therapy and multimodal imaging, which are promising alternatives in treating a variety of ailments. Materials having layered 2D structures have received a lot of attention since graphene was discovered in 2004 as a result of their proven biochemical and physical characteristics that set them apart from their bulk counterparts.¹ Utilising novel 2D-based systems with fascinating features for versatile technical applications is the major objective.² The topic emerged again with attention of scientific communities on graphene, the first 2D layered structure, and further led to a huge success in terms of applicability. Since then, dichalcogenides, phosphorenes, hexagonal boron nitride, *etc.* have been explored as 2D materials and extensively researched for various potential applications.^{3,4} A broad family of transition metal nitrides and/or carbides known as the MXenes was recently developed by the Gogotsi research team at Drexel University.⁵ To synthesize MXenes from 'MAX' phases, layers of 'A' element are particularly etched. The transition metal-based nitrides and carbides that make up the MAX phases are connected by the 'A' element to form strong bonding (ionic, metallic, and covalent) with the 2D layers.⁶ A typical MXene 2D flake has the general characteristic formula of Mn+1XnTx , which denotes the presence of carbon or

nitrogen intermingled with surface functions such as F, Cl, O, and OH, Sc, Ti, V, Cr, Mn, Fe, Y, Zr, Nb, Mo, Hf, Ta, and W.

A number of top-down synthesis methods including electrochemical etching,^{7,8} thermally driven electrochemical,⁹ hydrothermal techniques in the presence of NaOH¹⁰ and KOH solutions,¹¹ Lewis acid molten salt replacement reaction,¹² and salt-templated approaches¹³ were adopted. Amongst them recently fluorine-free synthesis methods are attracting considerable attention for their safe and promising gateway to chemical synthesis of MXenes (Fig. 1).

MXene nanosheets possess high specific surface areas making them suitable carriers of drugs or proteins with lots of anchoring sites and reservoirs. MXenes have intriguing physiochemical characteristics, such as photothermal conversion, X-ray attenuation, electron switching ability, and localized surface plasmon resonance, as well as biological behaviours, such as enzyme-assisted biodegradation, cellular endocytosis, distinctive biodistribution, and metabolism pathway, because of their ultrathin layered structure with almost single-atomic thickness.¹⁴ Owing to its 2D planar arrangement, hydrophilic nature, infinite and open possibilities towards functionalization and chemical substitution, substantial absorption characteristics in the near-infrared region, and excellent attributes, MXenes are considered one of the most favourable materials for use in biomedical uses. Despite diligent research on MXene,

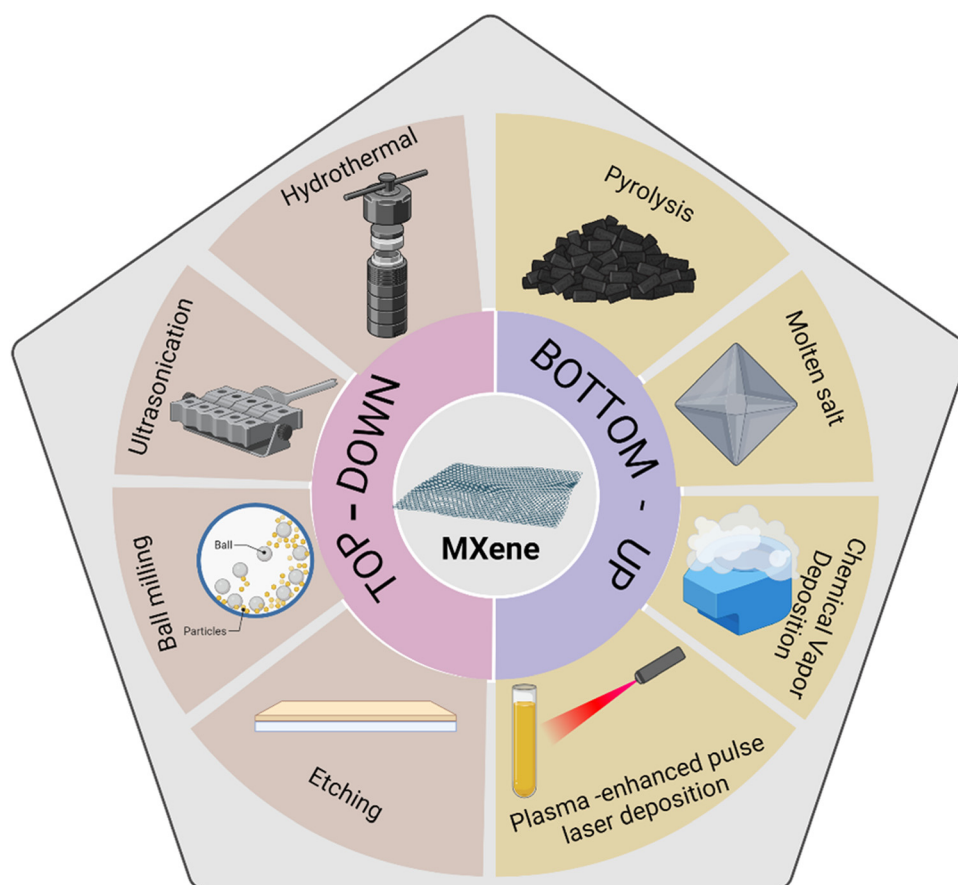


Fig. 1 Schematic of surface functionalization techniques for MXenes.



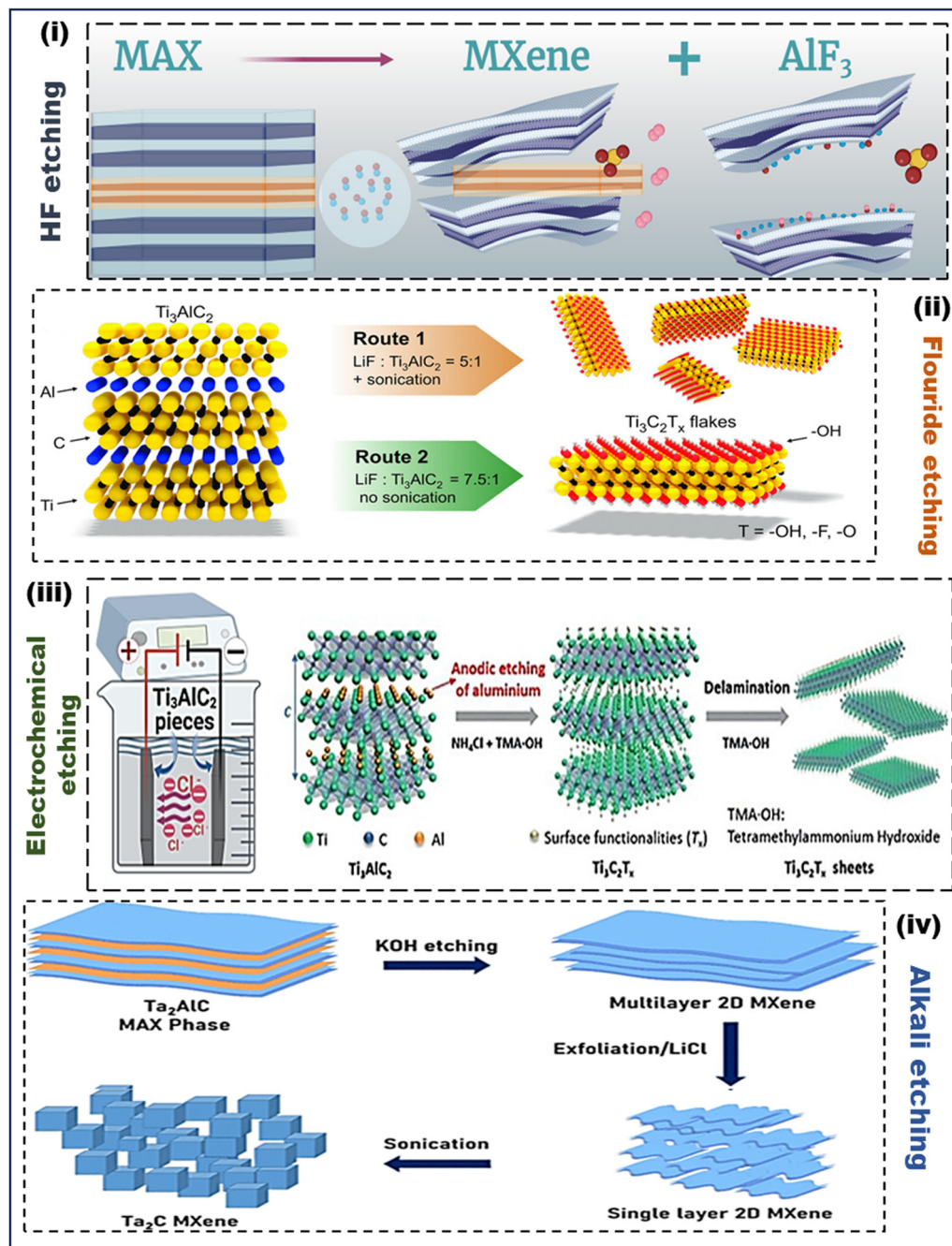


Fig. 2 Schematic of etching strategies for MXene production. (i) HF etching. Reproduced from ref. 28 with permission from Elsevier, copyright 2020, (ii) Fluoride etching. Reproduced from ref. 29 with permission from Wiley, copyright 2016. (iii) Electrochemical etching. Reproduced from ref. 30 with permission from Wiley, copyright 2018. (iv) Alkali etching. Reproduced from ref. 31 with permission from the Royal Society of Chemistry, copyright 2018.

MAX phase that could lead poor etching to yield MXenes. Furthermore, the resulting MXenes' separation from their precursor phase is quite challenging. Another impediment to alkali etching yields the formation of additional oxide/hydroxide layers, developed over the MAX phase. In one example, when 2 M KOH was used to etch Ti_3SiC_2 at a temperature of 200 °C *via* a hydrothermal reaction, it results in a core-shell MAX@ $\text{K}_2\text{Ti}_8\text{O}_{17}$ composite,³⁷ whereas NaOH caused the development of a $\text{Na}_2\text{Ti}_7\text{O}_{15}$ layer on the MAX phase, preventing the

process from yielding pure MXenes. The use of intense alkali for etching the MAX phase is effective, yielding extremely hydrophilic substances with F-free terminations. However, the risks of using concentrated alkali and high temperatures confine its use to the production of significant amounts of MXenes. Furthermore, the resulting chemical products are often multilamellar MXenes with accordion-like shape, which induce further intercalation and delamination to form mono-layer MXene nanosheets.³⁸



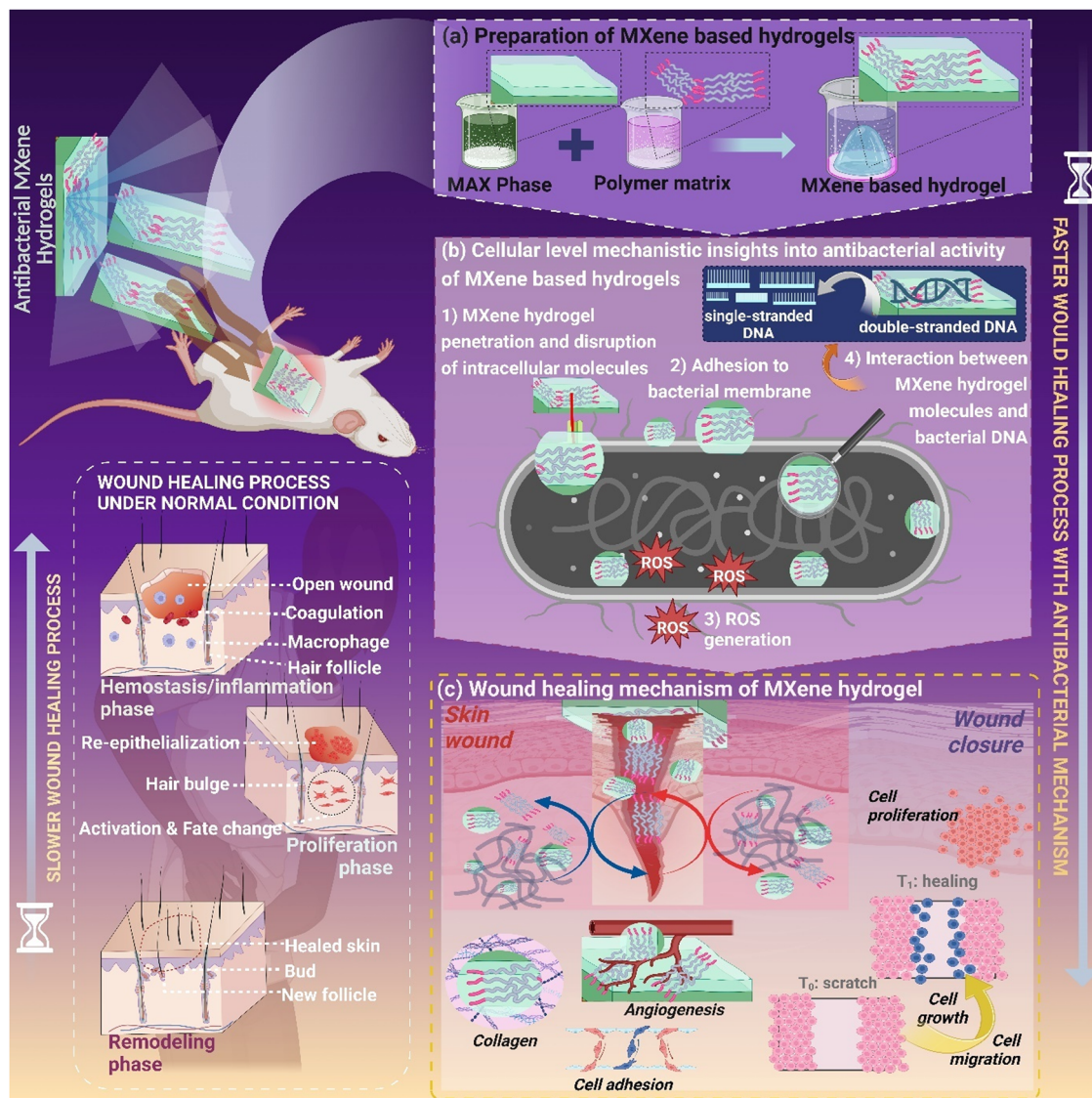


Fig. 5 Schematic of cellular level insights into MXene materials as potential antibacterial candidates for wound healing applications.

bactericide density for both Gram-positive and Gram-negative bacteria, which ultimately leads to the inhibition of biofilm formation.⁸⁰ In this case, antibiotic-resistant bacteria can be effectively combated with combinational therapy and multi-mechanism antimicrobial medicines that have synergistic effects.

As the threat of antibiotic resistance continues to rise, the antimicrobial potential of MXenes stands as a beacon of hope in the fight against bacterial infections in the biomedical field. MXenes with their unique optical/thermal characteristics, high electrical conductivity, hydrophilicity, electro-mechanical properties and tuneable physicochemical properties can be thought of as appealing candidates for the designing of innovative micro- and nano-systems with significant bactericidal potency. Overall, the primary and potential mechanisms by which MXenes/derivatives deactivate or eradicate pathogenic bacteria are the rupture of cell membranes of bacteria *via* the sharp

edges of nanoflakes of MXenes, the inhibition of nutrient intake, the generation of reactive oxygen species (ROS), and photo-thermal-driven bacterial deactivation. Compiling toxicological, pharmacological/pharmacokinetics, and associated antibacterial mechanisms can aid in the development of avant-garde MXene-derived composites wherein they exhibit potential antibacterial properties in subsequent eras.

4. Insights into the biomedical application prospect of MXene-derived nanostructured materials

4.1 Drug delivery applications

MXene-based nanocomposites have emerged as a promising and innovative solution in the field of drug delivery, offering significant advancements in the way therapeutic agents are



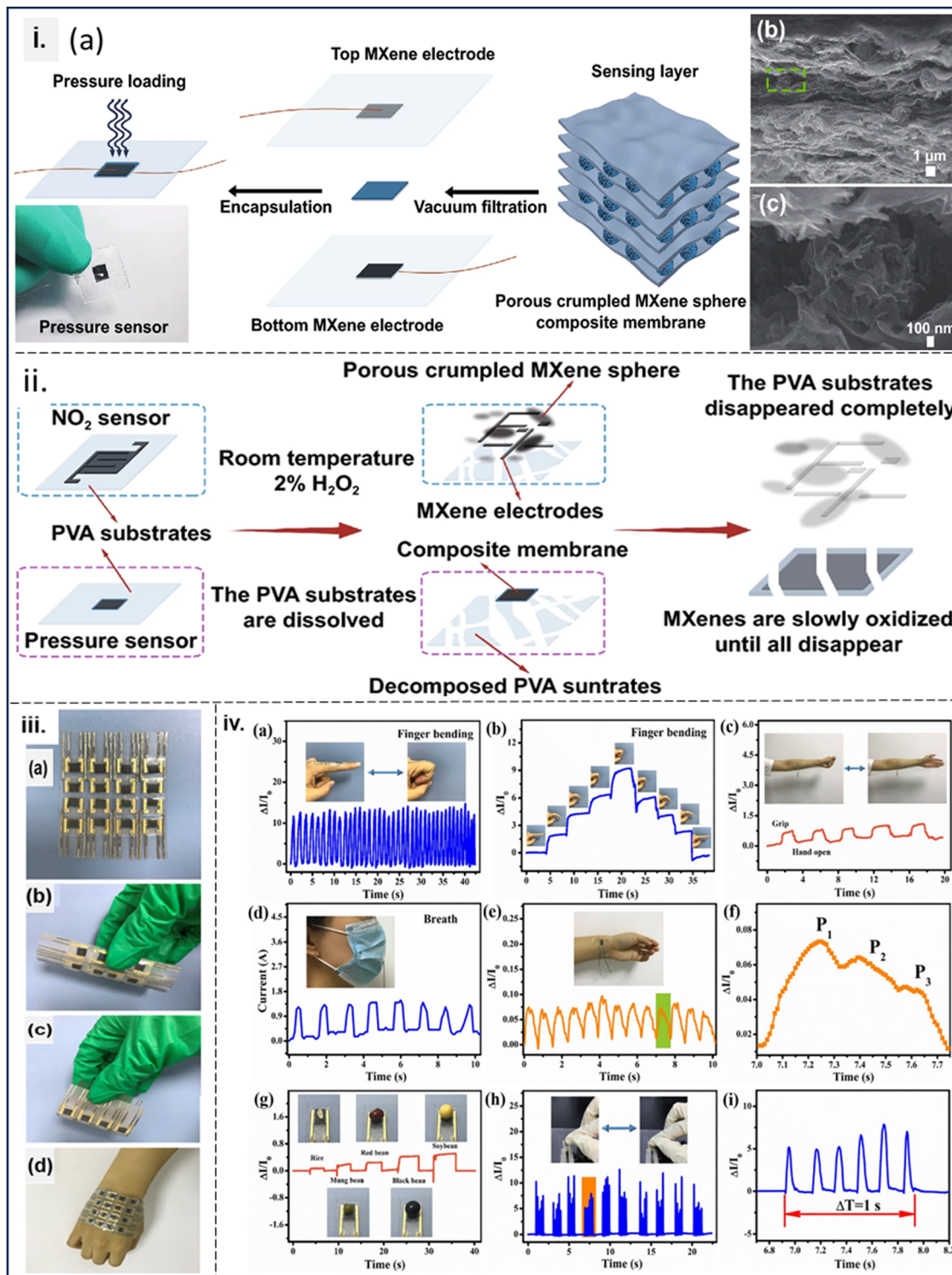
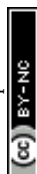


Fig. 8 (i) (a) Schematic of the pressure sensor fabrication based on MS-2-10 and a photograph of the fabricated pressure sensor. (b) Cross-section SEM image of the composite membrane and (c) the close-up image of porous crumpled MXene sphere in the green box. (ii) Schematic of the degradation process of the transient NO₂ and pressure sensors based on MS-2-10. Reproduced from ref. 136 with permission from Springer, copyright 2022. (iii) (a) Photograph of the assembled e-skin assembled from the MCF based pressure sensor with 4 × 4 pixels. Photographs of the E-skin (b) and (c) under different bending states and (d) attached onto the hand. (iv) Real-time sensing signal of the MCF-based pressure sensor towards (a) repetitive finger bending and (b) different bending angles. Real-time sensing signal recording of the pressure sensor for different human physiological monitoring, including (c) arm muscle contraction, (d) breath and (e) and (f) wrist pulse. (g) Real-time sensing signal recording of the pressure sensor upon several small items with different weights (from left to right: rice, mung bean, red bean, black bean and soybean). (h) and (i) Real-time sensing signal of the pressure sensor for imitated knocking of early stage Parkinson's disease. Reproduced from ref. 137 with permission from Elsevier, copyright 2021.



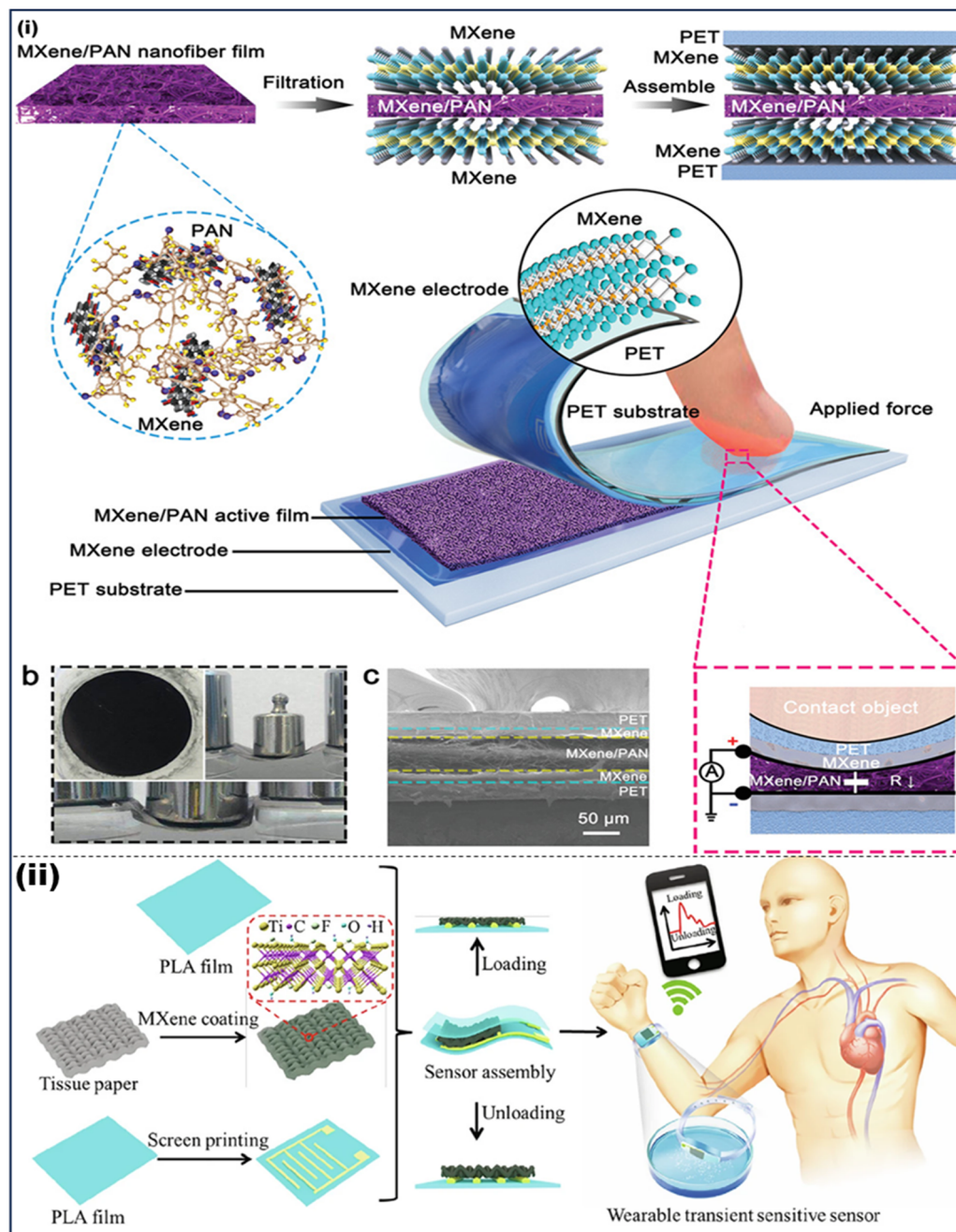


Fig. 9 (i) Schematic of the hydrophilic, conductive, and redox-active sandwich-like PSGO-PEDOT nanosheets and their incorporation into hydrogels. (a) Fabrication process of the MXene/PAN-based flexible pressure sensor with the MXene electrode and working mechanism (inset). (b) Optical image of the MXene/PAN thin film with MXene electrodes and their mechanical flexibility and strength. (c) SEM image of the flexible pressure sensor with the sandwich structure. Reproduced from ref. 140 with permission from Wiley, copyright 2021. (ii) Schematic for the procedure to fabricate MXene nanosheet-based flexible wearable transient pressure sensors. Reproduced from ref. 141 with permission from the American Chemical Society, copyright 2019.

sophistication, driven by smart communities, precision agriculture, innovative technologies, and advanced medical services.¹⁴² A recent development exemplifying this approach is the creation of a pristine MXene-based $\text{Ti}_3\text{C}_2\text{T}_x$ liquid ink tailored for large-scale printing applications. This innovation holds potential applications in the manufacturing of 3D and 4D printed sensing devices, aligning with the demand for environmentally beneficial outcomes. Geravand and colleagues¹⁴³

introduced an innovative biodegradable nano-filtration membrane by employing a hybrid nanocomposite made from polycaprolactone (PLC) and hydrophilic $\text{Ti}_3\text{C}_2(\text{OH})_2$ MXene sheets. This membrane was designed for the treatment of dyed aqueous solutions. Similarly, Zhang and collaborators¹⁴⁴ unveiled a remarkable biodegradable multipurpose pressure sensor. This sensor was created using cross-attached collagen fibers (CCFs) combined with MXene aerogel, demonstrating an



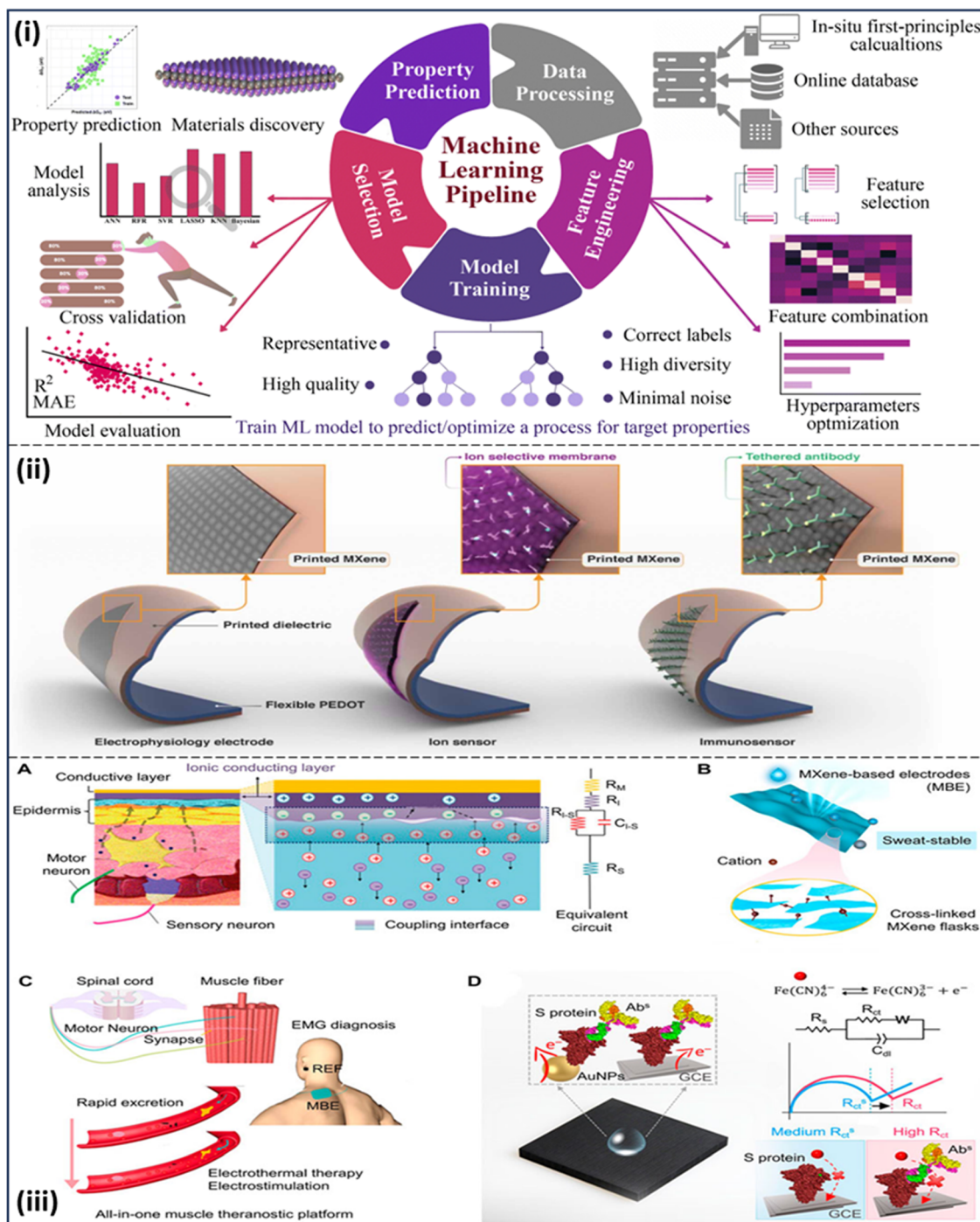


Fig. 10 (i) Workflow of the machine learning approach, starting from data processing, feature engineering, model training, model selection and property prediction for the screening of ideal HER catalysts from MXenes. From first-principles calculations, the materials space is generated from a large number of possible combinations of the selected elements and functionalization. Reproduced from ref. 177 with permission from the Royal Society of Chemistry, copyright 2023. (ii) Schematic of three MXene electrodes printed on flexible self-standing PEDOT substrates. The mode of sensing is governed by the surface functionality of the printed MXene device. (Left) Electrophysiology electrode. (Middle) MXene-based ion sensor with an ion-selective membrane on the top of the MXene layer. (Right) Immunosensor made of MXene film tethered with specific antibodies. Reproduced from ref. 178 with permission from IOPscience, copyright 2020. (iii) (A) A flexible skin-adherent electrode with minimal electrochemical impedance attached to the epidermis. An equivalent circuit model is shown to the right. (B) Bioderived, air-permeable, and sweat-stable MXene-based electrode (top), where structural crosslinking exists throughout the nanoscopic structure (bottom). (C) A MXene-based "theranostic" device to provide electrothermal therapy if muscle fatigue is detected. (D) Loading a peptide onto a label-free EIS biosensor increases its sensitivity. Reproduced from ref. 179 with permission from Frontiers, copyright 2023.

promotes cellular adhesion and proliferation which might instigate the phosphorus/calcium deposition, thereby increasing *in vitro* bio-mineralization and osseointegration explored in

tissue engineering applications.¹⁴⁷ Furthermore, their radio-opacity aids in monitoring implant placement and post-operative assessment (Fig. 11). As research in this field

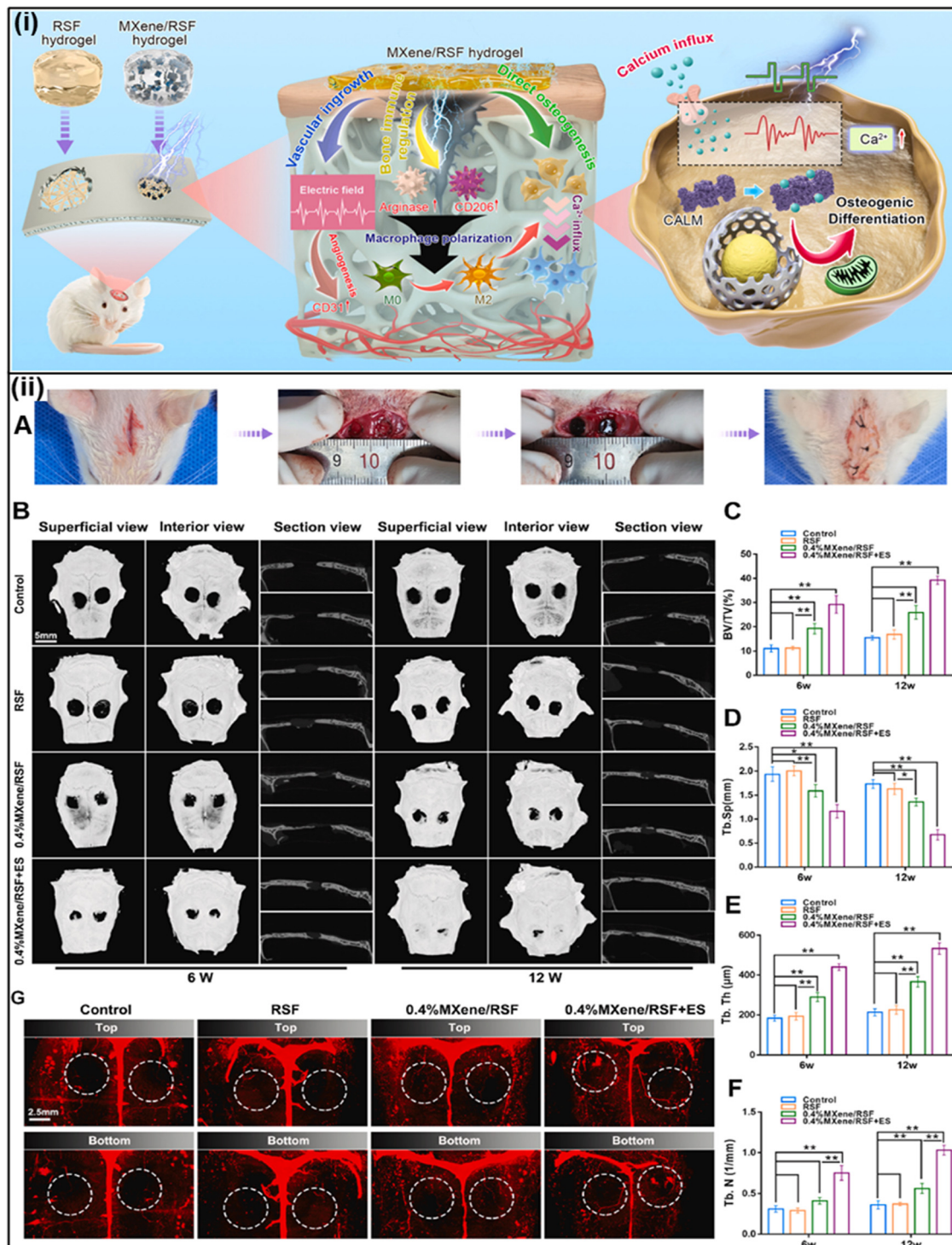


Fig. 11 (i) Conceptual and effective mechanisms of the electroactive MXene/RSF hydrogels to re-establish the electrical microenvironment for bone regeneration. (ii) MXene/RSF hydrogels with ES potential accelerated bone regeneration. (A) Procedure for the establishment of the calvarial defect model in SD rats. (B) Cranial bone regeneration at 6 and 12 weeks after implantation presented by micro-CT. (C)–(F) BV/TV, Tb.Sp, Tb.Th, and Tb.N results calculated based on micro-CT. (G) Representative images of 3D reconstruction of the blood vessels at 12 weeks post-implantation. Reproduced from ref. 198 with permission from KeAi Communications, copyright 2023.

