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## REPLY

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## Reply to comment on ‘3D melt electrowritten MXene-reinforced scaffolds for tissue engineering applications’

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### Abstract

Yang *et al* comment on our article by Zahrabi *et al* (2025 *Biofabrication* 17 045011 10.1088/1758-5090/adf803) titled ‘3D melt electrowritten MXene-reinforced scaffolds for tissue engineering applications’ reporting the first demonstration of melt electrowritten (MEW) MXene/PCL scaffolds and their pro-osteogenic cellular response without exogenous growth factors. Here, we respond by clarifying MXene’s role during MEW processing and its contribution to tissue scaffold properties by defining future research directions. Importantly, the MXene within the PCL scaffolds does not exhibit high electrical conductivity as pristine 2D MXene films do, since the investigated loadings are below the electrical percolation threshold. Therefore, bulk conductivity is not expected to dominate scaffold behavior. Instead, we attribute improved print resolution and stability to MXene-enabled interfacial and thermal effects that can stabilize the MEW jet and enhance filament definition. In addition, favorable interactions between MXene surface terminations and PCL strengthen interfacial adhesion and influence crystallization and degradation kinetics. We further discuss the surface functionalization strategies (e.g. APTES functionalization) that can improve MXene–polymer compatibility and may reduce oxidation susceptibility. Building on these points, we envision next steps including (i) investigation of osteoinductive signaling pathways mechanism, (ii) complementary *in vivo* assessment in standard bone-defect models, (iii) fabrication of scalable structures by the development of hybrid manufacturing routes combining with MEW such as extrusion/hydrogel casting or electrospinning, and (iv) AI-guided optimization using existing material composition and process–structure models as a design constraint.

We thank Yang *et al* for their positive and thoughtful highlights, and suggestions for the further improvement on our recent study. Their engagement reflects the growing interest in electroactive and MXene-based biomaterials for regenerative medicine.

The systematic integration of 2D electrically and thermally conductive MXene into melt electrowritten (MEW) polymer scaffolds remains comparatively understudied. In this study, we demonstrated the printability of MXene/PCL nanocomposite MEW scaffolds for the first time by improving the surface hydrophobicity of MXene by performing a (3-aminopropyl) triethoxysilane (APTES) functionalization to enhance compatibility with PCL. Building

on evidence that electro- and thermally- conductive 2D additives can beneficially tune MEW processability and scaffold performance, this approach improved print fidelity and resolution, boosted mechanical strength relative to pristine PCL, and mitigated undesirable bulk degradation and rapid mass loss. Our PCL/MXene nanocomposites achieve analogous, in key respects, superior enhancements in printability, degradation control, and mechanical strength. We attribute these improvements to the interfacial nano-topographic and chemical cues imparted by the few-layer MXene sheets. MXene’s high aspect ratio and nanoscale roughness promote flow-induced alignment and stabilize the MEW jet, expanding

the melt-processing window and sharpening filament definition. In addition, their high thermal conductivity improves heat dissipation during deposition, aiding faster filament solidification and dimensional fidelity. MXene surface terminations (e.g. –O/–OH/–F) provide favorable interactions with PCL ester groups, increasing interfacial adhesion and nucleation density, which together hinder bulk degradation. Importantly, our MXene loadings are below the electrical percolation threshold, so bulk conductivity is not expected. Therefore, the observed improvements arise from these interfacial and microstructural effects [1, 2]. Nevertheless, local interfacial electroactivity at cell–MXene interfaces, arising from surface charge, roughness, and capacitive effects, can occur without bulk percolation and influence biological effects and scaffold functionality. This can provide a local electrochemical environment and likely contributes to the observed enhanced cellular responses. Consistent with this interpretation, compared to pristine PCL, our PCL–MXene scaffolds enhanced MC3T3 cell proliferation and osteogenic differentiation without exogenous growth factors, and increased the compressive response. These enhancements are attributed to interfacial nano-topographic and chemical cues rather than macroscopic current flow. Such features could be strategically incorporated into layered constructs, for example, a mechanically supportive PCL extrusion core with an outer MEW PCL–MXene layer engineered for cell guidance and interfacial bioactivity. *In vivo* testing can be pursued as a complementary or collaborative study in a standard bone-defect model [3] to assess integration and repair.

PCL is a degradable polyester; however, under hydrolytic and enzymatic conditions, it erodes progressively, exposing and ultimately releasing embedded MXene domains as the polymer mass diminishes. MXene stability under physiological conditions remains a key research need. To enhance MXene–PCL compatibility and minimize oxidation, we employed surface functionalization of  $Ti_3C_2T_x$  (e.g. silane/APTES coupling or polymer-grafting strategies), which is anticipated to improve the stability, hydrophilicity and interfacial bonding within the polymer. Such approaches have proven effective in mitigating oxidation of metal particles in aqueous and physiological media [4].

3D MEW offers high microscale precision, but the technique is strongly affected by the 3D MEW process temperature, melt viscosity, and chemical stability of the polymers [5–7]. The introduction of MXene changed the PCL crystallization behavior, depending on its concentration, due to the thermally conductive properties of MXene. Accelerated crystallization of the PCL composite resulted in expedited solidification. This altered behavior led to reduced shape distortion. In general, however, hindering

printing in higher layers to obtain thicker constructs is limited in MEW. However, to address this, we can propose a hybrid route, such as combining solution electrospinning, hydrogel casting, or extrusion printing to form bulk, centimeter-scale construct, followed by MEW deposition to add microarchitecture and MXene functionality.


AI-driven optimization, such as Bayesian or machine learning methods, can be useful to identify optimal MXene concentrations and printing parameters, as recently demonstrated in bioprinting workflows [8]. Our response surface methodology models already capture the quantitative relationships between MEW inputs (printing speed ( $mm\ min^{-1}$ ), nozzle-to-collector distance (mm), feeding pressure (bar), and acceleration voltage (kV)) and output (fiber diameter) for pristine PCL and MXene/PCL. Using these data to train an interpretable model (e.g. Gaussian process regression) coupled with Bayesian optimization is technically straightforward and increasingly common in materials process design. This would enable rapid prediction over an expanded concentration window and active selection of the next experiments, yielding a concentration–parameter optimum under printability and cytocompatibility constraints [6, 9].

In conclusion, we are grateful to Yang *et al* for their constructive discussion, which situates our findings within broader advances in conductive biomaterials and hybrid fabrication. Our study demonstrates the feasibility and biological functionality of MXene-reinforced MEW scaffolds and points to future directions involving surface engineering, hybrid printing, AI-guided design, and vascularization. Together, these approaches can help realize the full translational potential of electroactive nanomaterial scaffolds.


## Data availability statement

No new data were created or analysed in this study.

## Author contributions

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Methodology (lead), Validation (equal),  
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