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Research Highlight

Hierarchical biomimetic strategy for dental enamel regeneration at the extreme nanoscale

Jinke Chang[1,2,*], **Jin-Chong Tan**[2,*] **and Alexander M Korsunsky**[2,*]

[1] State Key Laboratory for Manufacturing Systems Engineering, Xi'an Jiaotong University, Xi'an 710049, People's Republic of China
[2] Department of Engineering Science, University of Oxford, Oxford, Oxfordshire OX1 3PJ, United Kingdom

E-mail: jinke.chang@xjtu.edu.cn, jin-chong.tan@eng.ox.ac.uk and korsunskygroup@gmail.com

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1. From Hierarchical mineralisation to biomimetic manufacturing strategies

The fabrication of hierarchical mineralised nanomaterials remains a long-standing challenge in advanced manufacturing, as their performance is governed by structural control across molecular, nanoscale and mesoscale length scales. Dental enamel is an extreme example, combining exceptional stiffness, wear resistance and chemical stability through a highly ordered mineral hierarchy. Mature enamel consists of tightly aligned apatite crystallites organised into decussating prism architectures separated by interprismatic regions, and its outstanding mechanical properties depend critically on the fidelity of this organisation. Conventional approaches to enamel regeneration, including fluoride-based treatments and calcium phosphate delivery strategies, can increase mineral content but typically produce disordered surface layers, which fail to restore the crystallographic alignment and microscale architecture of native tissue. These approaches rely on surface precipitation and lack control over crystallographic orientation, preventing epitaxial growth from the underlying enamel. As a result, the regenerated layer is structurally discontinuous at the micro-interface, limiting stress transfer and reducing mechanical stability under functional loading. The challenge is therefore not simply to supply ions, but to recreate the interfacial and physicochemical conditions that govern mineral reconstruction across length scales, enabling hierarchical self-assembly from molecular interactions to fully developed structural motifs.

The incorporation of a biomolecular matrix into manufacturing processes offers a biomimetic route to the fabrication of hierarchical nanocrystals. Elastin-like recombinamers (ELRs) containing intrinsically disordered regions can be engineered to undergo controlled disorder–order transitions, giving rise to the highly oriented fibrils that provide directional cues for apatite nucleation[1]. This behaviour demonstrates that hierarchical mineralisation can be programmed through the supramolecular organisation of a designed protein matrix, producing aligned crystallites and prism-like structures. The introduction of microscale topographies into the strategy further showed that geometric confinement can bias nanocrystal co-alignment and direct anisotropic mineral growth across millimetre-scale regions[2]. This principle has a biological analogue in natural amelogenesis, where enamel crystal growth is spatially regulated within organised extracellular protein matrices and by ameloblast Tomes' processes. Together, these findings establish that supramolecular assembly, geometric confinement and the ionic environment act cooperatively to govern mineral architecture across length scales. A key obstacle, however, remained the interface with native enamel: earlier studies relied on synthetic substrates, whereas natural enamel presents heterogeneous chemistry and

* Authors to whom any correspondence should be addressed.

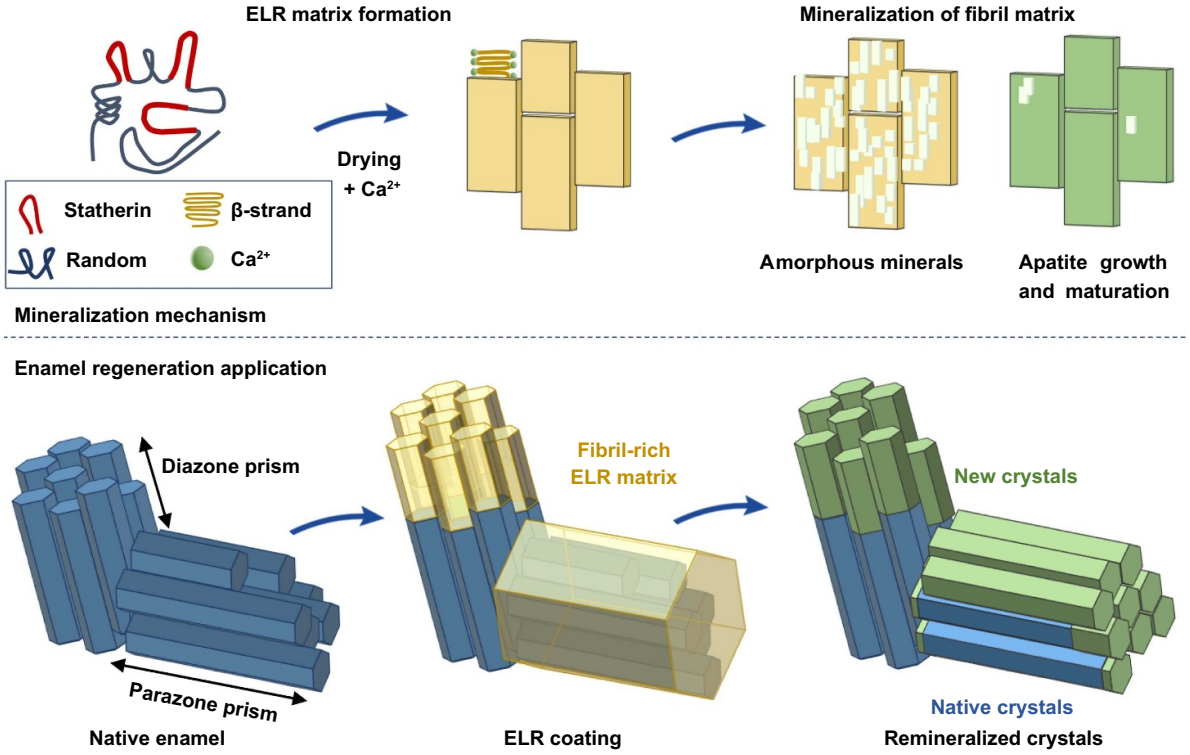

Figure 1. Human enamel regeneration based on biomimetic supramolecular protein matrix. Schematic overview of the ELR-driven mineralisation process and its application to enamel repair. ELR molecules assemble into a fibrillar matrix that concentrates calcium ions and orchestrates the transformation from amorphous precursors to aligned apatite crystallites. When applied to eroded enamel, this matrix guided the mineralisation process that promotes epitaxial extension of native crystals and re-establishes the characteristic prismatic and inter-prismatic architecture, leading to recovery of enamel structure and function. Figure artwork independently drawn by the authors, inspired by findings reported in[3].

structure, limiting matrix attachment and orientation-matched growth. Importantly, this interface challenge is not unique to dentistry but is common to many repair and remanufacturing scenarios involving complex material surfaces.

2. Supramolecular matrix–guided enamel regeneration

A recent advance demonstrates that structurally integrated enamel regeneration can be achieved directly at the native interface[3]. A supramolecular elastin-like recombinamer matrix assembles into β-sheet-rich fibrillar networks that mimic the developing enamel scaffold and concentrate calcium ions at their surfaces, enabling the formation of an amorphous precursor that transforms into aligned apatite (Figure 1). When applied to eroded enamel, the matrix establishes an organised interfacial environment that enables epitaxial continuation of native crystallites and reconstruction of prismatic and interprismatic architectures. The regenerated layer exhibits hardness (H, (1.4 $\pm$ 0.3) GPa) and elastic modulus (E, (58.3 $\pm$ 16.7) GPa), comparable to native enamel (H = 2.5–4 GPa; E = 50–90 GPa), and maintains resistance to wear and fracture under simulated physiological conditions. Impressively, no observable microstructural degradation was detected after prolonged mechanical wear (75 N for 2 weeks) and acid erosion in 0.1 M acetic acid (pH 4.0) for up to 2 days. This performance was achieved within a mineralised layer up to ~10 μm thick, formed over approximately ten days, with apatite nanocrystals (~50 nm in diameter and ~1 μm in length) closely matching native morphology. It should be noted that the mechanical measurements were likely obtained under optimised laboratory conditions, and the large variation in elastic modulus may reflect heterogeneous interfacial nucleation during remineralisation.

The performance arises from a transition from diffusion-driven surface precipitation to matrix-mediated mineralisation, in which supramolecular confinement regulates nucleation kinetics and suppresses rapid, disordered crystallisation. The matrix stabilises amorphous precursors and directs their transformation into oriented apatite, while molecular interactions impose anisotropic growth. The umbrella sampling simulations also indicated higher detachment energy of ELR fragments along the *a*-axis than the *c*-axis, favouring crystal growth along the *c*-axis. This confined, matrix-directed growth enables epitaxial extension from native enamel and restores interfacial structural coherence, distinguishing it from conventional surface-driven remineralisation strategies such as fluoride varnishes and amorphous calcium phosphate systems, which typically increase surface microhardness by ~10%–30% after repeated applications over days to weeks, but rarely

achieve prism-scale structural recovery or mechanically integrated interfaces.

3. Implications, challenges and outlook

The ability to regenerate enamel with restored hierarchy and functional performance marks a meaningful step in enamel repair[4]. By controlling the interfacial environment, this approach re-establishes crystallographic continuity and tissue-specific architecture directly on native enamel, shifting the focus from surface deposition to interface-directed reconstruction. However, the regenerated layer of about 10 μm remains far below the ∼0.5–2 mm thickness of natural enamel, representing only ∼0.5%–2% of native enamel thickness and leaving a gap of around two orders of magnitude relative to clinical needs as a substitute for conventional dental fillings. This confines its use to surface-level repair rather than bulk restoration. Progress toward broader application will depend on increasing mineralisation depth without disrupting structural coherence at the interface. Furthermore, the 10-day mineralisation timescale reflects the slow kinetics required for ordered crystal growth, creating a trade-off between structural fidelity and clinical practicality. Approaches such as gentle electric fields, ultrasound or temperature modulation may help accelerate ion transport and phase transformation, while scaffold-guided mineralisation strategies may provide a route toward thicker regenerated layers. Nevertheless, maintaining interfacial control, crystallographic orientation and epitaxial growth during accelerated mineralisation remains a central challenge.

Viewed alongside earlier advances in disorder–order transitions, confined mineral nucleation and topographically guided growth[5], this work defines a coherent framework for interface-controlled mineralisation with relevance beyond the field of dentistry. By regulating nucleation, crystallographic orientation and growth within a confined interfacial environment, this mechanism enables the re-establishment of structural continuity across heterogeneous or damaged surfaces. Although applications beyond enamel remain to be demonstrated, the central principle established here offers a useful framework for thinking about relative manufacturing problems in which functional performance depends on coherent growth across complex surfaces, including coatings and the repair of hierarchical ceramic or composite materials.

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ORCID iD

Jinke Chang 0000-0002-8335-1337

References

[1] Elsharkawy S et al. 2018. Protein disorder–order interplay to guide the growth of hierarchical mineralized structures. *Nat. Commun.* **9**, 2145.
[2] Deng X et al. 2021. Topographically guided hierarchical mineralization. *Mater. Today Bio* **11**, 100119.
[3] Hasan A et al. 2025. Biomimetic supramolecular protein matrix restores structure and properties of human dental enamel. *Nat. Commun.* **16**, 9434.
[4] Zhao H W et al. 2022. Multiscale engineered artificial tooth enamel. *Science* **375**, 551–556.
[5] Chang J K, Tavakol M, Besnard C, Korsunsky A M and Tan J-C. 2025. Biomimetic enamel-like crystals: a versatile platform for unraveling the basic mechanisms of demineralization and remineralization. *ACS Appl. Mater. Interfaces* **17**, 50505–50518.