Editorial

Beyond natural tooth enamel

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With the rapid development of aerospace, national defense technology, and biological hard-tissue repair, engineers and scientists always aim at the design and manufacture of composites with higher stiffness, viscoelasticity, strength, and toughness, but unfortunately, these properties—stiffness/viscoelasticity and strength/toughness—are generally thought to be mutually counteracted. The mixture of two intrinsically complementary components such as stiff ceramic and soft polymer is the classic strategy to ameliorate the foregoing conflicting performances. However, engineering materials fabricated by the "mixture" way are just a trade-off, that is, one property is enhanced accompanied by the weakening of the other one. Recently, Guo et al. reported a multiscale bio-design of hydroxyapatite (HA)-based composite (defined as artificial tooth enamel [ATE]; Figure 1) following the strategy of "synthesis of enamel-like nanoblocks and subsequent multiscale bio-assembly," which simultaneously exhibited high stiffness, hardness, viscoelasticity, strength, and toughness.[1]

Natural structural materials like tooth enamel, bones, and nacre usually possess excellent comprehensive mechanical properties thanks to their hierarchical structure and amorphous intergranular phase (AIP). Especially, tooth enamel (highly mineralized tissue), the outer shell of a tooth with several millimeters, is the hardest and strongest tissue in the human body to masticate food and is tough enough to resist impact and vibration during the continuous occlusal process. These excellent mechanical properties originate from enamel's hierarchical structure composed of 96 wt % parallelly arranged HA nanowires with AIP interconnected by biological proteins.[2,3] The comprehensive mechanical properties and hierarchical structure of tooth enamel have attracted wide interest from both materials science and clinical application. Therefore, mimicking enamel's

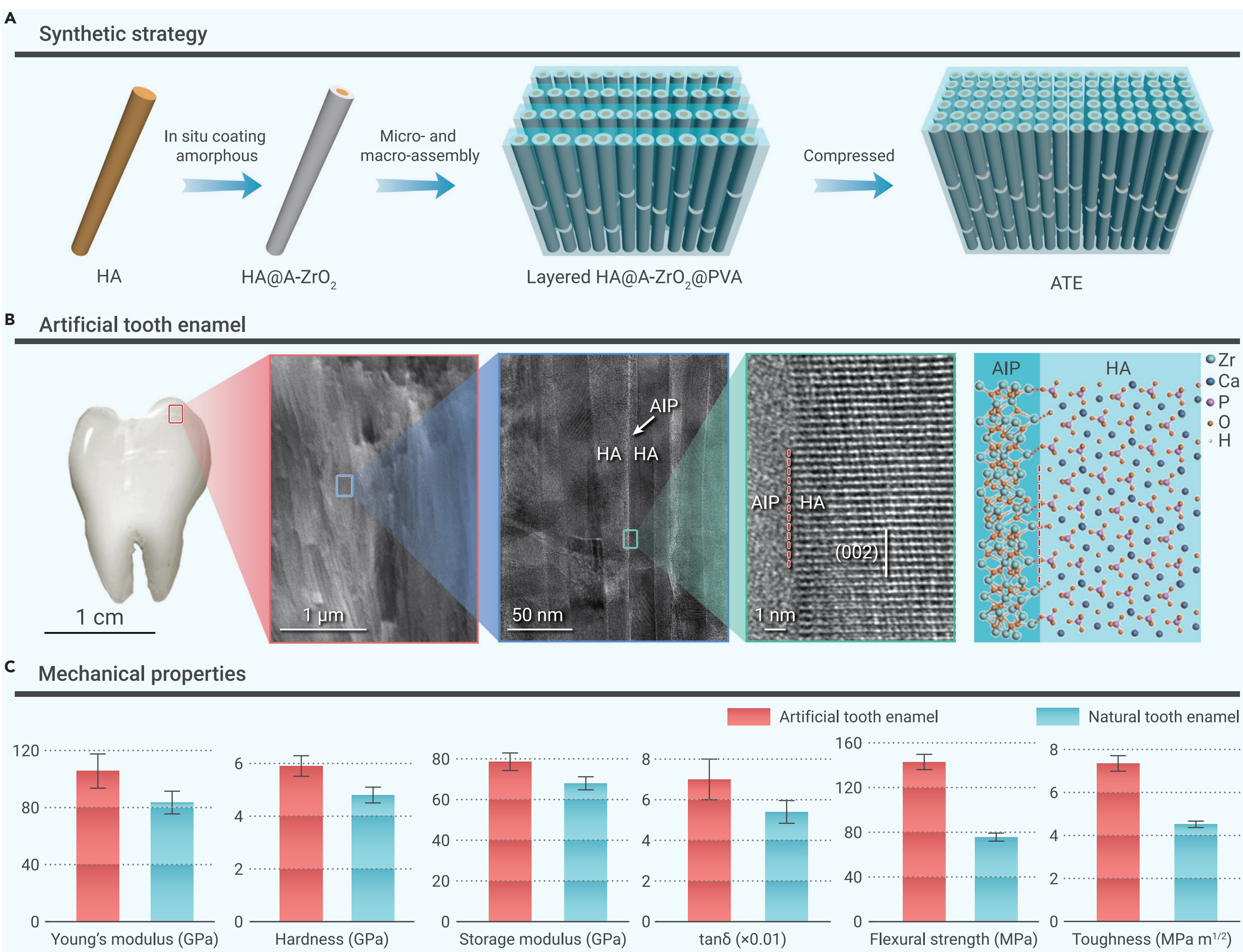

Figure 1. Artificial tooth enamel (ATE) and its mechanical performance (A–C) Hierarchical structure of synthetic strategy (A) and structure (B) of artificial tooth enamel (ATE), and comparison of the mechanical properties between NTE and ATE (C). HA, hydroxyapatite; AIP, amorphous intergranular phase; A-ZrO$_2$, amorphous ZrO$_2$; PVA, polyvinyl alcohol. (Credit: Lin Guo.)

structural characteristics in artificial engineering materials is highly desired to solve the knotty problems in mechanical enhancement and practical applications.

To duplicate the mechanical properties and hierarchical structure of natural enamel, an alternative way is to mimic the forming process of natural tooth enamel—mineralization. The enamel is produced by the cooperation of ameloblasts and amelogenin in the intricate oral environment. So, providing a similar environment (presence of amelogenin and suitable temperature) and reaction source (Ca^{2+}, PO_4^{3-}, Na^+, Mg^{2+}, and F^-) of the natural mineralization process might allow the formation of an enamel-like structure of artificial materials. Nevertheless, just as in the lengthy natural mineralization process, the man-made mineralization process is time consuming, taking typically a couple of weeks for several micrometers, whose size is far smaller than applications' demand.

Another way is the enamel-inspired assembly of micro/nano structural blocks. The micro-structure of tooth enamel is parallelly aligned ceramic columns, and therefore, synthesizing one-dimensional nanomaterials or an assembled array is able to mimic the tooth enamel. Kotov et al. reported an enamel-inspired zinc-oxide-based composite by sequential growth of a zincoxide nanowire array followed by layer-by-layer deposition of a polymeric matrix, whose mechanical properties were comparable with those of natural tooth enamel.[4] The thickness of this composite was up to dozens of micrometers within a couple of days, which was more efficient than the mineralization method, although it was still not suitable for practical engineering applications. Moreover, the AIP, which highly influenced the mechanical performance of tooth enamel, was ignored. It is well known that, similar to amorphous alloys with high hardness and excellent ductility, the amorphous ceramics enable stronger energy dissipation.

It is a great challenge to hierarchically mimic enamel (both parallelly arranged nanowires and presence of AIP) at macro scale before the work by Guo et al., even though the hierarchy is indeed vital for the enamel's mechanical performance and the macro size determines materials' applications. To realize the hierarchically mimetic design at macro scale, Guo et al. firstly made amorphous ZrO_2 thin layers *in situ* grown on HA nanowires as hybrid nanoblocks to introduce AIP and subsequently developed a dual-directional freezing method to make these hybrid nanoblocks' oriented assembly (Figure 1). After compression, an ATE with a hierarchical enamel-like structure and macro size (several centimeters) was synthesized (Figure 1). Impressively, the ATE simultaneously displayed high stiffness, hardness, strength, viscoelasticity, and toughness, exceeding the properties of enamel (Figure 1). The stiff structural support of oriented aligned nanowires, efficient organic/inorganic interface connection with AIP, and robust polymer confinement could produce a series of strengthening and toughening behaviors, including nanowire sliding, pull out, fracturing and crack splitting, bridging, and bunching, thus resulting in remarkable energy-dissipation capability and excellent mechanical properties in ATE.

The most significant characteristic of ATE is the presence of AIP. Given the long-term disorder atomic arrangement of amorphous material, it does not have the grain boundary and dislocation that are common in crystal material so that it always exhibits higher stiffness, hardness, and energy-dissipation capacity.[5] This is one key reason why introducing AIP obviously promotes material's mechanical performance. What's more, amorphous materials usually possess abundant unsaturated bonds that can form strong chemical connections with the HA nanowires and organic matrix to strengthen the interface. The strong interface restricts the fracture of ATE and significantly contributes to the excellent mechanical properties.

As an emerging field, the enamel-inspired design unavoidably has some challenges that need to be further explored and noticed. To begin with, unlike nacre and bone, research on natural enamel is still in its infancy, and most of it is focused on the micro structure and mechanical properties of natural enamel. The role of protein, initial formation, gradient structure, influence of the various constituents, transformation of amorphous precursor, and intrinsic interfacial interaction between amorphous and crystal need further study. Especially, the mimic of enamel's gradient structure and achieving the same constituents as tooth enamel in the artificial materials need numerous efforts because these characteristics of enamel highly influence the mechanical performance of enamel, though they have been hardly duplicated up to now. Benefitting from the rapid development of measurement techniques, the formation process and hierarchical structure of natural enamel will be more accurately revealed, and the underlying mechanical performance will be uncovered *in situ* at the atomic and nano scales so as to further guide the design and preparation of enamel-inspired composites. Based on the in-depth analysis of tooth enamel, assembly methods with more controllable parameters such as combination of mineralization and bio-assembly and magnetic-field or electric-field assembly will be developed to fully mimic the enamel and pursue extremely high mechanical performance.

Natural enamel faces serious threats from cariogenic bacteria, mechanical injury, and beverages in the oral cavity. Dental diseases not only endanger oral and maxillofacial functions but also induce systemic diseases (e.g., cardiovascular disease and digestive disease), which significantly reduce people's quality of life. Traditional enamel-repair materials, such as resin-based composites and ZrO_2 implants, are unsatisfied with the mismatch in mechanical properties and biocompatibility with the natural enamel. The ATE has a similar structure as natural enamel, and its mechanical properties, such as stiffness and hardness, can be tuned to the same as those of nature tooth enamel, which effectively protect healthy teeth from wear and fracture. Meanwhile, the viscoelasticity and toughness of ATE are superior to those of natural enamel, allowing the composites to withstand greater vibration and impact force.

Considering the application demand, mass production of ATE including both amorphous reinforced HA nanowires and larger-size assembly is essential. Throughout the synthetic strategy proposed by Guo et al., one can see that the hydrothermal synthesis of HA nanowires, hydrolysis coating of AIP, and oriented assembly of structural blocks are all highly efficient, and they lay the foundation for ATE's industrialization. However, there are still some problems that need to be solved, such as how to guarantee the uniformity of HA nanowires and AIP coatings when the yield of them increases to hundreds of kilograms from several grams, how to design the directional freezing instruments with larger size to implement the enamel-inspired assembly at a scale of several meters, and how to construct the ATE to a desired shape. These need further study, especially technology innovation cooperated with engineers.

In summary, this is the first time that the controlled preparation of centimeter-scale enamel-inspired composites with identical structure and mechanical properties to natural enamel so far by multiscale bionic design have been realized, done so by Guo et al. Endowing the high strength, toughness, stiffness, and viscoelasticity with engineering materials will have a profound impact on advanced engineering applications. The ATE has good continuity and can inspire many in-depth explorations on high-performance biomimetic composites, such as changing the composition to achieve the versatility of the composites and selecting stiffer inorganic components to obtain the record high stiffness or hardness composites. The design philosophy will open new opportunities in high-performance composites not only for tooth repair but also for other engineering applications, such as strengthening surfaces of devices or creating protective equipment.

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DECLARATION OF INTERESTS

The authors declare no competing interests.