MATERIALS SCIENCE

Lessons from tooth enamel

A remarkable composite material has been made that mimics the structure of tooth enamel. This achievement opens up the exploration of new composite materials and of computational methods that reliably predict their properties. SEE LETTER P.95

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Tooth enamel combines hardness and impact resistance[1,2], making it extremely durable — which is essential to the lifelong survival of toothed organisms, because most animals cannot replace their adult teeth. On page 95, Yeom *et al.*[3] report a tooth-enamel-inspired composite material in which a columnar architecture of hard constituents is interlaced with a soft polymer matrix. The material exhibits an unprecedented combination of stiffness, vibrational damping and low density. The work paves the way for strategies for the design of lightweight materials that could, for example, be used as damage-resistant alternatives to ceramic composites, which have high stiffness and hardness, but are brittle[4].

Organisms such as animals and plants have diversified and evolved in response to environmental pressures, including predation, climate and the availability of energy sources. Their tissues and minerals therefore often exhibit combinations of mechanical properties not found in synthetic materials. Composites are pervasive in natural materials, because combinations of different constituents and internal architectures can achieve specialized functions that cannot be attained by individual materials.

Synthetic composite materials have also been made, such as fibre composites that are extensively used in aircraft structures. However, the degree of complexity and structural hierarchy found in natural composites is much higher than that in synthetic materials[5,6]. This has prompted researchers to correlate the properties of natural composites with their functions, with the goal of identifying rules that can be used in the design and processing of new, high-performance materials — especially lightweight materials for automotive and aircraft applications. Of particular interest is the interplay of material constituents, internal architecture and constituent dimensions, and the effects of this interplay on properties[5–7].

Yeom *et al.* have achieved this goal for tooth enamel, using advances in nanoscience and engineering. A key challenge was to find a way to synthesize materials that have the same degree of organization as the natural material: tooth enamel consists of aligned, micrometre-scale columns of the mineral hydroxyapatite, bound within a matrix of organic material. In nature, the matrix is created before the inorganic columns, but Yeom *et al.* took a different approach. They first grew a carpet-like arrangement of nanowires made from zinc oxide (ZnO), which mimic the columns in enamel. They then filled the space between the columns with a polymeric matrix, layer by layer. By repeating these two steps, the authors prepared multilayers of columnar composites that have a high volume fraction of ZnO, and which contain features resembling those of the tooth enamel of many species (Fig. 1).

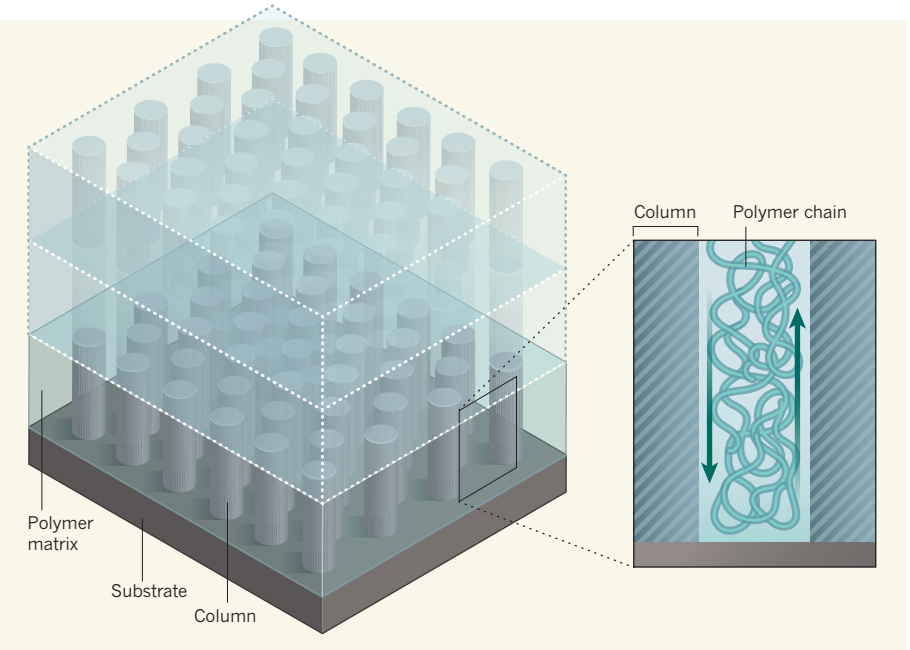

Figure 1 | A composite material inspired by tooth enamel. Yeom *et al.*[3] have prepared a composite in which micrometre-scale columns of zinc oxide are embedded in a polymer matrix — a structure that mimics that of tooth enamel. The material is prepared by growing a carpet of hard columns from a substrate, then surrounding the columns with a soft polymer matrix. The two steps are repeated to build up subsequent layers of the composite. The confinement of polymer molecules between columns (inset) and the slipping of polymer chains (arrows) at the interfaces between the columns and the matrix are key to the composite's outstanding combination of mechanical properties (high stiffness and viscoelasticity, but low density).

The researchers used a battery of nanometre-scale testing techniques developed and perfected in the past ten years to quantify the material properties of their composite. They found that it had a superior combination of stiffness and viscoelasticity (a mixture of viscosity and elasticity when the material undergoes deformation), with key properties in excess of those of most synthetic materials. The composite has excellent damping properties because of its viscoelasticity, and lower density than composites that incorporate large volume fractions of metals or ceramics. The high degree of control of the nanowire orientation, dimensions and density achieved by the authors is essential for the material's outstanding mechanical performance.

Yeom *et al.* also used molecular modelling to show that polymer confinement by the stiff crystal columns, and the slipping of polymer chains at the column–matrix interfaces, together probably explain the composite's superior viscoelasticity. Such comprehensive use of modern tools, from synthesis to characterization to analysis, has made the modern field of biomimetic materials possible.

Although Yeom and colleagues' synthetic process should allow columnar composites inspired by natural materials to be made in small sizes (areas of up to about 100 square centimetres, and thicknesses of several micrometres), scaling it up to make components that have the relatively large areas (up to square metres) and thicknesses (millimetres to centimetres) needed for practical applications is a challenge that needs to be addressed. The same challenge applies to many other bio-inspired composites that have highly organized architectures and hierarchical structures, and which require fine dimensional control of constituents. Nevertheless, several such bio-inspired materials have been manufactured on practically useful scales using a variety of processing techniques, including freeze-casting followed by mineralization[8], and additive manufacturing[9,10]. Although promising, these approaches require further development to attain the level of scalability and dimensional control required to achieve high-performance materials that are insensitive to defects[11].

Another interesting feature of Yeom and co-workers' study is the synergy between the material's architecture, constituents and dimensions and their effects on the material's mechanical response. The authors' findings highlight opportunities for using multiscale computational modelling of materials to predict the effects of new hierarchical architectures before attempting synthesis. Development of such models is an active area of research that will benefit from the type of advances in processing and experimentation discussed in the present paper. Indeed, the work by Yeom *et al.* and of others[8–10] demonstrates that emerging practical methods for investigating large libraries of constituents and for building new structural motifs will lead to unexplored, counter-intuitive materials behaviour — discoveries that might disrupt the frontiers of materials knowledge. ■

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CELL BIOLOGY

Stretched divisions

Many organ surfaces are covered by a protective epithelial-cell layer. It emerges that such layers are maintained by cell stretching that triggers cell division mediated by the force-sensitive ion-channel protein Piezo1. **See Letter p.118**

CARL-PHILIPP HEISENBERG

The integrity of epithelial-cell layers is essential for their protective and regulatory function in organ development and homeostasis. However, the integrity of an epithelial layer is subject to continual challenge from both mechanical and biochemical stimuli. Gudipaty *et al.*[1] reveal on page 118 how physical forces can control cell division to aid the maintenance of epithelial-layer integrity.

Epithelial layers are exposed to many mechanical and biochemical signals, which can be generated within the layers or arise from adjacent structures. There is increasing evidence that the interaction and feedback between these signals can affect epithelial-cell fate and behaviour through a phenomenon known as mechanosensation[2].

Gudipaty and colleagues investigated how the integrity of an epithelium is maintained when it loses cells, which could occur after cell death, for example. In such circumstances, the remaining cells have to stretch out to fill the gaps. To investigate the consequences of this stretching for layer integrity, the authors used a device that enabled them to stretch an epithelium *in vitro*. They observed that cellular stretching promotes epithelial-cell division, revealing a mechanosensitive means of linking cell stretching and the associated changes in tissue physical tension to the biochemical signalling pathways that control cell division (Fig. 1).

The authors found that cell stretching triggers epithelial-cell division by activating the force-sensitive ion-channel protein Piezo1 (ref. 3). This leads to an increase in the intracellular concentration of calcium ions (Ca^{2+}), the phosphorylation of ERK1/2 kinase protein and the expression of cyclin B protein, which controls cell division. Given that cell divisions in an underpopulated cell layer could reduce cell stretching and tension, a negative-feedback loop might exist that balances tissue tension and the rate of epithelial-cell division to keep fluctuations in tissue tension low and thereby preserve the layer integrity.

Cellular overcrowding in epithelia has

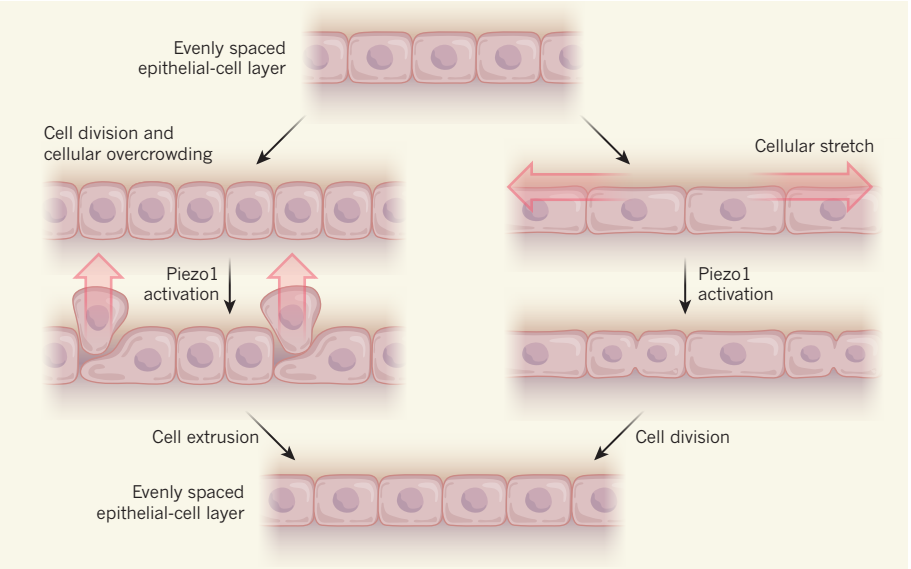

Figure 1 | Piezo1 maintains a stable, even layer of epithelial cells. If a layer of epithelial cells becomes overcrowded with more cells than usual in a given area, excess cells can be removed from the layer by a cell-extrusion process[4,5] mediated by the force-sensitive ion-channel protein Piezo1 (ref. 4). Conversely, if an epithelial layer becomes sparsely populated at the cellular level, cells in this region stretch to fill the space to maintain an intact epithelial barrier. Gudipaty *et al.*[1] observed that cellular stretching can trigger cell division, and that this process also requires the activation of Piezo1. Therefore, when an epithelial layer becomes overcrowded or underpopulated at the cellular level, Piezo1 is required to provide a stable, even layer of cells that maintains epithelial integrity.