

block songs were played for 135 days. Yet the observed copy ratio was skewed well beyond the null expectation. This implies that spring tutor copies in the prior study [11] might have been primed by exposure to those same song types during birds' first summers. More broadly, Mennill and colleagues [10] offer that mere "re-exposure" of previously-memorized summer models during spring blocks helps birds to cement their model choices, independent of other factors that favor specific learning outcomes. Given all of these new findings, the idea of training wild birds through loudspeakers no longer seems far-fetched; rather, it seems like the start of a new science meme, ready to be imitated.

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Epithelial Packing: Even the Best of Friends Must Part

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<https://doi.org/10.1016/j.cub.2018.08.055>

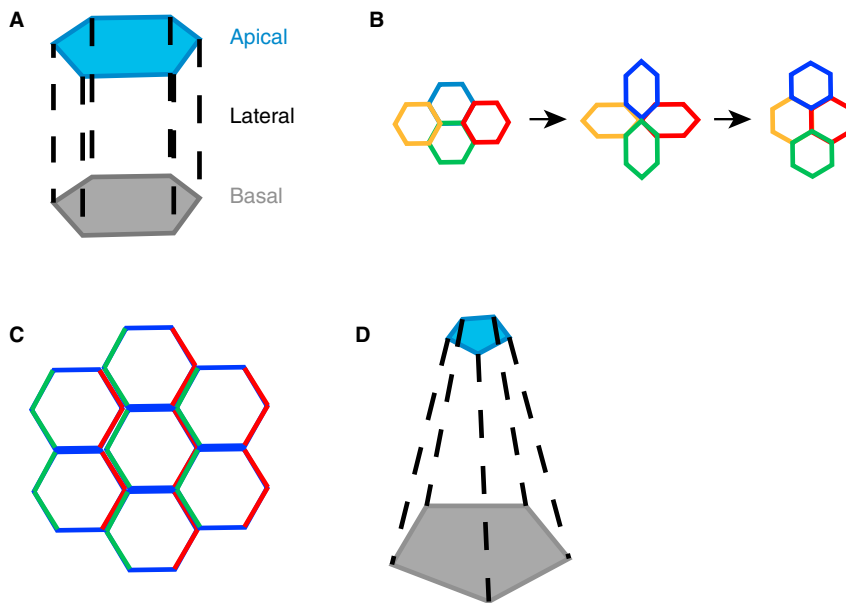
Textbooks commonly describe epithelia as tissues composed of regular arrays of prism-shaped cells. A recent study combining mathematical modeling with quantitative imaging has uncovered the scutoid, a new shape that is necessary for epithelial cells to pack into curved tissues.

Epithelial tissues are composed of cuboidal, columnar, or squamous cells that are packed together into sheets that line the surfaces of organs and organisms. Connections between epithelial cells can provide mechanical stability and serve as a barrier between compartments; consequently, the different surfaces of an epithelial cell

contain distinct sets of proteins that serve both mechanical and signaling functions. Within a simple epithelium, the basal surface of the cell contacts the basement membrane and thus contains receptors for the extracellular matrix. On the opposite side of the cell, the apical surface is oriented toward an internal cavity (or the outside of the organism)

and typically contacts air or liquid. The mechanical stability of the epithelium is provided by intercellular adhesions that form along the lateral surfaces and connect neighboring cells to each other. A new study by Gomez-Galvez *et al.* [1] now shows that, in order to form curved tissues, a subpopulation of epithelial cells must adopt a newly discovered shape in





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Figure 1. Building tissues of prisms and frusta.

(A) Parallel lateral surfaces generate prism-shaped cells. (B) T1 neighbor exchanges (also known as T1 transitions) permit convergence of regularly packed prism-shaped cells and lengthening of an epithelial tissue. (C) Asymmetric distribution of membrane-associated proteins (such as Frizzled and Van Gogh in the PCP pathway, represented as different colors in different regions of the cell) causes local and long-range polarization of epithelial cells. (D) Decreasing the relative size of the apical and basal membrane surfaces generates frustum-shaped cells.

which they form contacts with different neighbors on their apical side than on their basal side.

Some of the first considerations of cellular packing in epithelial tissues were described in the seminal work of D'Arcy Thompson [2], who was inspired by the similarities he observed between the geometries of cells within epithelial sheets and of bubbles within foams [3]. The shape of each bubble within a foam is controlled by surface tension, which minimizes the surface area of the bubble. In an ideal foam, this energetic minimization generates a hexagonal array of bubbles [4]. There is ample evidence to suggest that the shapes of individual cells are also influenced by surface tensions [5], namely cortical tension (due to cytoskeletal contractility at the plasma membrane) and intercellular surface tension (which decreases as adhesion to neighboring cells increases). As with bubbles in a foam, cells that contact each other within a tissue minimize their total surface area. Microscopy analysis of epithelial sheets in model systems, such as the *Drosophila* embryo and retina [6,7], have revealed that the apical and basal

surfaces of the cells within these tissues also form a (primarily) hexagonal array.

Until recently, imaging the full depth of lateral cellular boundaries within epithelial tissues *in vivo* has been challenging. Perhaps because of the analogies to foams, or perhaps because of simplicity, it has been commonly assumed that the apical and basal surfaces of each cell are connected by parallel lines (Figure 1A). The resulting three-dimensional (3D) shape is called a prism; more specifically, a hexagonal prism (six lateral edges) or, in some cases, a pentagonal prism (five lateral edges). Individual prisms can be packed together to form a flat sheet, such as is found in the epidermis. This regular packing has both physical and biological consequences. First, the two-dimensional (2D) shape of the apical surface is sufficient to define the 3D shape of the cell; this property has been exploited routinely in physical (theoretical) models that aim to define the mechanical properties of epithelial tissues [8]. Second, the overall geometry of a tissue can change if the prism-shaped cells adjust their connections to their neighbors. The most well-described neighbor exchange is

known as a T1 transition, which causes intercalation during axis elongation in a variety of developmental scenarios (Figure 1B). Third, a regular sheet of prism-shaped cells also enables the specification of long-range order, as is observed in the collective alignment of epithelial cells within the plane of the tissue that is driven by planar cell polarity (PCP). Such alignment permits proximal–distal, anterior–posterior, and cranial–caudal patterning over millions of cells, which is necessary for aligning hairs within the *Drosophila* wing blade or hair follicles within mammalian skin [9]. Core PCP components, including the transmembrane proteins Frizzled, Van Gogh, and Flamingo, localize to the plasma membrane on opposite sides of the cell, such that the proximal side of one prism forms contacts with the distal side of the neighboring prism (Figure 1C). As currently envisioned, long-range juxtacrine signaling is enabled by the regular packing of prism-shaped cells.

Curved epithelial sheets, which are formed by invagination, folding, or tubulogenesis, contain cells in which the apical and basal surfaces are of different sizes. The lines that connect the apical and basal vertices of cells within these tissues therefore are no longer parallel, and instead generate a pyramidal shape with the apex lopped off, known as a frustum (Figure 1D). The number of sides of the apical (or basal) surface still indicates the number and identity of a cell's neighbors. Cells can actively transition between prism and frustum shapes by actively decreasing or increasing their apical or basal membrane domains. Apical constriction and basal expansion have been observed across a wide range of morphogenetic epithelial tissues, and are well accepted as drivers of key developmental processes, including ventral furrow formation during gastrulation in *Drosophila* [10], invagination of the lens placode during morphogenesis of the vertebrate eye [11], and lateral branching during morphogenesis of the avian lung [12]. Of course, 2D models of the apical or basal surfaces of cells no longer approximate the 3D geometry of curved tissues, which recent efforts in computation and theory have attempted to resolve [13,14].

To understand the shapes of cells within curved epithelia, Gomez-Galvez

et al. [1] began by using a mathematical model to pack a cylindrical tube with a specified number of epithelial cells. Surprisingly, this mathematical model generated a subset of cells that had different neighbors contacting the apical and basal domains (Figure 2A). The 3D shape of these cells was neither a prism nor a frustum. Instead, these cells were characterized by one lateral face that changed planes, and therefore changed neighbors, along its length. The authors called this an apical–basal transition, akin to the T1 transition that occurs when prism-shaped cells within planar tissues rearrange and change neighbors. Surprisingly, the 3D shape itself had never before been characterized. The authors named it a ‘scutoid’ since it resembles the shape of the thorax of some beetles.

Their data suggest that, to pack curved surfaces efficiently, a subset of epithelial cells within a tissue must contact different neighbors at their apical and basal surfaces. The fraction of cells that adopt this scutoid morphology increases as the relative difference in curvature between the apical and basal surfaces of the tissues increases (Figure 2B). Quantitative image analysis revealed the presence of scutoid-shaped cells within the curved epithelia of the *Drosophila* salivary gland, egg chamber, and developing embryo, all of which showed evidence of apical–basal transitions. Cells with different neighbors at their apical and basal domains had been observed previously in the *Drosophila* leg imaginal disc [15] and the anterior pole of the embryo [16], although it is unclear whether these cells were scutoid-shaped. Future studies of epithelial tissues in other organisms will likely reveal the presence of scutoids across species.

Practically, the discovery of scutoids within epithelial tissues means that one can no longer assume the 3D shape of a cell by simply imaging its apical (or basal) membrane domain. This, of course, presents a problem for theorists who rely on the apical-shape assumption in crafting their mathematical and computational models [14]. This fact also raises several interesting questions for developmental biologists. First, how do prisms or frusta morph into scutoids in developing tissues? Studies of epithelial sheet and tube bending so far have focused on actomyosin-mediated forces that cause constrictions or neighbor

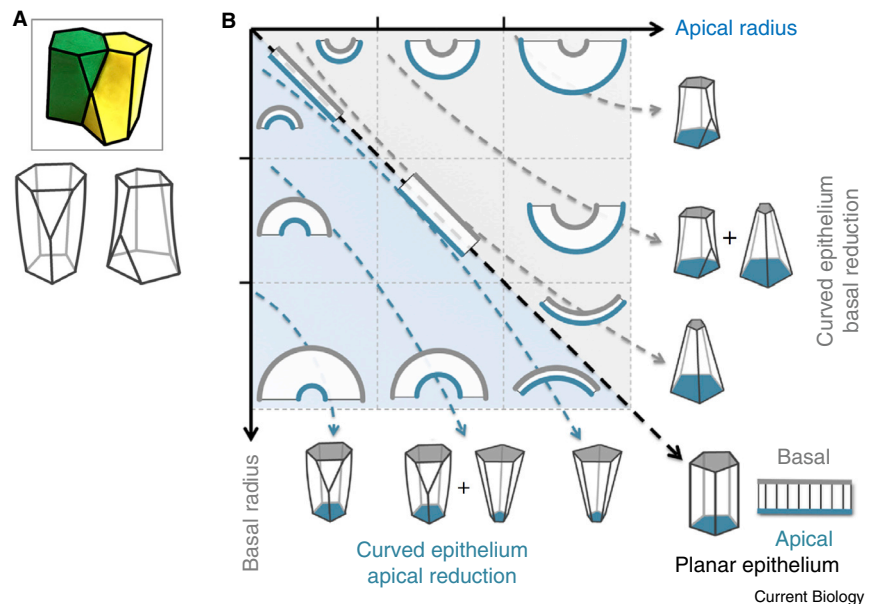


Figure 2. Curved tissues require scutoid-shaped cells, which have different neighbors at their basal and apical surfaces.

(A) To efficiently pack into curved tissues, epithelial cells adopt a scutoid morphology. Two scutoid-shaped cells (shaded in different colors) pack together, forming different neighbors on their apical and basal surfaces (top panel). Unlike prisms or frusta, the vertices of the apical and basal surfaces are not connected by lines in the scutoid (bottom panel). (B) Simple planar epithelia are composed of prism-shaped cells. Curved, relatively flat epithelial tissues are composed of frustum-shaped cells; in these tissues, the curvature of the apical and basal surfaces is approximately the same. The fraction of scutoid-shaped cells increases as the relative differences in curvature between the apical and basal surfaces increases. (Images adapted from [1] under a Creative Commons licence: <http://creativecommons.org/licenses/by/4.0/>.)

exchanges in the apical or basal surfaces. Scutoids would suggest the possibility for a complementary force-generating machinery in the lateral membrane of cells. Apical–basal transitions are similar to T1 neighbor exchanges, which can occur passively as an epithelial tissue is deformed globally [17] or actively as the cells involved change their shapes [18]. The mathematical model of Gomez-Galvez *et al.* [1] suggests that apical–basal transitions can result purely from tensile forces, but it remains unclear whether this is sufficient to generate stereotyped epithelial tissue bending *in vivo*. Curiously, the anisotropic cells of the *Drosophila* leg imaginal disc were found to elongate into isometric prisms during the morphogenesis of this tissue [15], suggesting the tantalizing possibility that the conversions between prisms, frusta, and scutoids are dynamic and reversible.

Second, what are the effects of scutoid-shaped cells on intercellular signaling within a tissue? How does the apical–basal transition affect the establishment and maintenance of juxtacrine signaling

that is necessary to generate local and long-range order, such as that downstream of the PCP pathway? Is asymmetry within the apical-most surface of a cell sufficient to establish polarity? Or is there a secondary or parallel cue that orients long-range polarity with information from the lateral and basal domains? Since cell shape plays such an important role in regulating cell phenotype, it is essential to understand whether the scutoid- and frustum-shaped subpopulations within a given tissue have different fates. As Thompson predicted, the geometrical rules of packing determine the arrangements of cells within a tissue, but these arrangements are likely to have consequences far beyond what he (or any of us) could have dreamed.

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Motor Control: Parietal Stimulation Prevents Voluntary Hand Movement

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<https://doi.org/10.1016/j.cub.2018.09.001>

Inhibition of action is commonly attributed to frontal cortex. A new study shows that intra-surgical stimulation of human posterior parietal cortex selectively prevents the initiation and execution of voluntary movement of the contralateral hand.

Making the right move at the right time is crucial for humans and animals alike. I am constantly reminded of this simple truth, for instance whenever trying to cross a busy street. In such situations I usually plan my way across the street in advance. Yet, my action plan needs to be withheld until there is a large enough traffic gap; and, if something unexpected happens, for example an approaching car suddenly accelerates, I might need to stop my plan at the very last second. What is going on in peoples' brains in such situations? How does our central nervous system realize the proactive and reactive inhibition of voluntary movement needed in everyday life? While we already have gained a quite decent understanding of how the brain

brings about goal-directed movement, much less is known about the ways it prevents specific actions and why. In this issue of *Current Biology*, Desmurget *et al.* [1] report that intra-surgical stimulation of posterior parietal cortex does inhibit the initiation and execution of voluntary hand movement with high selectivity. Their results provide novel clues about how this part of the human brain could assist us in achieving optimal performance through action inhibition.

The stimulation technique used by Desmurget *et al.* [1] is referred to as direct electrical stimulation. Direct electrical stimulation is first of all a clinical tool, which can be used to identify areas that subserve important functions, such as

language. Such functional mapping can help neurosurgeons to reduce post-operative deficits in their patients whenever there is need to resect brain tissue [2,3]. For instance, in case of Desmurget *et al.*'s [1] patients, intra-surgical mapping was required to inform the neurosurgeon prior to tumor removal. Direct electrical stimulation provides researchers with rare and valuable insights into human brain function through its direct — though artificial — interference with neuronal processing [2,3].

Direct electrical stimulation is widely known through the work of Wilder Penfield and Edwin Boldrey [4] in the 1930s. Penfield and Boldrey used direct electrical stimulation for a clinical

