Shape changes and elastic dewetting of adherent epithelia

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Epithelial tissues play a fundamental role in various morphogenetic events during development and early embryogenesis. Although epithelial monolayers are often modeled as two-dimensional (2D) elastic surfaces, they distinguish themselves from conventional thin elastic plates in three important ways: the presence of an apical-basal polarity, spatial control and variability of cellular thickness, and their nonequilibrium active nature. Here, we develop a minimal continuum model of a planar epithelial tissue as an active elastic material that incorporates all these features. We start from a full three-dimensional (3D) description of the tissue and derive an effective 2D model that captures both the apical-basal asymmetry and the spatial geometry of the tissue, through the curvature of the apical surface. By identifying four distinct sources of activity, we find that bulk active stresses arising from actomyosin contractility and growth compete with boundary active tensions due to localized actomyosin cables and lamellipodial activity, to generate the various states spanning the morphospace of a planar epithelium. Our treatment hence unifies elastic dewetting and 3D shape deformations of substrate-adhered tissues. Finally, we discuss the implications of our results for some biologically relevant processes such as tissue folding at the onset of lumen formation.

Living tissues are capable of remarkable deformations and dramatic shape changes key to many developmental processes. The diversity of resulting morphogenetic motifs arises from a rich interplay of cell-cell interactions, morphogen gradients and cytoskeletal activity. While the appearance of form along with functionality in living organisms over the course of development involves a plethora of complex biochemical and physiological processes, it has become increasingly clear that mechanics and material approaches offer useful principles to understand the collective organization of cellular matter. In this regard, an important goal of tissue mechanics is to characterize and classify the mechanisms by which thin 2D sheets of cells can fold and deform into 3D shapes. Understanding how shape in biological systems emerges from the spontaneous organization of active processes at the molecular scale remains a grand challenge in biology. It additionally has far reaching implications for the design of self-shaping functional materials.

A common approach to modeling epithelial tissue mechanics is in analogy with thin sheets of passive elastic or fluid media. An important distinction though is that cells actively consume energy to remodel the tissue architecture, thereby allowing the tissue to realize exotic nonequilibrium mechanical properties, ranging from active jammed states to ultradeformable and rupture resistant solids. In addition, epithelial tissues are intrinsically polarized along the apical-basal axis of the constituent cells, with the basal surface often adhered via a basement membrane to a substrate. This polar asymmetry in conjunction with bulk active stresses, either due to actomyosin contractility or growth, can lead to geometric incompatibilities that shape the tissue. Importantly, apicobasal polarized active stresses act as torques that compete with both cell-cell and cell-substrate adhesion to pattern differential spatial curvature in the tissue by locally varying the cellular thickness. Previous work has addressed this in the context of the 3D morphology of single epithelial cells, while continuum modeling on the tissue scale has primarily been restricted to constant thickness shape changes or free monolayers neglecting substrate adhesion.
context of wound healing assays and micropatterned tissue cultures, epithelial spreading driven by cellular migration and boundary localized active tensions have also been analyzed in the plane without regard to 3D tissue morphology. In the very different context of active suspensions, the wetting properties and shapes of orientationally ordered liquid crystalline drops have been shown to be controlled by an active disjoining pressure and depend on the kinds of topological defects present.

In this paper we derive an effective 2D description for epithelial tissues that accounts for apical-basal polarity, cell-cell interactions and cell-substrate adhesion within an active elastic continuum model. Importantly, apical-basal polarity affects both passive and active sectors of tissue mechanics. By exploiting the separation of scales in a thin monolayer, we perform a systematic reduction of the 3D equations of active mechanics to 2D, while retaining the cellular thickness as a dynamical variable. The structure of our equations is consistent with a recently proposed general phenomenological description of active surfaces, with the inclusion of traction forces due to cell-substrate interactions and an explicit derivation of model parameters. By incorporating four distinct sources of cellular activity through nonequilibrium stresses and boundary tensions, our model allows a unified treatment of planar dewetting and apical shape change of substrate-adhered tissues. In particular, we include i) nonequilibrium contributions from bulk contractile stresses due to the apical-medial actomyosin cytoskeleton, ii) extensile stresses generated by cell growth, iii) an apically localized supracellular actomyosin cable that serves as a “purse-string”, and iv) polarized lamellipodial activity that promotes cell migration at the free boundary of the tissue. The competition of extensile and contractile forces between the boundary and the bulk of the tissue determines its morphology as a function of tissue size and the stiffness of the focal adhesions bound to the substrate. Working within a simplified 1D setting, we obtain steady-state solutions of our equations that characterize the different possible shapes through the curvature of the apical surface and the in-plane contraction or expansion of the tissue, identifying the latter as an elastic analog of dewetting or wetting. A cartoon of the shapes predicted by our model is shown in Fig. [1].

In Sec. [1] we introduce the continuum description of an adherent tissue and outline the reduction from 3D to an effective 2D model that incorporates in-plane deformations and variations in the shape of the apical surface. Some details of the tissue parameterization are given in Appendix [A]. In Sec. [2] we examine stationary profiles of the apical surface, tissue deformation and the cellular stress obtained analytically for a one dimensional (1D) geometry corresponding to a tissue layer homogeneous in one of the in-plane directions. In Sec. [3] we examine the competition of various active extensile and contractile stresses in controlling tissue shape and identify two transitions, one associated with change in shape of the apical surface, the other with change of in-plane tissue size that we describe as an elastic wetting-dewetting transition. Finally we conclude in Sec. [4] with a brief discussion of the relevance of our model to *in-vitro* experiments of tissue folding and lumen formation.

1 The model

We model an epithelial tissue as a 3D elastic material that is thin in one dimension and adhered to a planar rigid substrate. In the absence of inertia, mechanical equilibrium implies force balance for the 3D stress tensor $\Sigma_{ab}$ which gives $\partial_b \Sigma_{ab} = 0$. Here and in the following, Greek indices run over all three material coordinates $\{x, y, z\}$, while Roman indices run over only two dimensions, orthogonal to the thin direction, which we take to be $z$. Writing out the force balance equations, we then have

$$\partial_j \Sigma_{ij} + \partial_i \Sigma_{ij} = 0, \quad (1)$$
$$\partial_j \Sigma_{ij} + \partial_z \Sigma_{zz} = 0. \quad (2)$$

The rest configuration of the tissue has a linear dimension given by $2L_0$ and thickness $h_0$. In the Lagrangian frame, $z = 0$ is identified with the basal surface of the tissue and $z = h_0$ is the apical surface (see Fig. 2). Slowly varying deformations in the $(x, y)$ plane then occur on the scale $\sim L_0$, while deformations along $z$ are much more rapid, varying on the scale of $h_0$. As $h_0/L_0 \ll 1$, Eqs. [1,2] generate a hierarchy of stress scales

$$\Sigma_{zz} \ll \Sigma_{zz} \ll \Sigma_{ij}. \quad (3)$$

This geometric separation of scales underlies the reduction of the 3D model to an effective 2D one, just as for passive shells and plates. Integrating over $z$, the average 2D stress $\langle \sigma \rangle$ and bending moment $\langle M \rangle$ appear as the first two moments of $\Sigma$,

$$\sigma_{ij} = \int_0^{h_0} dz \Sigma_{ij}, \quad (4)$$
$$M_{ij} = \int_0^{h_0} dz \int_0 h_0 dz \Sigma_{ij}. \quad (5)$$

Averaging Eq. [1] over $z$, we obtain an equation for in-plane force balance:

$$\partial_j \sigma_{ij} = T_i, \quad (6)$$

where we use $\Sigma_{ij}|_{z=h_0} = 0$ as the apical surface is a free surface typically in contact with a fluid, and $T_i \equiv \Sigma_{ij}|_{z=0}$ is the traction force exerted by the tissue on the substrate. Doing the same for

| I. | II. |
|---|---|
| Wetting + Convex | Dewetting + Convex |
| III. | IV. |
| Wetting + Concave | Dewetting + Concave |

Fig. 1 A sketch of the different tissue morphologies that are possible in our model. The red dashed lines mark the extent of the undeformed tissue.
the bending moment as can integrate by parts to get the torque balance as
\[ \partial_i \partial_j M_{ij} = f_n, \] (7)
where we employ the symmetry of the stress tensor \( \langle \Sigma_{ij} = \Sigma_{ji} \rangle \) and set \( f_n \equiv \Sigma_{ij} \vert_{z=0} - \Sigma_{ij} \vert_{z=h} \) as the net normal force exerted by the tissue. Note that, in the simplest setting within the reduced 2D description, we have three relevant degrees of freedom to capture the total deformation of the tissue, two in-plane displacements and the thickness of the tissue. Eqs. (a) and (b) provide a sufficient number of constraints to solve the problem, ensuring it is well-posed. If we wish to retain more degrees of freedom to describe the tissue deformation within an effective 2D model, we can do so by deriving further balance equations for higher moments of \( \Sigma_{ij} \) to obtain a consistent description. Given the general setup, we now specialize to the case at hand with a specific constitutive model for the tissue as an active solid.

### 1.1 Constitutive relations

The stress tensor has contributions from both passive elasticity and active stresses \( \langle \Sigma = \Sigma^f + \Sigma^a \rangle \). Assuming a Hookean constitutive law for an isotropic solid, the elastic stress is given by
\[ \Sigma^f_{ab} = 2\mu \varepsilon_{ab} + \lambda \delta_{ab} \varepsilon_{vv}, \] (8)
where \( \varepsilon_{ab} \) is the full 3D strain tensor and \( \mu, \lambda \) are the 3D Lamé parameters. The active stress \( \Sigma^a_{ij} \) includes two terms, a contractile stress arising from force dipoles exerted by the actomyosin cytoskeleton and an extensile stress accounting for cellular growth. Apicobasal polarity allows us to distinguish the active stress in the \( z \) direction versus in the plane, so we separately write
\[ \Sigma^a_{ij} = m_0 \delta_0 \xi_j + \Omega \delta_j, \quad \Sigma^a_{zz} = m \xi \xi_j, \] (9)
where \( m \) is the local density of contractile units, such as phosphorylated myosin motors bound to actin filaments. For simplicity, we take the actomyosin network to be isotropic in the plane with \( \xi_j > 0 \) controlling the average contractile activity in the plane and along the apicobasal axis respectively. Growth enters as an isotropic extensile pressure \( (\Omega < 0) \) solely in the plane, and we disregard growth in the \( z \) direction. An important feature of apicobasal polarity is that the actomyosin cortex is spatially localized near the apical surface. Neglecting any basal myosin, we write
\[ m(z) = m_0 \frac{\sinh(z/\ell)}{\sinh(h_0/\ell)}, \] (10)
where \( m_0 \) is the concentration of active units at the apical surface and \( \ell \) is a localization length. Such a profile can be obtained by solving a dynamical equation for the volumetric actomyosin density, \( \delta m \approx D \partial^2_t + \nabla^2 m \) that combines spatial diffusion \( (D) \) and turnover of actomyosin units on a time scale \( \tau \), while additionally imposing a fixed average \( m \) in the cell to capture the mean pool of functional actomyosin whose value is tightly regulated by the cell. For simplicity, we neglect any strain coupling here. For \( t \gg \tau \) and to lowest order in \( \nabla^2 \), \( m \) adopts the same profile as in Eq. (9) with the localization length \( \ell = \sqrt{D\tau} \).

To complete the model reduction to 2D, we follow the standard Kirchoff-Love procedure and set \( \Sigma_{zz} = 0 \), as justified by the hierarchy in Eq. (3). This gives,
\[ \varepsilon_{zz} = \frac{\Sigma_{zz} + \bar{\lambda} \varepsilon_{kk}}{2\mu + \bar{\lambda}}. \] (11)
Next we set \( \Sigma_{zz} \approx 0 \implies \varepsilon_{zz} \approx 0 \). This permits us to parametrize the \( z \) dependence of the strain \( \varepsilon_{ij} \) (see Appendix A for derivation) as,
\[ \varepsilon_{ij}(z) = \frac{1}{2} \left( \partial_i u_j + \partial_j u_i - h_0 \frac{z}{h_0} \right) \partial_i \partial_j h, \] (12)
where \( u \) is the in-plane displacement and \( h \) is the local thickness of the deformed tissue. Here we have assumed that the basal surface \( z = 0 \) does not delaminate from the substrate it is adhered to, and can hence only deform in the plane. We work to linear order in both \( u \) and \( h \), as appropriate for small deformations. A fully covariant and nonlinear generalization is easily possible as has been recently done for active surfaces.

Upon using Eqs. (a) and (b) along with Eq. (12) we obtain \( \sigma = \sigma^f + \sigma^a + \sigma^g \), where
\[ \sigma^g_{ij} = 2\mu u_{ij} + \lambda \delta_j u_{ik} - \frac{\mu h_0}{6} \partial_i \partial_j h - \delta_j \frac{h_0}{12} \nabla^2 h, \] (13)
\[ \sigma^f_{ij} = \left[ \xi_j - \xi_i \left( \frac{v}{1 - v} \right) \right] m_0 \delta_i, \quad \sigma^a_{ij} = h_0 \Omega \delta_j. \] (14)

The 2D linearized strain tensor is \( \varepsilon_{ij} = (\partial_i u_j + \partial_j u_i)/2 \) and the 2D Lamé parameters and Poisson ratio are
\[ \mu = \bar{\mu} h_0, \quad \lambda = 2\bar{\mu} \frac{\bar{\lambda} h_0}{(2\bar{\mu} + \bar{\lambda})}, \quad \nu = \frac{\lambda}{2\mu + \lambda}. \] (15)

In general we expect \( \xi_j \gg \xi_i \), as a result, \( \sigma^g_{ij} > 0 \) signalling in-plane contractility. Also note the presence of \( \partial_i \partial_j h \) in the elastic
part of the stress tensor, which though unusual, is a natural consequence of apicobasal polarity in passive mechanics, as expected of asymmetric membranes.\(E_{12}\) We similarly express the moment tensor as \(M\)

\[
M_{ij} = \frac{h_0}{2} \sigma_{ij} + \frac{\mu}{2} \sigma_{ij} + \frac{\mu}{20} \partial_i \partial_j h - \delta_i^j \frac{\lambda}{20} \nabla^2 h. \tag{16}
\]

In all the averages involving \(m(z)\) (Eq. \(E_{10}\)), we assume \(\ell \ll h_0\), i.e., the actomyosin density is strongly localized to the apical surface. The first two terms in the moment tensor equation above (Eq. \(E_{16}\)) also reflect the apico-basal polarization of the tissue. The first term \(h_0 \sigma^z/2\) is a “passive” contribution that appears because the basal surface is flat and adhered to a substrate, as a result of which the average force taken to act on the mid-plane of the tissue generates a torque on the apical surface. The second term \(h_0 \sigma^z/2\) is an active torque generated by the asymmetric \(z\)-profile of the actomyosin density (Eq. \(E_{10}\)). The final two terms in Eq. \(E_{16}\) are the usual elastic components of the bending moment due to the curvature of the apical surface. Similar active moments have been obtained using inhomogeneous activity profiles in the context of active shells through constant thickness surfaces. While recent work\(^{33}\) has derived a reduced description of epithelial monolayers keeping track of the tissue thickness, the role of apical-basal polarity was only included in the passive part of the mechanics, and active torques as in Eq. \(E_{16}\) were missed.

Finally, we specify the constitutive equation for the traction \((T)\) and normal forces \((f_n)\) to complete the model description. Assuming the substrate is rigid, we use a viscoelastic model to capture the deformation and turnover of the focal adhesions attached to the substrate. In addition, we introduce an internal in-plane polarization \(p\) that directs individual cell motion. Combining the two, we have\(^{34,32}\)

\[
T = Y_s u + \Gamma_p \partial_\perp u - f p, \tag{17}
\]

where \(Y_s\) is the stiffness of the focal adhesion complexes and \(\Gamma_p\) is the effective friction with the substrate. The active propulsion force \(f p\) accounts for cellular crawling and migration due to actin treadmilling within lamellipodia. In confluent epithelia, the polarization \(p\) is appreciable only near the boundary of the colony\(^{32,35,52}\). Following Ref.\(^{36}\) we model the polarization quasi-statically, assuming the tissue is unpolarized in the bulk, and the polarization points along the outward normal at the tissue boundary. Writing to linear order \(\partial_\perp p = -a p + K \nabla^2 p\), with \(a\) a decay rate and \(K\) an elastic constant, we neglect any strain coupling and set \(\partial_\perp p \approx 0\) to get

\[
p = \delta_p \nabla^2 p, \tag{18}
\]

where \(p \cdot \nabla = 1\) along the tissue boundary (\(\nabla\) is the outward normal). The localization length \(\ell_p = \sqrt{K/a}\) controls the penetration of the polarization into the bulk of the tissue. We assume that the propulsion force is the dominant contribution of the polarization, though an extensile active stress \(\sim \zeta' y_p\) \((\zeta' < 0)\) is also generally present. The latter can be viewed as renormalizing the boundary tension (see Sec.\(^{1,2}\) given the edge localized profile of \(p\), and we neglect it henceforth.

The normal force on the tissue has a similar constitutive equation, combining an effective friction \((\Gamma_{\perp})\) and an apical surface tension \((\gamma)\) to give

\[
f_n = \Gamma_{\perp} \partial_\perp h - \gamma \nabla^2 h. \tag{19}
\]

Note that, here we use the fact that the basal surface does not delaminate from the substrate, hence only vertical distortions of the apical surface, through \(h\), contribute to the normal force. Unlike active membranes with pumps\(^{35}\), a mean density of actomyosin units at the apical surface \((m_0 \neq 0)\) does not actively induce a finite normal velocity. Instead, bending deformations of the apical surface distort the cytoskeletal network that generates a restoring force \(\sim \gamma \nabla^2 h\), through its contractility.

To summarize, using Eqs. \(E_{6}\) and \(E_{7}\), the full set of dynamical equations for the in-plane displacements \((u)\) and the tissue thickness \((h)\) are

\[
\Gamma_{\perp} \partial_\perp u + Y_s u = \mu \nabla^2 u + (\mu + \lambda) \nabla \cdot u + \nabla \cdot (\sigma^c + \sigma^f) - \frac{B h_0}{12} \nabla \nabla^2 h + f p, \tag{20}
\]

\[
\Gamma_{\parallel} \partial_\parallel h = \gamma \nabla^2 h - \kappa \nabla^4 h + \frac{h_0}{2} \sigma^c + \frac{h_0}{2} \nabla \cdot (Y_s u + \Gamma_{\perp} \partial_\perp u - f p). \tag{21}
\]

Here, we have defined \(B = 2\mu + \lambda\) as the bulk modulus and \(\kappa = B h_0^2/40\) as the bending rigidity of the tissue. Until now, we have addressed three sources of cellular activity, through a contractile stress \((\sigma^c)\), growth \((\sigma^f)\) and a propulsion force \((/p)\). The final source of activity appears in the boundary conditions and is discussed below.

### 1.2 Boundary conditions

Along with the equations of mechanical equilibrium given in Eqs. \(E_{20}\) and \(E_{21}\) we have to specify the boundary conditions for \(\sigma\) and \(M\). In doing so we include the presence of a contractile actomyosin cable that is apically localized at the boundary. The assembly of such a supracellular structure is known to operate in key morphogenetic events\(^{47,48}\) and wound healing\(^{34,39,50}\). The simplest way to account for this is through a boundary line tension of strength \(\Lambda\) localized at the apical surface of the tissue (see Fig. 3). One can easily show that this also results in an effective boundary torque \(\sim h_0 \Lambda\). Hence we have

\[
\sigma \cdot \nabla \psi = -\Lambda C \psi, \tag{22}
\]

\[
M \cdot \nabla \psi = -h_0 \Lambda C \nabla \psi, \tag{23}
\]
around the edge of the tissue. Note that, as expected, the tangential components of both $\sigma$ and $M$ vanish, while the normal components are balanced by the contractile line tension ($\Lambda > 0$) along with the boundary curvature ($C$). As before, $\mathbf{v}$ is the unit outward normal at the boundary. The various forces acting on the tissue are schematically shown in Fig. 3. In the following, we will analyze the steady states of the equations we have derived and interpret the solutions in terms of shape changes in the epithelial monolayer.

2 Stationary Solution in 1D

For simplicity, we shall work in 1D and assume the tissue is homogeneous in the $y$-direction. This turns out to be sufficient to explain the main features of the model. A more detailed treatment of other geometries is left for future work. We choose our coordinate system so that the undeformed tissue has $-L_0 \leq x \leq L_0$. Setting $\partial_{h}u_{x} = \partial_{h}h = 0$, it is convenient to recast Eqs. 29, 30 in terms of $\sigma_{xx} \equiv \sigma$ and the mean curvature of the apical surface $H = \partial_{y}^2 h$.

The equations then read

$$\varepsilon_{0} \partial_{x}^{2} \sigma = \sigma - \sigma^{\epsilon} - \sigma^{\delta} + \frac{B h_{0}}{12} H - f \varepsilon_{0} \partial_{h} p,$$

$$\varepsilon_{h} \partial_{x}^{2} H = H + \frac{h_{0}}{2 l_{p}^{2}} \partial_{x}^{2} (\sigma + \sigma^{a}) .$$

The stress and curvature relaxation length scales are $\ell_{\sigma} = \sqrt{B Y_{c}}$ and $\ell_{H} = \sqrt{k_{H} / f}$, respectively, where the bulk modulus $B = 2 \mu + \lambda$ as before. The active stresses are taken to be spatially constant, $\sigma_{xx}^{\epsilon} \equiv \sigma^{\epsilon} > 0$ and $\sigma_{xx}^{\delta} \equiv \sigma^{\delta} < 0$, while the polarization $p(x)$ solves Eq. 18 with $p(\pm L_0) = \pm 1$ to give

$$p(x) = \frac{\sinh(x / \ell_{p})}{\sinh(L_{0} / \ell_{p})},$$

which is sketched in Fig. 4. The full analytical solution of the above equations along with the requisite boundary conditions ($\sigma(\pm L_0) = -\Lambda, M(\pm L_0) = -h_{0}\Lambda$) is not very illuminating. Instead it is instructive to consider the case where surface tension dominates bending elasticity, allowing us to neglect $\partial_{H}^{2} H \ll H$ and directly slave the tissue curvature to the stress profile as

$$H \approx - \frac{h_{0}}{2 l_{p}^{2}} \partial_{x}^{2} \sigma,$$

where $\sigma^{\epsilon}$ has dropped out as it is a constant. Of course, this approximation will fail close to the tissue boundary where, in particular, the line tension $\Lambda > 0$ requires $H(L_{0}) = h_{0}(\sigma^{\epsilon} + 3\Lambda)/2 k > 0$ at the edge. Substituting Eq. 27 into Eq. 24, we find that, in this limit, apico basal polarity simply affects the passive mechanics by enhancing the stress relaxation length scale to $L_{0}^{2} = L_{0}^{2} + (B h_{0} / 24 \gamma)$. So we have

$$L_{0}^{2} \partial_{x}^{2} \sigma - \sigma = - \left( \sigma^{\epsilon} + \sigma^{\delta} + f \varepsilon_{0} \partial_{h} p \right).$$

Upon imposing $\sigma(\pm L_0) = -\Lambda$, we obtain the spatial stress profile in the tissue to be

$$\sigma(x) = \sigma_{a} - (\Lambda + \sigma_{a}) \frac{\cosh(x / L_{0})}{\cosh(L_{0} / L_{0})} + \frac{f \varepsilon_{0} \ell_{p}}{\ell_{p}^{2} - L_{0}^{2}} \left[ \cosh(x / \ell_{p}) \cosh(L_{0} / \ell_{p}) \right] - \coth \left( \frac{L_{0}}{\ell_{p}} \right) \cosh(x / L_{0}) \cosh(L_{0} / L_{0}) \right] .$$

We have combined the two bulk active stresses into $\sigma_{a} = \sigma^{\epsilon} + \sigma^{\delta}$.

When actomyosin contractility dominates growth $\sigma_{a} > 0$ and when growth dominates $\sigma_{a} < 0$. With these approximations Eq. 27 directly gives us the curvature profile of the apical surface as

$$H(x) = \frac{h_{0}}{2 \ell_{p}^{2}} \left[ \frac{(\Lambda + \sigma_{a}) \cosh(x / L_{0})}{L_{0}^{2} \cosh(L_{0} / L_{0})} - \frac{f \varepsilon_{0} \ell_{p}}{\ell_{p}^{2} - L_{0}^{2}} \left[ \frac{\sinh(x / \ell_{p})}{\sinh(L_{0} / \ell_{p})} \right] - \left( \frac{L_{0}}{\ell_{p}} \right) \cosh \left( \frac{L_{0}}{\ell_{p}} \right) \cosh(L_{0} / L_{0}) \right] .$$

Similarly, using the steady state in-plane force balance $\partial_{x} \sigma = Y_{p} u_{s} - f p$, we find the displacement of the tissue to be

$$u_{s}(x) = - \frac{(\Lambda + \sigma_{a}) \sinh(x / L_{0})}{Y_{p} L_{0} \cosh(L_{0} / L_{0})} + \frac{f \sinh(x / \ell_{p})}{Y_{p} \sinh(L_{0} / \ell_{p})} + \frac{f \varepsilon_{0} \ell_{p}}{\ell_{p}^{2} - L_{0}^{2}} \left[ \frac{\sinh(x / \ell_{p})}{\sinh(L_{0} / \ell_{p})} \right] - \frac{L_{0}}{\ell_{p}} \coth \left( \frac{L_{0}}{\ell_{p}} \right) \sinh(L_{0} / L_{0}) \right] .$$

3 Active shaping of planar epithelia

We now use the above solution (Eqs. 29, 30, 31) to interpret and characterize the morphology of an adhered epithelium. The curvature of the apical surface at the center of the tissue $H(0)$ and the displacement at the edge $u_{s}(L_{0})$ serve as simple “order parameters” characterizing the shape of the tissue. Note that, when $H(0) > 0$, the apical surface curves up, away from the substrate, adopting an upward concave profile (“valley shaped”), while for $H(0) < 0$, we have an upward convex profile (“dome shaped”) for the apical surface of the tissue. Separately, the in-plane displacement of the tissue edge $u_{s}(L_{0})$ tracks the overall expansion ($u_{s}(L_{0}) > 0$) or contraction ($u_{s}(L_{0}) < 0$) of the tissue with respect to its undeformed state. We shall interpret this as an elastic version of epithelial wetting ($u_{s}(L_{0}) > 0$) or dewetting ($u_{s}(L_{0}) < 0$),...
in analogy with its fluid counterpart.\textsuperscript{37,39}

### 3.1 Role of growth, contractility and the actomyosin cable

We shall first consider the simple case where the polarized motility of the leading cells at the edge of the epithelium is absent, by setting $f = 0$. The competition between adhesion to the substrate and elastic and active stresses creates a spatially inhomogeneous stress profile in the resting tissue sheet. If active stresses are homogeneous, as we consider, the length scale controlling spatial inhomogeneities $\sim L_0$ is determined primarily by the relative strength of tissue to focal adhesion elasticity. In this case, the stress profile is monotonic between $x = 0$ and $x = L_0$, and symmetric across $x = 0$. As expressed in Eq. 27, spatial inhomogeneities in the stress alone result in a nonvanishing curvature of the apical surface with $H \propto -\partial^2 \sigma$ (a homogeneous stress profile always yields a flat surface).

It is possible to obtain a change in the sign of $H(x)$ even in the absence of line tension from the actomyosin cable ($\Lambda = 0$), simply from the competition between contractile and extensile uniform active stresses, as in this case $H(x) \propto \sigma_a$, with $\sigma_a = \sigma^e + \sigma^c$. Additionally, $u_c(L_0) \propto -\sigma_a \sinh(L_0/L_0)$ (from Eq. 31), hence the sign of $\sigma_a$ controls the behavior as follows:

- If contractile stresses exceed extensile ones ($\sigma_a > 0$), then the tissue stress is everywhere contractile (positive, like a negative pressure) and maximum at the center of the tissue. Correspondingly, $H(x) > 0$, i.e., the apical surface is shaped like a valley, as one would physically expect from a decrease in internal pressure, and $u(L_0) < 0$, i.e., the tissue is dewetted (see Fig. 1 image IV).

- If extensile stresses exceed contractile ones ($\sigma_a < 0$), then the tissue stress is everywhere extensile (negative, like a positive pressure) and maximum at the edges of the tissue. Correspondingly, $H(x) < 0$, i.e., the apical surface is shaped like a dome, as one would physically expect from an increase in internal pressure, and $u(L_0) > 0$, i.e., the tissue wets the substrate (see Fig. 1 image I).

Reinstating the actomyosin cable tension $\Lambda > 0$ makes the stress profile more negative, with now contractile behavior (and $H(x) > 0$) arising when $\Lambda + \sigma_a > 0$ and extensile (and $H(x) < 0$) arising when $\Lambda + \sigma_a < 0$, upon neglecting the irrelevant constant $\sigma_a$ offset (see Eq. 29). This can be reformulated in terms of the value of $\Lambda$ required for the two different shapes, with

$$\Lambda_c = -\sigma_a = -\left(\sigma^e + \sigma^c\right).$$

So a curvature transition can only occur if $|\sigma^e| > |\sigma^c|$ (as $\sigma^e < 0$, being extensile, and we must have $\Lambda_c > 0$). The displacement field of the tissue at the boundary is in this case is $u_c(L_0) \propto -(\Lambda + \sigma_a) \sinh(L_0/L_0)$ (Eq. 51). As a result the tissue also undergoes an elastic dewetting to wetting transition at a value of $\Lambda$ that coincides with the change in apical surface curvature. Hence, we find

- $\Lambda > \Lambda_c$: contractile behavior with the stress peaked at the middle of the contracted (dewetted) tissue leading to a valley-shaped apical surface and dewetted tissue (see Fig. 1 image IV).

- $\Lambda < \Lambda_c$: extensile behavior with the stress peaked at the edges of the expanded (wetted) tissue leading to a dome-shaped apical surface and wetting tissue (see Fig. 1 image I).

In short, when growth dominates contractility ($\sigma_a < 0$), an increase in the tension of the actomyosin cable beyond the threshold $\Lambda_c$ causes the tissue to transition from dome-shaped to valley-shaped. The spatial profile of the stress and curvature are plotted in Fig. 5. For a large tissue ($L_0 \gg L_0$), one always has

$$\sigma(0) \simeq \sigma_a, \quad H(0) \simeq 0.$$  \hspace{1cm} (33)

Since $\sigma(L_0) = -\Lambda < 0$, and the stress is monotonic, one then has $\sigma(x) < 0$ everywhere (see Fig. 5) if $\sigma_a < 0$ (required for $\Lambda_c$ to exist). Hence the stresses are always extensile, but can still be maximum in the middle or at the edges, with a corresponding change in the sign of $H(x)$ depending on the value of $\Lambda$ relative to $\Lambda_c$. In this case the value of $H(0)$ alone, being exponentially small in a large tissue, does not provide a good criterion for the sign of the curvature, while the full curvature profile is still meaningful. On the other hand, when contractile active stresses dominate growth, the apical surface always adopts a valley like profile and the tissue dewets from the surface, no matter the strength of the actomyosin line tension.

### 3.2 Role of polarized cell motility

Now for $f \neq 0$, we have an additional length scale $\ell_p$ in the problem that can compete against $L_0$, allowing both the stress and curvature profile to become nonmonotonic on $0 \leq x \leq L_0$. This yields two distinct $\Lambda$ thresholds, one for change in curvature of the apical surface and the other for tissue dewetting, allowing for the four tissue shapes shown schematically in Fig. 1.

Before we address the fully general case, let us first switch off all bulk sources of activity ($\sigma_a = 0$). While $\sigma(L_0) = -\Lambda < 0$ still, the stress at the center of the tissue can change sign and so can its curvature $(\partial^2 \sigma)$. The propulsive force at the edge of the tissue enhances the stress in a region of width controlled roughly by

![Fig. 5 The stress and curvature distribution across the tissue with a bulk active stress ($\sigma_a$) and a boundary tension ($\Lambda$). For dominantly extensile stresses ($\sigma_a < 0$), there is a finite threshold $\Lambda_c = -\sigma_a$ (Eq. 32) for the tension beyond which the curvature of the apical surface changes sign. The spatial profiles of $\sigma(x)$ and $H(x)$ are plotted here in units where $B = 1$ and $L_0 = 1$, neglecting $\ell_p$, for (a) $\Lambda < \Lambda_c$ and (b) $\Lambda > \Lambda_c$. Note that the stress at the boundary of the tissue is given by $-\Lambda$ as required by the boundary condition.](image-url)
max($L_\sigma$, $\ell_p) \ll L_0$, leading (for a sufficiently large $f$) to a positive stress peak $\sim f\ell_p$ localized near the boundary (see Fig. 6). The physics in this case is akin to that of a stretched rubber band attached to a rigid surface, with the pre-stretch combining the net competition between the contractile ring and the propulsive force.

Putting back the bulk active stress $\sigma_a$, the nonmonotonic stress profile persists, which in turn allows for two distinct transition thresholds for the apical curvature change and for elastic dewetting. Setting $x = 0$ in Eq. 30, we have

$$H(0) = \frac{h_0}{2Y\cosh(L_0/L_\sigma)} \left[ \sigma_a - (fL_c - \Lambda) \right], \quad (34)$$

$$L_c = \frac{\ell_p^2}{\ell_p (\ell_p + L_0^2)} \left[ \frac{L_0^2 \cosh(L_0/L_\sigma) - \ell_p^2 \cosh(L_0/\ell_p)}{\sinh(L_0/\ell_p)} \right]. \quad (35)$$

The length scale $L_c$ represents the effective region over which the propulsive force accumulates stress and affects the apical surface curvature. Using the fact that $x^2 \cosh(1/x)$ is a positive and monotonically decreasing function until its minimum at $x \approx 0.48$, one can show that $L_c > 0$ for $\ell_p, L_\sigma \lesssim 0.48L_0$. Note that $L_c$ also remains smooth and finite for $\ell_p = L_\sigma$, and is hence a legitimate length scale in the physical regime of interest. For $\ell_p \ll L_\sigma$ in a large tissue ($L_0 \gg L_\sigma, \ell_p$), we have $L_c \approx \ell_p(\ell_p/L_\sigma)^2$ as expected. Interestingly though, for $\ell_p \approx L_\sigma$, we find $L_c \approx L_\sigma(\ell_p^2/2L_0^2)\ell_p$ and when $\ell_p \gg L_\sigma$, $L_c$ grows exponentially large in the tissue size. This dramatic enhancement of the region of influence of the polarized motility for $\ell_p \gtrsim L_\sigma$ through the tissue and focal adhesion elasticity is reminiscent of similar collective force transmission seen in expanding monolayers.51

From Eq. 34 we immediately find that $H(0)$ changes sign at a threshold actomyosin cable tension,

$$\Lambda_c = fL_c - \sigma_a. \quad (36)$$

As expected, the propulsive force increases the threshold for the tissue shape transition. So for

- $\Lambda > \Lambda_c$: tissue adopts a valley-shaped apical surface.
- $\Lambda < \Lambda_c$: tissue adopts a dome-shaped apical surface.

Recall that $L_\sigma$ can be very large in a large tissue when $\ell_p \gtrsim L_\sigma$, which suggests that such a shape transition can only be realistically observed in smaller tissues or when the polarization is very strongly localized ($\ell_p \ll L_\sigma$). Of course this only refers to the curvature near the center of the tissue. The nonmonotonic spatial profile of the stress and curvature implies that the shape of the apical surface can also change close to the boundary. A representative plot of such a curvature profile is shown in Fig. 6.

Distinct from the curvature change, the displacement of the tissue boundary changes sign at a different threshold for $f \neq 0$, given by

$$\Lambda_d = fL_d - \sigma_a. \quad (37)$$

To see this we set $x = L_0$ in Eq. 31 to obtain

$$u_c(L_0) = \frac{1}{YL_\sigma} \tanh \left( \frac{L_0}{L_\sigma} \right) \left[ -\sigma_a + (fL_d - \Lambda) \right], \quad (38)$$

$$L_d = \frac{L_\sigma}{\tanh(L_0/L_\sigma)} \left[ 1 + \frac{\ell_p^2}{\ell_p^2 - L_\sigma^2} \left( 1 - \frac{\ell_p(\ell_p/L_\sigma)}{L_\sigma \tanh(L_0/\ell_p)} \right) \right]. \quad (39)$$

Here $L_d$ is the length scale that captures the influence of the propulsive force on the tissue displacement. For a large tissue, we have

$$L_d \approx L_\sigma - \frac{\ell_p^2}{(\ell_p + L_\sigma)}, \quad L_\sigma, \ell_p \ll L_0. \quad (40)$$

which is positive as $L_\sigma > \ell_p$. Unlike $L_c$, $L_d$ is independent of the tissue size for a large tissue, irrespective of the ratio $\ell_p/L_\sigma$ and is primarily controlled by the stress penetration depth $L_\sigma$. This highlights the distinction between the force transmission mechanisms that control curvature and shape of the tissue versus its size and wetting properties. It is useful to contrast this with Ref. 39, where a size dependent dewetting transition was observed in an epithelial tissue modeled as an active fluid, which albeit different, is nonetheless similar to our elastic model. The main distinction lies in the strength of cell-substrate adhesions ($Y_s$), which in Ref. 39 is considered negligible, resulting in $L_d \approx L_0$, whereas, we work in the strongly adhered limit with $L_\sigma \ll L_0$. As a consequence, our elastic dewetting transition is size independent. On the other hand, for weak substrate adhesion, we can replace $L_\sigma$ by $L_0$ in Eq. 40 thereby recovering the size dependence seen Ref. 39.

From Eq. 38, we easily find that $u_c(L_0)$ changes sign at the value $\Lambda = \Lambda_d$ given in Eq. 37. Hence, as we change $\Lambda$, we go through a dewetting transition, where for

- $\Lambda > \Lambda_d$: the tissue is globally contracted and dewets from the substrate.
- $\Lambda < \Lambda_d$: the tissue is globally extended and wets the substrate.

Importantly though, when $\ell_p \ll L_\sigma, \Lambda > \Lambda_c$, while for $\ell_p \gtrsim L_\sigma$, $\Lambda_d < \Lambda_c$ and $\Lambda_d$ is then size dependent. As $\Lambda_c \neq \Lambda_d$ when $f \neq 0$, we find

\footnote{Of course, as before, when the bulk active stresses are dominantly contractile ($\sigma_a > 0$), either transition exists only for a sufficiently large propulsive force.}
that our model predicts four different morphological states for the tissue as sketched in Fig. 1. An illustrative morphological “phase diagram” is shown in Fig. 7 for $\sigma_a > 0$, in the $\Lambda-f$ plane. Note that, just like the stress profile, the tissue displacement is also nonmonotonic in general (see Fig. 5). So while the edge of the tissue contracts from its rest length when $\Lambda > \Lambda_d$, the center of the tissue can be locally extended due to the stress being more extensile there and vice-versa. As a result, while our simple characterization in terms of just $H(0)$ and $u_c(L_0)$ is easy to understand, the full tissue shape and stress profile can be accessed in experiments through imaging and traction force microscopy allowing for more stringent tests of our theory.

3.3 Role of apical bending rigidity

Until now, we focused on the minimal model where the bending rigidity of the apical surface $\kappa$ was neglected in favour of its surface tension $\gamma$. This allowed us to take $\ell_H = \sqrt{\kappa/\gamma} \to 0$ and slave $H$ to the stress profile (Eq. 27). Reintroducing a finite but small $\ell_H \ll \ell_a, \ell_p$ does not change the above results, but larger values of $\ell_H$ do affect the tissue morphology and the transitions in qualitative ways. While the curvature is once again slaved to the total stress in the bulk of the tissue, this is no longer the case on scales $\sim \ell_H$ near the boundary. Using the fact that the contractile ring generates a boundary torque that enforces $H(L_0) \propto (\sigma^c + 3\Lambda) > 0$, we see that, close to the tissue boundary, the variation of the curvature on a length scale $\sim \ell_H$ provides an additional effective source of localized stress in Eq. 24 through the passive term $(Bh_0/12)H$. As a result, we find an extra positive contribution $\sim (\sigma^c + 3\Lambda)$ to the force balance equation localized over a region $\ell_H$ from the boundary. This additional contribution enters at the same level as the polarization term, but with the opposite sign. Hence, we can easily extend our previous results by viewing the effect of a finite $\ell_H$ as providing an additional contractile force near the edge spread out over a region of size $\ell_H$, akin to an effective negative propulsive force. This is a direct consequence of apico-basal polarity in the tissue that permits active torques on the apical surface. An immediate implication is that, in the absence of extensile forces, such as arising from growth or polarized cell motility ($f = \sigma^g = 0$), neither a curvature nor a dewetting transition can occur in the tissue, even for finite $\ell_H$. Alternately, even in the absence of polarized motility ($f = 0$), for a finite $\ell_H$ and $\sigma_a < 0$, the curvature change and dewetting transitions now don’t coincide. The various states and transition boundaries, including a finite $\ell_H$ as well, are plotted in the morphological phase diagram shown in Fig. 7.

4 Conclusion

In this paper, by using a lubrication approximation, we have developed a simple 2D elastic model for epithelial tissues strongly adhered to a flat rigid substrate. Crucially, we incorporate both apico-basal polarity in the tissue and the local variation of cellular thickness, allowing us to address the consequences of active stresses on tissue shape. The morphology of a resting epithelium is decided by a competition between bulk and boundary active stresses in conjunction with the elasticity of the tissue and sub-
strate adhesion. We distinguish two kinds of transitions, one concerning the curvature of the apical surface and another for the in-plane size change of the tissue, interpreting the latter as an elastic analog of dewetting. The basic physics underlying these shape changes is transparent: extensile stresses (like positive internal pressure) cause the apical surface to be “dome-shaped” and locally expand the tissue, while contractile stresses (like negative pressure) do the opposite, as expected.

Within a minimal model that neglects the bending rigidity of the apical surface, the curvature \( H \) can be slaved entirely to the total stress in the tissue. In this limit, the transition of either tissue shape or size are decided by a balance of bulk active stresses including contractility and growth \( \sim \sigma^c + \sigma^g \), the actomyosin cable tension \( \sim \Lambda \) and the net stress \( -fL_{c,d} \) arising from cellular motility at the leading edge (remember that \( -f \mathbf{p} \) is the force exerted by the tissue). The length scale \( L_{c,d} \) over which propulsive forces are transmitted is decided by the elastic parameters and differs in general for the two transitions. In particular, \( L_c \) can be size dependent, while \( L_d \) is not in general for a large tissue. Including a finite bending rigidity has a similar effect as an effective negative propulsive force as a result of a cumulative transmission of stress from the boundary active torque generated by the contractile actomyosin cable. Although we only consider homogeneous bulk active stresses, an edge localized spatial profile of either growth or contractility would also have the same effect as the propulsive force, only with the overall sign determined by the stress contribution being mostly contractile or extensile.

In the past few years, there has been a growing understanding on the mechanical basis of tissue morphogenesis in controlled settings, such as in organoids\cite{52}. Recent in-vitro experiments\cite{53,54} demonstrate that epithelial tissues can initiate lumen formation through a folding transition when exposed to a bath of extracellular matrix. It is conceivable that such a shape change is triggered by a mechanism involving competing bulk and boundary active stresses as in our model. A useful test would be to measure the stress profile along with the tissue curvature and compare against our continuum results, as has been done previously for expanding monolayers viewed as an active fluid\cite{55}, though without reference to apical curvature. More recently, active torques arising from a polarized distribution of actomyosin have been experimentally quantified in freely suspended epithelia\cite{56}, highlighting the importance of such torques in bending tissues. Our work provides insight into the routes by which active forces can shape planar stationary epithelia, and extending these results to curved surfaces and time-dependent nonlinear phenomena are the next immediate challenges.

5 Conflicts of interest

There are no conflicts to declare.

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7 Appendices

A Parametrizing the strain tensor

In this Appendix, we parametrize the tissue deformation in terms of in-plane displacements (\( \mathbf{u} \)) and a height field for the tissue thickness (\( h \)). This is done by enforcing \( \epsilon_{iz} = 0 \) as stated in the main text. Writing the 3D position of any point in tissue as \( \mathbf{R} \), we have the identity

\[
\mathbf{R}(x,y,z) = \mathbf{R}_0(x,y) + \int_0^z dz' \partial_z \mathbf{R}(x,y,z'),
\]

where \( \mathbf{R}_0 \equiv \mathbf{R}(z=0) = 0 \) and \( \mathbf{R}_0 \hat{z} = 0 \) as the basal surface is attached to a planar substrate. In the undeformed tissue, \( \partial_z \mathbf{R} = \hat{z} \) and it continues to specify the normal to a local \( x-y \) section of the deformed tissue as well. Writing \( \partial_z \mathbf{R} = \hat{z} + \mathbf{w} \), where \( \mathbf{w} \) is a small deflection, we set \( 2\epsilon_{iz} = 0 \partial_z \mathbf{R}_0 + \partial_z \mathbf{R}_i = 0 \) to linear order in \( \mathbf{w} \). Consistency requires that

\[
w_i = -\int_0^z dz' \partial_z w_i(z'), \quad i = x,y,
\]

while \( w_z \) is not constrained as of yet. As the basal surface is planar, \( \partial_z \mathbf{R}(z=0) = \hat{z} \), hence \( w_z(z=0) = 0 \). The thickness of the tissue being small, we Taylor expand \( w_z \) as a function of \( z \) and retain the lowest order term, which is

\[
w_z = \frac{z}{h_0} W(x,y).
\]

This simple linear interpolation is a convenient ansatz for the 3D deformation of the tissue and is the most dominant term for a thin tissue. The function \( W(x,y) \), as we will see, is related to the local thickness of the tissue. Using this parametrization in Eq.~\ref{eq:41} we obtain \( \mathbf{R} = \mathbf{r} + \mathbf{U} \), where \( \mathbf{r} = (x,y,z) \) is the undeformed material coordinate and the 3D displacement \( \mathbf{U} \) is

\[
U_i = u_i - \frac{z^2}{6h_0} \partial_i W, \quad U_z = \frac{z^2}{2h_0} W,
\]

having introduced the in-plane 2D displacement \( \mathbf{u} \) such that \( \mathbf{R}_0 = (x + u_x, y + u_y, 0) \). The deformed thickness of the tissue is obtained
from \( \dot{z} \cdot \mathbf{R}(z = h_0) = h \), which relates \( W \) and \( h \) as

\[
W = 2 \left( h - h_0 \over h_0 \right). \tag{45}
\]

Hence, \( W \) is exactly the strain in the \( z \)-direction. This completes our parametrization of the 3D displacement, from which it is trivial to obtain the strain tensor quoted in the main text (Eq. \[12\]).

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