

Supplementary Materials for

Active curling of epithelial monolayers dominated by actin cytoskeleton mechanics

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1. Phenomenological model of epithelial monolayers.

Corresponding to the composition of multiscale structural model [see Fig. 1], in our theoretical analysis, the cellular model is divided into three parts in parallel: the cell membrane, the cytoskeleton (CSK), and the cytoplasm. The cell membrane and cytoplasm are scaling-law viscoelastic materials^{32, 49}, and their creep responses are expressed as $J(t) = (1/E_{\text{mem}}^0)t^{-\alpha}$ and $J(t) = (1/E_{\text{cyto}}^0)t^{-\alpha}$, where their elastic moduli are calculated to be $E_{\text{mem}}^0 = 1.96 \text{ kPa}$ and $E_{\text{cyto}}^0 = 4.89 \text{ kPa}$ ⁴⁹, respectively [see Fig. S1(a) and (b)]. The slopes of creep curves are the scaling-law exponent, and both exponents of cell membrane and cytoplasm are calculated as $\alpha = \alpha_m = \alpha_c = 0.46$. Fig. S1(c) shows the typical stress-strain curve of the cytoskeleton for stress hardening³², which can be expressed as $\sigma = E_{\text{csk}}^0 (e^{\lambda \varepsilon} - 1)/\lambda$ where the elastic modulus is calculated to be $E_{\text{csk}}^0 = 1.41 \text{ kPa}$ and the stress hardening coefficient is calculated to be $\lambda = 4.45$ ⁴⁹. Without the pre-tension, the differential modulus is equal to the elastic modulus ($E_{\text{csk}} = E_{\text{csk}}^0$).

Therefore, the phenomenological model of epithelial monolayers is established, consisting of three branches: a fractional element-springpot representing the cell membrane, a spring element representing the cytoskeleton, and a fractional element-springpot representing the cytoplasm, as shown in Fig. S1(d). Its relaxation function and creep function can be written as $E(t) = E_{\text{csk}} + E_{\text{mem}} t^{-\alpha} + E_{\text{cyto}} t^{-\alpha}$, where $E_{\text{mem}} = E_{\text{mem}}^0 (\sin \alpha \pi / \alpha \pi)$ and $E_{\text{cyto}} = E_{\text{cyto}}^0 (\sin \alpha \pi / \alpha \pi)$ are the instantaneous relaxation moduli of cell membrane and cytoplasm⁴⁹, respectively.

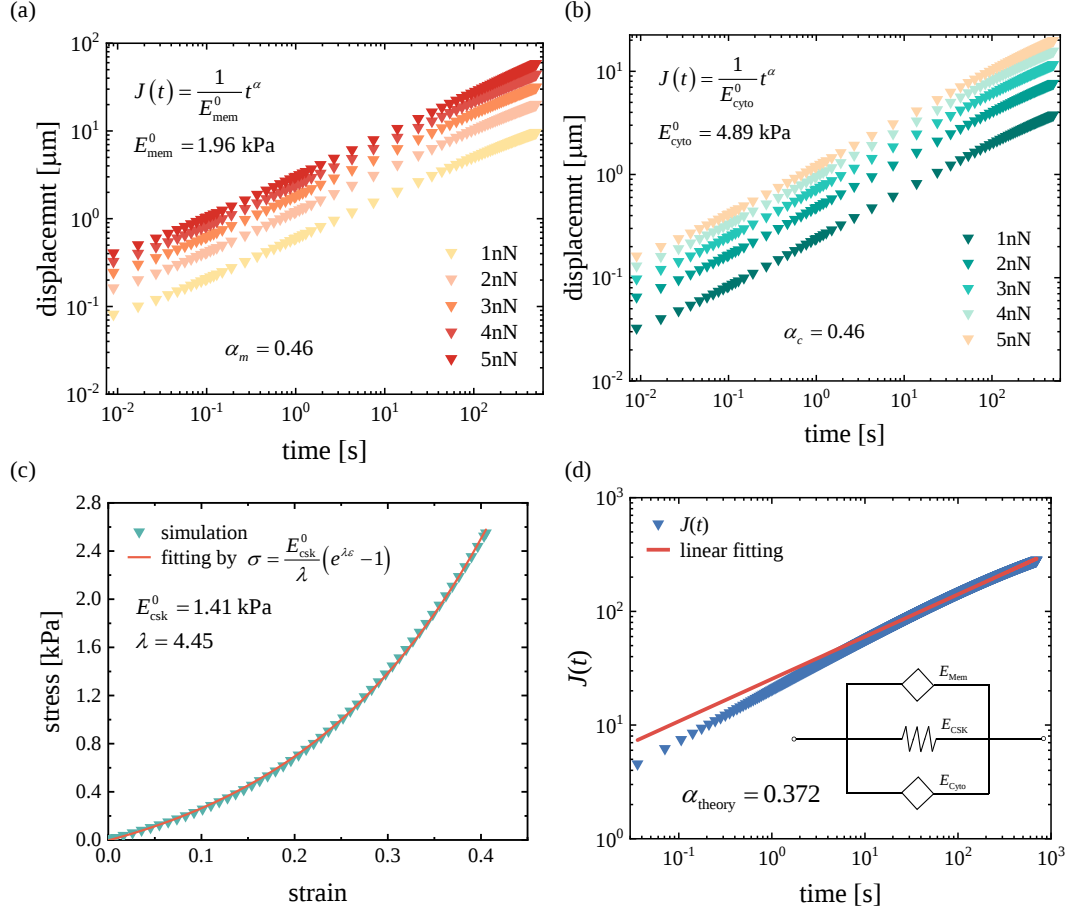


Fig. S1. Phenomenological model of epithelial monolayers. Creep curves of (a) the cell membrane and (b) the cytoplasm with respect to time under different step forces, respectively. (c) Stress-strain curves of the cytoskeleton. The curve can be fitted by the typical stress hardening function $\sigma = (E_{\text{csk}}^0 / \lambda) (e^{\lambda \epsilon} - 1)$, where the elastic modulus and the stress hardening coefficient are $E_{\text{csk}}^0 = 1.41$ kPa and $\lambda = 4.45$, respectively. (a) Creep curves for a phenomenological model of epithelial monolayers. The phenomenological model consists of three branches: a fractional element-springpot representing the cell membrane, a spring element representing the cytoskeleton, and a fractional element-springpot representing the cytoplasm. The scaling-law exponent is $\alpha_{\text{theory}} = 0.372$.

2. Deflection function w_1 of a plate with three sides simply supported and one side free under the deflection $(w)_{x=\pm a/2}$.

To obtain the analytical solution of the spontaneous curling of epithelial tissue, we decompose it into the superposition of three cases, as illustrated in Fig. 4 in the main text. Then, we derive the deflection function in each of the three cases respectively.

Treating a plate with three sides simply supported and one side free as Case 1, in this case, the boundary conditions are

$$\begin{cases} (w)_{x=0} = 0, \left(\frac{\partial^2 w}{\partial x^2} \right)_{x=0} = 0 \\ (w)_{x=\frac{a}{2}} = \sum_{m=1,3,5,\dots}^{\infty} a_m \sin \frac{m\pi y}{b}, \\ (w)_{y=0,b} = 0, \left(\frac{\partial^2 w}{\partial y^2} \right)_{y=0,b} = 0 \end{cases} \quad (S1.1)$$

where a_m is the subsidence shape function. The deflection function w_1 can be expressed as

$$w_1 = - \sum_{m=1}^{\infty} X_m \sin \frac{m\pi y}{b}, \quad (S1.2),$$

where X_m is the shape function. Substituting Eq. (S1.2) into the elastic bending equation

$$D\nabla^4 w = 0, \quad (S1.3),$$

we can obtain

$$\frac{d^4 X_m}{dx^4} - 2 \left(\frac{m\pi}{b} \right)^2 \frac{d^2 X_m}{dx^2} + \left(\frac{m\pi}{b} \right)^4 X_m = 0. \quad (S1.4)$$

The general solution of Eq. (S1.4) is

$$X_m = A_m \sinh \frac{m\pi x}{b} + B_m \frac{m\pi x}{b} \cosh \frac{m\pi x}{b} + C_m \cosh \frac{m\pi x}{b} + D_m \frac{m\pi x}{b} \sinh \frac{m\pi x}{b}. \quad (S1.5)$$

Then, the deflection function satisfies the boundary conditions for Y-sides can be expressed as

$$w_1 = - \sum_{m=1,2,3,\dots}^{\infty} \left(\begin{aligned} &A_m \sinh \frac{m\pi x}{b} + B_m \frac{m\pi x}{b} \cosh \frac{m\pi x}{b} \\ &+ C_m \cosh \frac{m\pi x}{b} + D_m \frac{m\pi x}{b} \sinh \frac{m\pi x}{b} \end{aligned} \right) \sin \frac{m\pi y}{b}. \quad (S1.6)$$

To satisfy the boundary conditions at $x=0$, there should be $C_m = D_m = 0$. By substituting it into the boundary conditions at $x=a/2$ and considering $\alpha_m = m\pi a/(2b)$, we obtain

$$\begin{cases} A_m \sinh \alpha_m + B_m \alpha_m \cosh \alpha_m = a_m \\ A_m (1 - \mu) \sinh \alpha_m + B_m [(1 - \mu) \alpha_m \cosh \alpha_m + 2 \sinh \alpha_m] = 0 \end{cases}, \quad (\text{S1.7})$$

and

$$\begin{cases} A_m = \frac{a_m}{2 \sinh \alpha_m} \left[2 + \frac{(1 - \mu) \alpha_m}{\tanh \alpha_m} \right] \\ B_m = -\frac{(1 - \mu) a_m}{2 \sinh \alpha_m} \end{cases}. \quad (\text{S1.8})$$

Finally, we can derive the deflection function w_1 in Case 1 as

$$w_1 = - \sum_{m=1,3,5,\dots}^{\infty} \left[\frac{(1 - \mu) a_m}{2 \sinh \alpha_m} \left(\left(\frac{2}{(1 - \mu)} + \frac{\alpha_m}{\tanh \alpha_m} \right) \sinh \frac{m\pi x}{b} - \frac{m\pi x}{b} \cosh \frac{m\pi x}{b} \right) \sin \frac{m\pi y}{b} \right]. \quad (\text{S1.9})$$

3. Deflection function w_2 of a plate with four sides simply supported under the active actin filaments distribution field $N(z)$.

For a plate with simply supported boundaries on all four sides (Case 2), the boundary conditions can be treated as:

$$\begin{cases} (w)_{x=\pm a/4} = 0, (M_x)_{x=\pm a/4} = 0 \\ (w)_{y=0,b} = 0, (M_y)_{y=0,b} = 0 \end{cases}, \quad (\text{S2.1}).$$

By considering the relationship between displacement deflections and moments, we can express Eq.(S2.1) as

$$\begin{cases} (w)_{y=0,b} = 0, \left(\frac{\partial^2 w}{\partial y^2} \right)_{y=0,b} = -\frac{M_p}{D} \\ (w)_{x=\pm a/4} = 0, \left(\frac{\partial^2 w}{\partial x^2} \right)_{x=\pm a/4} = -\frac{M_p}{D} \end{cases},$$

where $D = Eh^3/12(1 - \mu^2)$ represent the bending stiffness of epithelial tissues and

$M_p = E\xi/(1 - \mu) \int_{-h/2}^{h/2} N \cdot z dz$ is the equivalent active bending moment. Similarly, the

deflection function w_2 can be expressed as

$$w_2 = \sum_{m=1,2,3,\dots}^{\infty} X_m \sin \frac{m\pi y}{b} - \frac{M_p}{2D} (y-b)y, \quad (S2.2)$$

and the general solution of the shape function X_m is the same as Eq. (S1.4). As the deflection function w_2 is an even function, it can be obtained as $A_m = B_m = 0$. Then we can derive the expression of the deflection function w_2 as

$$w = \sum_{m=1,2,3,\dots}^{\infty} \left(C_m \cosh \frac{m\pi x}{b} + D_m \frac{m\pi x}{b} \sinh \frac{m\pi x}{b} \right) \sin \frac{m\pi y}{b} - \frac{M_p}{2D} (y-b)y. \quad (S2.3)$$

Substituting Eq. (S2.3) into the boundary conditions on $x=a/4$ and assigning the values of β_m as $m\pi a/(4b)$, we can obtain

$$\begin{cases} \sum_{m=1,2,3,\dots}^{\infty} (C_m \cosh \beta_m + D_m \beta_m \sinh \beta_m) \sin \frac{m\pi y}{b} = \frac{M_p}{2D} (y-b)y \\ \left(\frac{m\pi}{b} \right)^2 \sum_{m=1,2,3,\dots}^{\infty} [(C_m + 2D_m) \cosh \beta_m + D_m \beta_m \sinh \beta_m] \sin \frac{m\pi y}{b} = \frac{M_p}{D} \end{cases}. \quad (S2.4)$$

Expanding the right term of the Eq. (S2.4) sign to a single trigonometric series, we get

$$\begin{cases} \frac{M_p}{2D} (y-b)y = \sum_{m=1,2,3,\dots}^{\infty} \left[\frac{2}{b} \int_0^b \frac{M_p}{2D} (y-b)y \sin \frac{m\pi y}{b} dy \right] \sin \frac{m\pi y}{b} \\ = \sum_{m=1,2,3,\dots}^{\infty} \frac{2b^2 M_p}{Dm^3 \pi^3} (\cos m\pi - 1) \sin \frac{m\pi y}{b} \\ \frac{M_p}{D} = \sum_{m=1,2,3,\dots}^{\infty} \left[\frac{2}{b} \int_0^b \frac{M_p}{D} \sin \frac{m\pi y}{b} dy \right] \sin \frac{m\pi y}{b} \\ = \sum_{m=1,2,3,\dots}^{\infty} \frac{2M_p}{Dm\pi} (\cos m\pi - 1) \sin \frac{m\pi y}{b} \end{cases}. \quad (S2.5)$$

Then, we obtain

$$\begin{cases} C_m \cosh \beta_m + D_m \beta_m \sinh \beta_m = \frac{2b^2 M_p}{Dm^3 \pi^3} (\cos m\pi - 1) \\ (C_m + 2D_m) \cosh \beta_m + D_m \beta_m \sinh \beta_m = \frac{2b^2 M_p}{Dm^3 \pi^3} (\cos m\pi - 1) \end{cases}, \quad (S2.6)$$

$$\begin{cases} C_m = \frac{2b^2 M_p}{Dm^3 \pi^3 \cosh \beta_m} (\cos m\pi - 1) \\ D_m = 0 \end{cases} \quad (S2.7)$$

In this way, we obtain the final form of the deflection function w_2 as

$$w_2 = -\frac{4b^2 M_p}{D\pi^3} \sum_{m=1,3,5,\dots}^{\infty} \frac{\cosh \frac{4\beta_m x}{a}}{m^3 \cosh \beta_m} \sin \frac{m\pi y}{b} - \frac{M_p}{2D} (y-b)y. \quad (S2.8)$$

To facilitate the superposition, we translate the Y -axis leftward by $a/4$, and obtain

$$w_2 = -\frac{4b^2 M_p}{D\pi^3} \sum_{m=1,3,5,\dots}^{\infty} \frac{\cosh \left(\frac{4\beta_m x}{a} + \beta_m \right)}{m^3 \cosh \beta_m} \sin \frac{m\pi y}{b} - \frac{M_p}{2D} (y-b)y. \quad (S2.9)$$

To solve the subsidence shape function a_m , it is necessary to further obtain the equivalent shear force on the free sides of both Case 1 and Case 2. The resultant force on the free sides is zero, implying that the equivalent shear force of Case 1 and Case 2 satisfies the following relation:

$$\left(\overline{F}_{Qx}^1 + \overline{F}_{Qx}^2 \right)_{x=\frac{a}{2}} = 0. \quad (S2.10)$$

where

$$\begin{aligned} \overline{F}_{Qx}^1 &= -D \left[\frac{\partial^3 w}{\partial x^3} + (2-\mu) \frac{\partial^3 w}{\partial x \partial y^2} \right]_{x=\frac{a}{2}} \\ &= -\frac{D\pi^3 (1-\mu)^2}{2b^3} \sum_{m=1,3,5,\dots}^{\infty} \left[\frac{a_m m^3}{\sinh^2 \alpha_m} \left(\frac{3+\mu}{1-\mu} \frac{\sinh(2\alpha_m)}{2} + \alpha_m \right) \sin \frac{m\pi y}{b} \right], \end{aligned} \quad (S2.11)$$

$$\begin{aligned} \overline{F}_{Qx}^2 &= -D \left[\frac{\partial^3 w}{\partial x^3} + (2-\mu) \frac{\partial^3 w}{\partial x \partial y^2} \right]_{x=\frac{a}{2}} \\ &= \frac{4(3-\mu)M_T}{b} \sum_{m=1,3,5,\dots}^{\infty} \left(\beta_m \tanh \beta_m \sin \frac{m\pi y}{b} \right). \end{aligned} \quad (S2.12)$$

Finally, we can obtain the subsidence shape function a_m as

$$a_m = \frac{16b^2(3-\mu)M_p\beta_m \tanh \beta_m \sinh^2 \alpha_m}{Dm^3\pi^3(1-\mu)^2 \left(\frac{3+\mu}{1-\mu} \sinh 2\alpha_m + 2\alpha_m \right)}. \quad (S2.13)$$

4. Deflection function w_3 of a plate with the trilateral simply supported and one-edge free under adjacent trilateral active bending moment M_p .

The microelement deformation energy of a plate dV is expressed as $dV = -\frac{1}{2} [M_x w_{,xx} + M_y w_{,yy} - 2M_{xy} w_{,xy}] dx dy$. Considering $M_p = 0$, we can obtain

$$dV = \frac{D}{2} \left[(w_{,xx} + w_{,yy})^2 - 2(1-\mu)(w_{,xx} w_{,yy} - w_{,xy}^2) \right] dx dy. \quad (S3.1)$$

Then, the bending deformation energy of the entire plate V is given:

$$V = \frac{D}{2} \iint \left[(w_{,xx} + w_{,yy})^2 - 2(1-\mu)(w_{,xx} w_{,yy} - w_{,xy}^2) \right] dx dy. \quad (S3.2)$$

For a four-sided simply supported rectangular plate without free edges, the bending deformation energy of the entire plate V can be expressed as

$$V = \frac{D}{2} \iint (\nabla^2 w)^2 dx dy. \quad (S3.3)$$

In Case 3, the deflection function w_3 can be expressed as

$$w_3 = \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} E_{mn} \sin \frac{2n\pi x}{a} \sin \frac{m\pi y}{b}. \quad (S3.4)$$

Combining Eq. (S3.4) and Eq. (S3.3), we can obtain the expression of the bending deformation energy as

$$V = \frac{\pi^4 ab D}{16} \sum_{m=1,3,5,\dots}^{\infty} \sum_{n=1,3,5,\dots}^{\infty} E_{mn}^2 \left(\frac{4n^2}{a^2} + \frac{m^2}{b^2} \right)^2, \quad (S3.5)$$

$$\delta V = \frac{\pi^4 ab D}{8} \left(\frac{4n^2}{a^2} + \frac{m^2}{b^2} \right)^2 E_{mn} \delta E_{mn}. \quad (S3.6)$$

The curvature of the bending surface of the plate along three edges ($x=0$, $y=0$ and $y=b$) are

$$\begin{cases} (w_{,x})_{x=0} = \pm \frac{2\pi}{a} \sum_{m=1,3,5,\dots}^{\infty} \sum_{n=1,3,5,\dots}^{\infty} nE_{mn} \sin \frac{m\pi y}{b} \\ (w_{,y})_{y=0,b} = \pm \frac{\pi}{b} \sum_{m=1,3,5,\dots}^{\infty} \sum_{n=1,3,5,\dots}^{\infty} mE_{mn} \sin \frac{2n\pi x}{a} \end{cases}, \quad (\text{S3.7})$$

Therefore, the increment of curvature can be obtained as

$$\begin{cases} \delta(w_{,x})_{x=0} = \pm \frac{2m\pi}{a} \sin \frac{n\pi y}{b} \delta E_{mn} \\ \delta(w_{,y})_{y=0,b} = \pm \frac{n\pi}{b} \sin \frac{2m\pi x}{a} \delta E_{mn} \end{cases}. \quad (\text{S3.8})$$

Then the work done by the torque is

$$\begin{aligned} \delta W &= -\int_0^b M_T \frac{2m\pi}{a} \sin \frac{n\pi y}{b} dy \delta A_{mn} - \int_0^{\frac{a}{2}} M_T \frac{n\pi}{b} \sin \frac{2m\pi x}{a} dx \delta A_{mn} \\ &= -\left(\frac{4mb}{na} + \frac{na}{mb} \right) M_T \delta A_{mn}. \end{aligned} \quad (\text{S3.9})$$

According to $\delta V + \delta W = 0$, we can get

$$E_{mn} = -\frac{8M_T}{\pi^4 Dab} \left(\frac{4m^2}{a^2} + \frac{n^2}{b^2} \right)^{-2} \left(\frac{4mb}{na} + \frac{na}{mb} \right). \quad (\text{S3.10})$$

Together, the deflection function w_2 is expressed as

$$\begin{aligned} w_3 &= \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} E_{mn} \sin \frac{2m\pi x}{a} \sin \frac{n\pi y}{b} \\ &= -\frac{8M_p}{\pi^4 D} \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} \left(\frac{1}{mn} \right) \left(\frac{a^2 b^2}{4m^2 b^2 + n^2 a^2} \right) \sin \frac{2m\pi x}{a} \sin \frac{n\pi y}{b}. \end{aligned} \quad (\text{S3.11})$$

To solve the subsidence shape function $\bar{a}_m$, it is necessary to further obtain the equivalent shear force of Case 1 and Case 3 on the free sides, whose resultant force is zero, namely that

$$\left(\bar{F}_{Qx}^1 + \bar{F}_{Qx}^3 \right)_{x=\frac{a}{2}} = 0, \quad (\text{S3.12})$$

where

$$\begin{aligned} \bar{F}_{Qx}^3 &= -D \left[\frac{\partial^3 w}{\partial x^3} + (2-\mu) \frac{\partial^3 w}{\partial x \partial y^2} \right]_{x=\frac{a}{2}} \\ &= \frac{16M_T}{\pi} \sum_{m=1,3,5,\dots}^{\infty} \sum_{n=1,3,5,\dots}^{\infty} \left(\frac{1}{n} \right) \left(\frac{4m^2}{a^2} + \frac{n^2}{b^2} \right)^{-1} \left(\frac{4m^2}{a^2} + (2-\mu) \frac{n^2}{b^2} \right) \sin \frac{n\pi y}{b} \end{aligned} \quad (S3.13)$$

Then, we can obtain the subsidence shape function $\bar{a}_m$ as

$$\bar{a}_m = \frac{32M_p \sinh^2 \alpha_m \sum_{i=1,3,5,\dots}^{\infty} \left(\frac{4i^2}{a^2} + \frac{m^2}{b^2} \right)^{-1} \times \left(\frac{4i^2}{a^2} + (2-\mu) \frac{m^2}{b^2} \right)}{D\pi^4 (1-\mu)^2 m^4 \left(\frac{3+\mu}{1-\mu} \frac{\sinh(2\alpha_m)}{2} + \alpha_m \right)}. \quad (S3.14)$$

In summary, by superimposing the above problems, the elastic solution of the half problem in the main text can be obtained:

$$\begin{aligned} w &= w_1 + \bar{w}_1 + w_2 + w_3 \\ &= - \underbrace{\sum_{m=1,3,5,\dots}^{\infty} \left[\frac{(1-\mu)a_m}{2 \sinh \alpha_m} \left(\left(\frac{2}{(1-\mu)} + \frac{\alpha_m}{\tanh \alpha_m} \right) \sinh \frac{m\pi x}{b} - \frac{m\pi x}{b} \cosh \frac{m\pi x}{b} \right) \sin \frac{m\pi y}{b} \right]}_{w_1} \\ &\quad - \underbrace{\sum_{m=1,3,5,\dots}^{\infty} \left[\frac{(1-\mu)\bar{a}_m}{2 \sinh \alpha_m} \left(\left(\frac{2}{(1-\mu)} + \frac{\alpha_m}{\tanh \alpha_m} \right) \sinh \frac{m\pi x}{b} - \frac{m\pi x}{b} \cosh \frac{m\pi x}{b} \right) \sin \frac{m\pi y}{b} \right]}_{\bar{w}_1} \\ &\quad - \underbrace{\frac{4b^2 M_p}{D\pi^3} \sum_{m=1,3,5,\dots}^{\infty} \frac{\cosh \left(\frac{4\beta_m x}{a} + \beta_m \right)}{m^3 \cosh \beta_m} \sin \frac{m\pi y}{b} - \frac{M_p}{2D} (y-b)y}_{w_2} \\ &\quad - \underbrace{\frac{8M_p}{\pi^4 D} \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} \left(\frac{1}{mn} \right) \left(\frac{a^2 b^2}{4m^2 b^2 + n^2 a^2} \right) \sin \frac{2m\pi x}{a} \sin \frac{n\pi y}{b}}_{w_3}. \end{aligned} \quad (S3.15)$$

According to the elastic-viscoelastic correspondence principle, the elastic bending equation Eq. (S1.3) is transformed into

$$\int_0^t D(t-\tau) \cdot d\nabla^4 w(x, y, t) d\tau = 0, \quad (S3.16)$$

which is Eq. (6) in the main text. In addition, the viscoelastic solution [Eq. (8) in the main text] can be obtained by replacing the bending modulus D of the elastic solution [Eq. (S3.15)] with $D(t)$.

5. Buckling promotes spontaneous curling under larger compression loading.

Fig. S2(a) shows the time evolution curves of the rotation angle $\theta_{y\max}$ of epithelial tissues curling under different loading strains. Compared with Fig. S2(b), the buckling makes the curve significantly different from others [Fig. S2(a)]. In other words, under larger compression forces, the spontaneous curling and buckling of epithelial tissues are superimposed on each other and the buckling behavior further promotes the curling. In addition, the active post-buckling behavior (spontaneous recovery) observed in our simulations [Fig. S2(b)] is in agreement with the experiment of Wyatt et al.²⁵. They suggested that actomyosin controls the planarity and folding of epithelia in response to compression. Thus, the active force allows epithelia to buffer against deformation²⁵ and drives the tissue to form and retain complex mechanical behaviors, such as spontaneous curling.

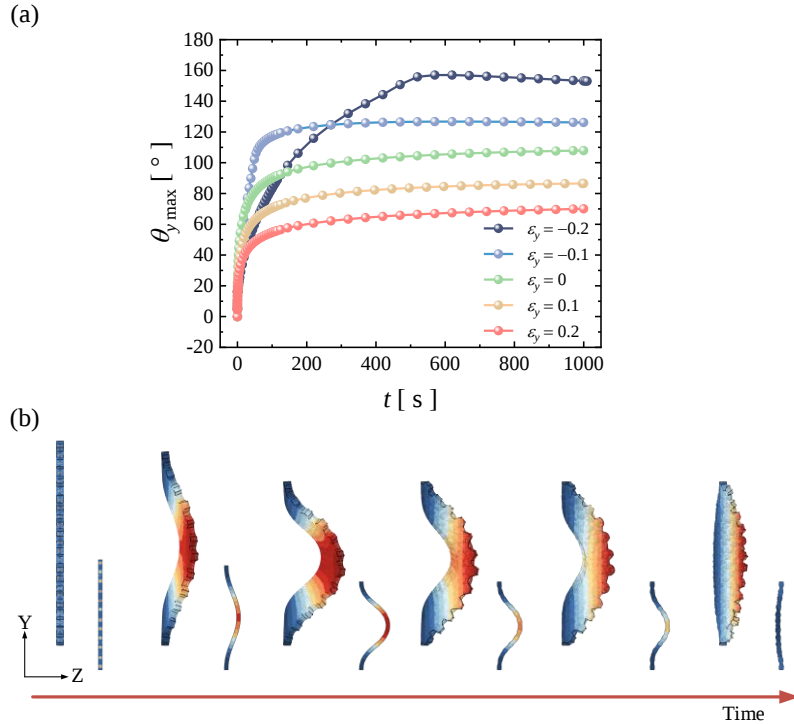


Fig. S2. Evolution of curling of epithelial tissues over time. (a) Time evolution curve of the rotation angle $\theta_{y\max}$ of epithelial tissue curling under different loading strains. In our simulation, the step load is approximated by a linear loading in a short time (within 1 s). (b) Shape transformation of epithelial tissues with time under the superposition of buckling and curling with the strain

$\varepsilon_y = -0.2$. The epithelial monolayer buckles and gradually flattens under the active force over time. The small picture in the lower right corner shows the model bending YZ -profile.