## Supplementary Information

## 1. Full set of equations associated with models 1-3

### 1.1. Rheological equations

We present here the full set of equations associated with models 1-3, where the cell-production rate $k_{\mathrm{p}}$ in the epithelium is imposed as a function of distance from the epithelium-stroma interface. For the epithelium, the rheology is that of an incompressible viscous fluid with shear viscosity $\eta \ddagger$ and the source term $k_{\mathrm{p}}$, which encompasses cellular division and apoptosis:

$$
\begin{align*}
\partial_{\alpha} v_{\alpha} & =k_{\mathrm{p}} \\
\sigma_{\alpha \beta}^{\prime} & =\eta\left(\partial_{\alpha} v_{\beta}+\partial_{\beta} v_{\alpha}\right) \\
\partial_{\alpha} \sigma_{\alpha \beta} & =0 . \tag{1}
\end{align*}
$$

Here, $v_{\alpha}$ is the cell-velocity field and $\sigma_{\alpha \beta}$ the total stress tensor, which has been split into $\sigma_{\alpha \beta}^{\prime}$ defined above and a remaining diagonal part $-p_{\mathrm{e}} \delta_{\alpha \beta}$, where $p_{\mathrm{e}}$ is the tissue pressure. The third equation is the force-balance condition.

In models 1-3, the rate of cellular production takes the form of a single exponential with a characteristic decay length $l$ :

$$
\begin{equation*}
k_{\mathrm{p}}(z)=k \exp \left(-\frac{z-L}{l}\right)-k_{0} . \tag{2}
\end{equation*}
$$

The steady-state thickness of the epithelium $H$ is then related to the constant $k_{0}$ introduced above by the relation:

$$
\begin{equation*}
k_{0}=k \frac{l}{H}\left[1-\exp \left(-\frac{H}{l}\right)\right], \tag{3}
\end{equation*}
$$

which insures that cell velocity vanishes at the apical surface of the epithelium, or equivalently that the total number of cells is globally conserved.

In the case of model 1 , the stroma is described as an incompressible elastic solid:

$$
\begin{align*}
\partial_{\alpha} u_{\alpha} & =0 \\
\sigma_{\alpha \beta}^{\mathrm{s}} & =\mu\left(\partial_{\alpha} u_{\beta}+\partial_{\beta} u_{\alpha}\right) \\
\partial_{\alpha} \sigma_{\alpha \beta}^{\mathrm{s}} & =0 . \tag{4}
\end{align*}
$$

Here, $\mu$ is the shear modulus of the elastic material and $u_{\alpha}$ its displacement field with respect to its resting configuration. The total stress tensor $\sigma_{\alpha \beta}^{\mathrm{s}}$ has been similarly split into two parts, $\sigma_{\alpha \beta}^{\mathrm{s}}$ and $-p_{\mathrm{s}} \delta_{\alpha \beta}$, with $p_{\mathrm{s}}$ the stroma pressure.
$\ddagger$ For simplicity, we assume a ratio of $\frac{2}{3}$ between bulk and shear viscosities.

In the case of model 2 , the stroma is described as an incompressible viscous fluid:

$$
\begin{align*}
\partial_{\alpha} v_{\alpha}^{\mathrm{s}} & =0 \\
\sigma_{\alpha \beta}^{\mathrm{s}} & =\eta_{\mathrm{s}}\left(\partial_{\alpha} v_{\beta}^{\mathrm{s}}+\partial_{\beta} v_{\alpha}^{\mathrm{s}}\right) \\
\partial_{\alpha} \sigma_{\alpha \beta}^{\mathrm{s}} & =0, \tag{5}
\end{align*}
$$

where $\eta_{\mathrm{s}}$ is the stroma viscosity and where the decomposition of the stress tensor $\sigma_{\alpha \beta}^{\mathrm{s}}=\sigma_{\alpha \beta}^{\prime \mathrm{s}}-p_{\mathrm{s}} \delta_{\alpha \beta}$ is similar as before.

For model 3, the constitutive equation is that of a material that behaves elastically at short times with a shear modulus $\mu$ and flows at long times with a shear viscosity $\eta_{\mathrm{s}}$. These two quantities define a relaxation time $\tau=\eta_{\mathrm{s}} / \mu$ that marks the transition between the two regimes. To linear order, we get the following Maxwell model:

$$
\begin{equation*}
\left(\tau \partial_{t}+1\right) \sigma_{\alpha \beta}^{\mathrm{s}}=\eta_{\mathrm{s}}\left(\partial_{\alpha} v_{\beta}^{\mathrm{s}}+\partial_{\beta} v_{\alpha}^{\mathrm{s}}\right), \tag{6}
\end{equation*}
$$

to which must be added the condition for incompressibility $\partial_{\alpha} v_{\alpha}^{\mathrm{s}}=0$ and the forcebalance equation $\partial_{\alpha} \sigma_{\alpha \beta}^{\mathrm{s}}=0$ (with $\sigma_{\alpha \beta}^{\mathrm{s}}=\sigma_{\alpha \beta}^{\mathrm{s}}-p_{\mathrm{s}} \delta_{\alpha \beta}$ ). Note that, since we investigate our model only to linear order in perturbations around a state where the velocity field vanishes uniformly in the stroma, the current linear Maxwell model suffices.

### 1.2. Boundary conditions

The boundary conditions at the apical surface of the epithelium read, to linear order:

$$
\begin{align*}
\sigma_{\mathrm{nt}} & =0 \\
\sigma_{\mathrm{nn}} & =\gamma_{\mathrm{a}} \delta H^{\prime \prime} \\
v_{z} & =\delta \dot{H} . \tag{7}
\end{align*}
$$

Here and throughout the paper, the indices ' $n$ ' and ' $t$ ' denote spatial coordinates in the directions respectively normal and tangential to the interface under consideration. The normal coordinate is oriented positively from the 'lower' compartment toward the 'upper' compartment according to the conventions of figure 1 of the main text (here from the epithelium toward the lumen). We also make use of the following notations for the partial derivatives of any field $\phi(x, t): \phi^{\prime \prime}=\partial^{2} \phi / \partial x^{2}$ and $\dot{\phi}=\partial \phi / \partial t$. At the epithelium-stroma interface, we have:

$$
\begin{align*}
\sigma_{\mathrm{nn}}^{\mathrm{s}} & =\sigma_{\mathrm{nn}}+\gamma_{\mathrm{i}} \delta h^{\prime \prime} \\
\sigma_{\mathrm{nt}} & =\xi\left(v_{\mathrm{t}}-\dot{u}_{\mathrm{t}}\right) \\
\sigma_{\mathrm{nt}}^{\mathrm{s}} & =\xi\left(v_{\mathrm{t}}-\dot{u}_{\mathrm{t}}\right) \\
\dot{u}_{\mathrm{n}} & =v_{\mathrm{n}} \\
u_{z} & =\delta h \tag{8}
\end{align*}
$$

for the elastic stroma, and

$$
\begin{aligned}
\sigma_{\mathrm{nn}}^{\mathrm{s}} & =\sigma_{\mathrm{nn}}+\gamma_{\mathrm{i}} \delta h^{\prime \prime} \\
\sigma_{\mathrm{nt}} & =\xi\left(v_{\mathrm{t}}-v_{\mathrm{t}}^{\mathrm{s}}\right)
\end{aligned}
$$

$$
\begin{align*}
\sigma_{\mathrm{nt}}^{\mathrm{s}} & =\xi\left(v_{\mathrm{t}}-v_{\mathrm{t}}^{\mathrm{s}}\right) \\
v_{\mathrm{n}}^{\mathrm{s}} & =v_{\mathrm{n}} \\
v_{z}^{\mathrm{s}} & =\dot{\delta h} \tag{9}
\end{align*}
$$

for either the viscous or the viscoelastic stroma. At the bottom of the stroma $(z=0)$, the displacement vanishes, which reads:

$$
\begin{equation*}
u_{x}=u_{y}=0 \quad \text { and } \quad u_{z}=0 \tag{10}
\end{equation*}
$$

for the elastic case, and

$$
\begin{equation*}
v_{x}^{\mathrm{s}}=v_{y}^{\mathrm{s}}=0 \quad \text { and } \quad v_{z}^{\mathrm{s}}=0 \tag{11}
\end{equation*}
$$

for the two other models.

### 1.3. Unperturbed solution

In the case of an unperturbed, flat configuration, the solution in the stroma is trivial, with vanishing displacement and pressure fields. In the epithelium, the velocity and pressure fields read:

$$
\begin{align*}
& v_{z}^{0}=k l\left[1-\exp \left(-\frac{z-L}{l}\right)\right]-k_{0}(z-L) \\
& p_{\mathrm{e}}^{0}=2 \eta k_{\mathrm{p}} \tag{12}
\end{align*}
$$

where $k_{\mathrm{p}}$ is given by equation (2). The components of the total stress tensor are zero except for $\sigma_{x x}^{0}=\sigma_{y y}^{0}=-p_{\mathrm{e}}^{0}=-2 \eta k_{\mathrm{p}}$. Note that this form of the unperturbed solution in the epithelium is independent of the stroma rheology.

### 1.4. Perturbed equations

Labelling all perturbed fields with a prefix ' $\delta$ ', we obtain the linearized continuity equation in the epithelium as $\partial_{\alpha} \delta v_{\alpha}=k_{\mathrm{p} \mid z-\delta h}-k_{\mathrm{p} \mid z} \simeq-\left(\partial k_{\mathrm{p}} / \partial z\right) \delta h$, since $(z-\delta h)$ is the new distance between the point of coordinate $z$ in the epithelium and the perturbed epithelium-stroma interface $\delta h$. This leads to:

$$
\begin{equation*}
\partial_{\alpha} \delta v_{\alpha}=\frac{k}{l} \exp \left(-\frac{z-L}{l}\right) \delta h . \tag{13}
\end{equation*}
$$

The other bulk equations in (1) as well as those describing the stroma retain their exact same form as before, now in terms of the perturbed quantities.

To linear order in perturbations, the Fourier modes in the $x$ and $y$ directions decouple, such that it is sufficient to study a deformation $\delta h$ of the epitheliumstroma interface translationally invariant in the $y$ direction with the complex form $\delta h(x, t)=\delta h(q) \exp (\omega t+\mathrm{i} q x)$. Consequently, all perturbed fields have the same form and the dependence in the wave number $q$ will be implicit in the equations given below. Expressing the stress-tensor and velocity components in the boundary conditions (7) to
(11) in the original reference frame with axes $(x, z)$ leads to the following set of equations. At the apical surface of the epithelium, we have:

$$
\begin{array}{ll}
\eta\left(\partial_{x} \delta v_{z}+\partial_{z} \delta v_{x}\right) & =-2 \mathrm{i} q \eta k_{\mathrm{p}} \delta H \\
2 \eta \partial_{z} \delta v_{z}-\delta p_{\mathrm{e}} & =-\gamma_{\mathrm{a}} q^{2} \delta H \\
\delta v_{z} & =\left(\partial_{t}-k_{\mathrm{p}}\right) \delta H, \tag{14}
\end{array}
$$

where the different quantities are expressed at $z=L+H$, since further corrections due to displacements of the interface are second order. Here, the cell-production rate at the apical surface $k_{\mathrm{p}}=k_{\mathrm{P} \mid z=H+L}=k \exp (-H / l)-k_{0}$ appears because of the non-trivial, unperturbed velocity field in the epithelium.

At the epithelium-stroma interface, the expression of the boundary conditions depend on the stroma rheology. For the elastic stroma of model 1, we have:

$$
\begin{array}{ll}
2 \mu \partial_{z} \delta u_{z}-\delta p_{\mathrm{s}} & =2 \eta \partial_{z} \delta v_{z}-\delta p_{\mathrm{e}}-\gamma_{\mathrm{i}} q^{2} \delta h \\
\eta\left(\partial_{x} \delta v_{z}+\partial_{z} \delta v_{x}\right)+2 \mathrm{i} q \eta k_{\mathrm{p}} \delta h & =\xi\left(\delta v_{x}-\delta \dot{u}_{x}\right) \\
\mu\left(\partial_{x} \delta u_{z}+\partial_{z} \delta u_{x}\right) & =\xi\left(\delta v_{x}-\delta \dot{u}_{x}\right) \\
\delta \dot{u}_{z} & =k_{\mathrm{p}} \delta h+\delta v_{z} \\
\delta u_{z} & =\delta h, \tag{15}
\end{array}
$$

where the different quantities are evaluated at $z=L$. Here again, the terms containing the cell-production rate at the epithelium-stroma interface $k_{\mathrm{P} \mid z=L}=k-k_{0}$ come from the presence of the unperturbed solution in the epithelium. For the viscous stroma of model 2 , the conditions read:

$$
\begin{array}{ll}
2 \eta_{\mathrm{s}} \partial_{z} \delta v_{z}^{\mathrm{s}}-\delta p_{\mathrm{s}} & =2 \eta \partial_{z} \delta v_{z}-\delta p_{\mathrm{e}}-\gamma_{\mathrm{i}} q^{2} \delta h \\
\eta\left(\partial_{x} \delta v_{z}+\partial_{z} \delta v_{x}\right)+2 \mathrm{i} q \eta k_{\mathrm{p}} \delta h & =\xi\left(\delta v_{x}-\delta v_{x}^{\mathrm{s}}\right) \\
\eta_{\mathrm{s}}\left(\partial_{x} \delta v_{z}^{\mathrm{s}}+\partial_{z} \delta v_{x}^{\mathrm{s}}\right) & =\xi\left(\delta v_{x}-\delta v_{x}^{\mathrm{s}}\right) \\
\delta v_{z}^{\mathrm{s}} & =k_{\mathrm{p}} \delta h+\delta v_{z} \\
\delta v_{z}^{\mathrm{s}} & =\delta \dot{h} . \tag{16}
\end{array}
$$

Finally, for the viscoelastic stroma of model 3, we have:

$$
\begin{array}{ll}
2 \eta^{\mathrm{s}} \partial_{z} \delta v_{z}^{\mathrm{s}}-\left(\tau \partial_{t}+1\right) \delta p_{\mathrm{s}} & =\left(\tau \partial_{t}+1\right)\left[2 \eta \partial_{z} \delta v_{z}-\delta p_{\mathrm{e}}-\gamma_{\mathrm{i}} q^{2} \delta h\right] \\
\eta\left(\partial_{x} \delta v_{z}+\partial_{z} \delta v_{x}\right)+2 \mathrm{i} q \eta k_{\mathrm{p}} \delta h & =\xi\left(\delta v_{x}-\delta v_{x}^{\mathrm{s}}\right) \\
\eta_{\mathrm{s}}\left(\partial_{x} \delta v_{z}^{\mathrm{s}}+\partial_{z} \delta v_{x}^{\mathrm{s}}\right) & \\
\delta v_{z}^{\mathrm{s}} & =\xi\left(\tau \partial_{t}+1\right)\left(\delta v_{x}-\delta v_{x}^{\mathrm{s}}\right) \\
\delta v_{z}^{\mathrm{s}} & =k_{\mathrm{p}} \delta h+\delta v_{z}  \tag{17}\\
& =\dot{\delta h} .
\end{array}
$$

## 2. Results for model 1

We start by the presentation of the mode structure for model 1 , where the stroma is elastic.

### 2.1. Asymptotic behaviour of the modes

We obtain three relaxation modes, of which we can analyze the asymptotic behaviours in the limits of large and small wave numbers, respectively. More complete expressions including higher-order terms can be found in section 5. In the limit of large wave numbers $q$, the relaxation modes associated with the epithelium-stroma interface and with the apical surface of the epithelium decouple, since their characteristic decay lengths are of order $q^{-1}$, which in this limit is much smaller than the epithelium thickness $H$. To constant order in a systematic expansion in $q^{-1}$, we get the following expressions:

$$
\begin{align*}
& \omega_{1} \simeq-\frac{\gamma_{\mathrm{i}}}{2 \eta} q-\frac{\mu}{\eta}+k-k_{0} \\
& \omega_{2} \simeq-\frac{\gamma_{\mathrm{a}}}{2 \eta} q+k \mathrm{e}^{-H / l}-k_{0} \\
& \omega_{3} \simeq-2 \frac{\mu}{\xi} q-\frac{\mu}{\eta} \tag{18}
\end{align*}
$$

The two first modes correspond to a balance of surface-tension and cell-production forces, to which in the first mode the elastic resistance of the stroma also contributes. The third mode corresponds to a balance of tangential stress and surface friction at the epithelium-stroma interface.

In the limit of small wave numbers, systematic expansions to leading order yield:

$$
\begin{align*}
& \omega_{1} \simeq-\frac{36 \mu}{\eta} \frac{1}{H^{3} L^{3}} \frac{1}{q^{6}} \\
& \omega_{2} \simeq-\frac{\mu}{4 \eta} \frac{1}{H L} \frac{1}{q^{2}} \\
& \omega_{3} \simeq k \mathrm{e}^{-H / l}-k_{0} . \tag{19}
\end{align*}
$$

The divergence of the two first modes to minus infinity is due to the elastic resistance of the stroma to uniform compressions. The third mode has a finite limit, which can be derived by integrating the continuity equation at $q=0$ over the height of the epithelium to leading order in perturbations. This limit therefore comes purely from mass-conservation in the epithelium and, as we shall see, reappears independently of the stroma rheology.

### 2.2. Influence of the different parameters

A study of the influence of the main parameters on the stability of the system for model 1 has been presented in [1] and is therefore only summarized here. The quantities destabilizing the system when they are increased are the epithelial viscosity $\eta$, the celldivision rate $k$, the thickness of the dividing region $l$ at constant cell-production $k$, and the thickness of the stroma $L$. This is due to the fact that the present instability originates from viscous shear stresses in the epithelium due to the differential flow of cells. This differential flow itself originates from non-uniform cell division along the interface due to its perturbations. The driving force for the instability can therefore be augmented either by increasing the epithelial viscosity at constant cell flow (increasing
$\eta$ ), increasing the cellular flow at constant epithelial viscosity (increasing $k$ ), or by increasing its extent (increasing $l$ ). The dependence in $L$ is explained by the fact that a thicker elastic stroma resists a given amplitude of displacements less for the same elastic modulus $\mu$. Stabilizing factors are the elastic shear modulus of the stroma $\mu$, the interfacial tension $\gamma_{\mathrm{i}}$ and the apical surface tension $\gamma_{\mathrm{a}}$.

### 2.3. Oscillatory regimes

In some parameter regimes, the relaxation of the system can be oscillatory. This can be seen from the crossing of the real parts of two of the relaxation modes and the associated occurrence of non-zero imaginary parts, which corresponds to an oscillatory response of the system in this range of wave numbers. This is the case for example in the model studied here when either the rate of cell division $k$ or the epithelium-stroma friction coefficient $\xi$ is increased, as illustrated in figure 1 . Such oscillatory behaviours however


Figure 1. Relaxation modes $\omega$ as a function of the wave number $q$ for model 1. (A) Parameter values are as follows: $\eta=10 \mathrm{MPa} \cdot \mathrm{s}, \mu=100 \mathrm{~Pa}, \gamma_{\mathrm{i}}=10 \mathrm{mN} \cdot \mathrm{m}^{-1}$, $\gamma_{\mathrm{a}}=1 \mathrm{mN} \cdot \mathrm{m}^{-1}$ (all estimated from [2]), $k=8.6$ divisions per day (estimated from [3]), $\xi=10 \mathrm{GPa} \cdot \mathrm{s} \cdot \mathrm{m}^{-1}$ (estimated from [4]), $H=L=300 \mu \mathrm{~m}$ and $l=200 \mu \mathrm{~m}$ (estimated from [5]). The three relaxation modes are real. Note that only one of these modes shows a region where it is positive, corresponding to an unstable system. (B) The same curves are displayed while zooming onto a smaller region of wave-number values. (C) The rate of cell division $k$ is changed to 16 divisions per day, and (D) the value of the epithelium-stroma friction coefficient $\xi$ instead is changed to $100 \mathrm{GPa} \cdot \mathrm{s} \cdot \mathrm{m}^{-1}$. Real parts are shown in the upper sub-panels (indices 1) and imaginary parts in the lower sub-panels (indices 2 ).
never occur with an associated positive real value of the complex-conjugated modes. We therefore expect these predicted oscillations to not be observable in actual biological systems. Such oscillatory relaxations however could in principle be observed in in-vitro systems prepared away from their steady-state configuration.

## 3. Results for model 2

We now present the mode structure for model 2, where the stroma is viscous.

### 3.1. Asymptotic behaviours of the modes

We now have two relaxation modes. In the limit of large wave numbers and to constant order in a systematic development in $q^{-1}$, they read:

$$
\begin{align*}
& \omega_{1} \simeq-\frac{\gamma_{\mathrm{i}}}{2\left(\eta+\eta_{\mathrm{s}}\right)} q+\frac{\eta}{\eta+\eta_{\mathrm{s}}}\left(k-k_{0}\right), \\
& \omega_{2} \simeq-\frac{\gamma_{\mathrm{a}}}{2 \eta} q+k \mathrm{e}^{-H / l}-k_{0} . \tag{20}
\end{align*}
$$

The second expression is identical to the one obtained previously for model 1 , since it corresponds to the relaxation mode of the apical surface, which decouples from the stroma dynamics in this limit. In the long-wavelength limit, we get, to leading order:

$$
\begin{align*}
& \omega_{1} \simeq k \mathrm{e}^{-H / l}-k_{0} \\
& \omega_{2} \simeq-\frac{L^{2}\left[3 H \gamma_{\mathrm{a}}+2 L\left(\gamma_{\mathrm{a}}+\gamma_{\mathrm{i}}\right)\right]}{6 \eta_{\mathrm{s}}} q^{4} . \tag{21}
\end{align*}
$$

The first expression here was also found in the case of an elastic stroma, since it corresponds to pure mass conservation in the epithelium and is therefore independent of the stroma rheology, as already commented. The second mode goes to zero by negative values as the wave number tends to zero. Therefore, the system is always stable for sufficiently small wave numbers, but in this case the relaxation time diverges in the limit of infinitely long wavelengths, contrary to what happens for an elastic stroma. This stems from the fact that the relaxation here is associated with lubrication-like viscous flows over large distances in the tangential direction rather than elastic relaxations over short distances in the normal direction. Expressions to next-to-leading order can be found in section 5 .

### 3.2. Mode structure and parameter dependences

The influence of the different parameters in this case are similar to the case of an elastic stroma, and have been discussed in [1]. Here again, only one relaxation mode shows a region where it becomes positive, corresponding to an unstable interface (figure 2A). Here however, we rarely get crossing of the modes and associated oscillatory relaxations as presented previously for an elastic stroma. Illustrations of the effect of an increased cell-division rate as well as that of an increased friction at the epithelium-stroma interface are shown in figures 2 B and 2 C . We can see that, contrary to the case of an elastic stroma, the epithelium-stroma friction coefficient has little influence on the mode structure, and that neither of these two parameter variations entrains a crossing of the modes and the occurrence of oscillatory relaxations. However, for very specific values of the parameters, oscillatory regimes do occur. We investigate in figure 3 an oscillatory regime that takes place in a narrow window of parameter values.


Figure 2. Relaxation modes $\omega$ as a function of the wave number $q$ for model 2. (A) The parameters are the same as in figure 1 A , except for $\eta_{\mathrm{s}}=10 \mathrm{kPa} \cdot \mathrm{s}($ instead of $\mu)$, $\gamma_{\mathrm{i}}=1 \mathrm{mN} \cdot \mathrm{m}^{-1}$ and $k=0.86$ divisions per day. (B) The rate of cell division $k$ is changed to 8.6 divisions per day. (C) The value of the friction coefficient $\xi$ instead is changed to $100 \mathrm{GPa} \cdot \mathrm{s} \cdot \mathrm{m}^{-1}$. (D) The viscosity of the stroma $\eta_{\mathrm{s}}$ instead is changed to $20 \mathrm{MPa} \cdot \mathrm{s}$, which makes it twice as large as the epithelium viscosity $\eta$ in this case.


Figure 3. Relaxation modes $\omega$ as a function of the wave number $q$ for model 2 , starting from a parameter set where oscillatory relaxations occur. (A) Parameters are the same as in figure 2 A , except for $\gamma_{\mathrm{i}}=10 \mathrm{mN} \cdot \mathrm{m}^{-1}$. The interface is stable, but the relaxation is oscillatory in a finite interval of wave numbers, for which the real parts of the two modes merge (imaginary parts not shown). (B) The friction coefficient $\xi$ is changed to $100 \mathrm{GPa} \cdot \mathrm{s} \cdot \mathrm{m}^{-1}$, which has little influence. (C) The cell-division rate $k$ instead is changed to 4.3 divisions a day. The interface is now unstable at small wave numbers. Crossing of the modes happens without oscillations at a wavelength of about $12 \mu \mathrm{~m}$. (D) Lowering instead $k$ to 0.4 divisions per day prevents the modes from crossing. (E) Increasing $\gamma_{\mathrm{i}}$ to $20 \mathrm{mN} \cdot \mathrm{m}^{-1}$ has a similar effect, while ( F ) decreasing it to $2 \mathrm{mN} \cdot \mathrm{m}^{-1}$ makes the interface unstable, pushes the crossing of the modes to short wavelengths (here about $6 \mu \mathrm{~m}$ ) and eliminates the oscillations, similarly to what happens in panel (C).

In figures 2 A and 2 D , we investigate the dependence of the mode structure on the stroma viscosity $\eta_{s}$, and find that the instability can occur when either of the two fluids - the epithelium or the stroma - is the more viscous one. This is contrary to the case of a standard viscous fingering instability, the Saffman-Taylor instability, which
corresponds to the situation where two fluids of different viscosities are displaced in a Hele-Shaw cell [6] by an external pressure gradient [7, 8]. In this latter case indeed, the instability develops only when the fluid displacing the other one is that of lower viscosity, otherwise the interface remains flat.

## 4. Complementary information associated with models 4-6

The bulk rheological equations for the epihtelium and stroma have been presented in section 1 for models 1-3, and remain the same here for the respective models 4-6, where only the cell-production rate $k_{\mathrm{p}}$ entering equation (1) changes. The coupling of this function to the local concentration of nutrients is presented in the main text, section 4. We present here the unperturbed solution to this set of equations as well as the perturbed equations to linear order around that steady state.

### 4.1. Unperturbed solution

Similarly to models $1-3$, the solution in the flat, unperturbed configuration is independent of the stroma rheology, but because of the coupling to nutrient diffusion, this solution is different from that exposed previously. In the stroma, we get a linear dependence of the nutrient concentration as a function of $z$ :

$$
\begin{equation*}
\rho_{\mathrm{s}}^{0}=\bar{\rho}_{0}-\frac{\sqrt{c D}}{D_{\mathrm{s}}}\left[A_{\mathrm{n}}^{0} \sinh (\alpha H)-B_{\mathrm{n}}^{0} \cosh (\alpha H)\right](z-l+d), \tag{22}
\end{equation*}
$$

where $\alpha=\sqrt{c / D}$ and where $A_{\mathrm{n}}^{0}$ and $B_{\mathrm{n}}^{0}$ are further given by:

$$
\begin{align*}
& A_{\mathrm{n}}^{0}=\frac{\bar{\rho}_{0}}{\cosh (\alpha H)+\frac{\alpha d D}{D_{\mathrm{s}}} \sinh (\alpha H)+\frac{v_{\text {off }}}{\alpha D}\left[\sinh (\alpha H)+\frac{\alpha d D}{D_{\mathrm{s}}} \cosh (\alpha H)\right]}, \\
& B_{\mathrm{n}}^{0}=-\frac{v_{\text {off }}}{\alpha D} A_{\mathrm{n}}^{0} . \tag{23}
\end{align*}
$$

In the epithelium, we get:

$$
\begin{align*}
\rho^{0} & =A_{\mathrm{n}}^{0} \cosh (\alpha \bar{z})+B_{\mathrm{n}}^{0} \sinh (\alpha \bar{z}) \\
k_{\mathrm{p}}^{0} & =\kappa_{1}\left[A_{\mathrm{n}}^{0} \cosh (\alpha \bar{z})+B_{\mathrm{n}}^{0} \sinh (\alpha \bar{z})\right]-\kappa_{0} \\
v_{z}^{0} & =\frac{\kappa_{1}}{\alpha}\left[A_{\mathrm{n}}^{0} \sinh (\alpha \bar{z})+B_{\mathrm{n}}^{0} \cosh (\alpha \bar{z})\right]-\kappa_{0} \bar{z}-B_{\mathrm{n}}^{0} \frac{\kappa_{1}}{\alpha} \\
p_{\mathrm{e}}^{0} & =2 \eta k_{\mathrm{p}}^{0}, \tag{24}
\end{align*}
$$

where $\bar{z}=z-(L+H)$ and where the parameter $\kappa_{0}$ is fixed by imposing that the tissue velocity vanishes at the apical surface of the epithelium:

$$
\begin{equation*}
\kappa_{0}=\frac{\kappa_{1}}{\alpha H}\left[A_{\mathrm{n}}^{0} \sinh (\alpha H)-B_{\mathrm{n}}^{0} \cosh (\alpha H)+B_{\mathrm{n}}^{0}\right] . \tag{25}
\end{equation*}
$$

The components of the total stress tensor are zero except for $\sigma_{x x}^{0}=\sigma_{y y}^{0}=-p_{\mathrm{e}}^{0}=-2 \eta k_{\mathrm{p}}^{0}$.

### 4.2. Perturbed equations for model 4-6

In terms of the perturbed fields, the bulk rheological equations are left unchanged in their form as compared with the equations associated with the total fields, since the original bulk equations are linear. However, they couple to the nutrient reactiondiffusion equations, which now read:

$$
\begin{align*}
\delta k_{\mathrm{p}} & =\kappa_{1} \delta \rho \\
\partial_{t} \delta \rho & =D \Delta \delta \rho-c \delta \rho \\
\partial_{t} \delta \rho_{\mathrm{s}} & =D_{\mathrm{s}} \Delta \delta \rho_{\mathrm{s}} . \tag{26}
\end{align*}
$$

The mechanical boundary conditions at the apical surface of the epithelium take the exact same expressions as those given in equation (14) in the context of models 1-3, only that $k_{\mathrm{p}}$ is now replaced by $k_{\mathrm{p} \mid z=L+H}^{0}=\kappa_{1} A_{\mathrm{n}}^{0}-\kappa_{0}$.

At the epithelium-stroma interface, we get the same conditions as in equations (15) to (17) depending on the stroma rheology, $k_{\mathrm{p}}$ being replaced by $k_{\mathrm{p} \mid z=L}^{0}=$ $\kappa_{1}\left[A_{\mathrm{n}}^{0} \cosh (\alpha H)-B_{\mathrm{n}}^{0} \sinh (\alpha H)\right]-\kappa_{0}$. At the anchoring boundary of the stroma, the displacement field vanishes. To this must be added the boundary conditions regarding the perturbed nutrient concentrations in the epithelium and stroma, respectively $\delta \rho$ and $\delta \rho_{\mathrm{s}}$. They read:

$$
\begin{array}{ll}
\delta \rho_{\mathrm{s} \mid z=L-d} & =0 \\
\rho_{\mid z=L+\delta h}^{0}+\delta \rho_{\mid z=L} & =\rho_{\mathrm{s} \mid z=L+\delta h}^{0}+\delta \rho_{\mathrm{s} \mid z=L} \\
D\left(\partial_{z} \rho_{\mid z=L+\delta h}^{0}+\partial_{z} \delta \rho_{\mid z=L}\right) & =D_{\mathrm{s}}\left(\partial_{z} \rho_{\mathrm{s} \mid z=L+\delta h}^{0}+\partial_{z} \delta \rho_{\mathrm{s} \mid z=L}\right) \\
D\left(\partial_{z} \rho_{\mid z=L+H+\delta H}^{0}+\partial_{z} \delta \rho_{\mid z=L+H}\right) & =-v_{\text {off }}\left(\rho_{\mid z=L+H+\delta H}^{0}+\delta \rho_{\mid z=L+H}\right) . \tag{27}
\end{array}
$$

Note that corrections of the interfaces' locations by a distance $\delta h$ or $\delta H$ in the perturbed fields lead to second-order terms and can therefore be ignored. These corrections however should be taken into account in the steady-state solutions where they contribute to linear order.

### 4.3. Fitting procedure for the comparison of models 1 and 4

In order to compare the results of models 1 and 4 in section 5 of the main text, we derive from model 4 a cell-production rate as a function of $z$ at steady state. We then fit the cell-production rate of model 1 to that function to generate the associated relaxation modes. We illustrate in figure 4 this fitting procedure, which gives a nearly perfect agreement between the two rate functions.

## 5. Assymptotic behaviours of the relaxation modes

Here, we present more detailed asymptotic expressions of the different relaxation modes of the different models, both in the short- and long-wavelength limits. We start with the model where the cell-production function is predefined and given by equations (2) and (3). We give the expressions whenever possible up to next-to-leading order.


Figure 4. Superposition of the cell-production functions at steady state for model 4 (curve (1)) and model 1 (curve (2)), following the fitting procedure described in the text. Parameters used to generate curve (1) are identical to those of figure 3A of the main text. The fitting parameters associated with curve (2) take the values $k=2$ division per day and $l=44 \mu \mathrm{~m}$.

### 5.1. Elastic stroma

With an elastic stroma (model 1), we have three relaxation modes, which are given in the short-wavelength limit by:

$$
\begin{align*}
& \omega_{1}^{\mathrm{el}}=-\frac{\gamma_{\mathrm{i}}}{2 \eta} q-\frac{\mu}{\eta}+k-k_{0}+O\left(\frac{1}{q}\right) \\
& \omega_{2}^{\mathrm{el}}=-\frac{\gamma_{\mathrm{a}}}{2 \eta} q+k \mathrm{e}^{-H / l}-k_{0}+O\left(\frac{1}{q}\right) \\
& \omega_{3}^{\mathrm{el}}=-2 \frac{\mu}{\xi} q-\frac{\mu}{\eta}+O\left(\frac{1}{q}\right) \tag{28}
\end{align*}
$$

and in the long-wavelength limit by:

$$
\begin{align*}
\omega_{1}^{\mathrm{el}}= & -\frac{36 \mu}{\eta} \frac{1}{H^{3} L^{3}} \frac{1}{q^{6}}-\frac{18 \mu}{5 \eta} \frac{2(H-L)^{2}-H L}{H^{3} L^{3}} \frac{1}{q^{4}}+O\left(\frac{1}{q^{2}}\right) \\
\omega_{2}^{\mathrm{el}}= & -\frac{\mu}{4 \eta} \frac{1}{H L} \frac{1}{q^{2}} \\
& -\left(\frac{k \mathrm{e}^{-H / l}-k_{0}}{2}+\frac{\mu}{\eta} \frac{10\left(H^{2}+L^{2}\right)+3 H L}{24 H L}+\frac{\mu}{L \xi}\right)+O\left(q^{2}\right) \\
\omega_{3}^{\mathrm{el}}= & k \mathrm{e}^{-H / l}-k_{0} \\
& -\left(k \mathrm{e}^{-H / l}-k_{0}\right)\left(\frac{2 k \mathrm{e}^{-H / l}(H+l) L \eta}{\mu}+\frac{2 H \eta}{\xi}-\frac{2 l L \eta k}{\mu}+H^{2}\right) q^{2} \\
& +O\left(q^{4}\right) . \tag{29}
\end{align*}
$$

### 5.2. Viscous stroma

With a viscous stroma (model 2), we have two relaxation modes, which are given in the short-wavelength limit by:

$$
\begin{align*}
& \omega_{1}^{\mathrm{v}}=-\frac{\gamma_{\mathrm{i}}}{2\left(\eta+\eta_{\mathrm{s}}\right)} q+\frac{\eta}{\eta+\eta_{\mathrm{s}}}\left(k-k_{0}\right)+O\left(\frac{1}{q}\right) \\
& \omega_{2}^{\mathrm{v}}=-\frac{\gamma_{\mathrm{a}}}{2 \eta} q+k \mathrm{e}^{-H / l}-k_{0}+O\left(\frac{1}{q}\right) \tag{30}
\end{align*}
$$

and in the long-wavelength limit by:

$$
\begin{align*}
& \omega_{1}^{\mathrm{v}}=k \mathrm{e}^{-H / l}-k_{0}-\left(k \mathrm{e}^{-H / l}-k_{0}\right)\left(1+\frac{2 \eta}{\xi H}+\frac{2 \eta L}{\eta_{\mathrm{s}} H}\right) H^{2} q^{2}+O\left(q^{4}\right) \\
& \omega_{2}^{\mathrm{v}}=-\frac{L^{2}\left[3 H \gamma_{\mathrm{a}}+2 L\left(\gamma_{\mathrm{a}}+\gamma_{\mathrm{i}}\right)\right]}{6 \eta_{\mathrm{s}}} q^{4}+\omega_{2}^{\mathrm{v}, 6} q^{6}+O\left(q^{8}\right) \tag{31}
\end{align*}
$$

Here, $\omega_{2}^{\mathrm{v}, 6}$ is a very long expression that is not particularly enlightening. In the case where $\gamma_{\mathrm{a}}=0$, it reads:

$$
\begin{align*}
\omega_{2}^{\mathrm{v}, 6}= & -\frac{L^{2}}{2 \eta_{\mathrm{s}}}\left\{\frac { \eta k } { 9 } \left[l\left(H^{2}-6 l^{2}\right)(3 H+2 L) \mathrm{e}^{-H / l}+12 L l^{3}+6 H^{3} l\right.\right. \\
& \left.\left.+2 H^{2} l(-9 l+2 L)+6 H l^{2}(3 l-2 L)\right]+\frac{L^{2} \gamma_{\mathrm{i}}}{5 \eta_{\mathrm{s}}}\left(6 L \eta_{\mathrm{s}}+5 H \eta\right)\right\} . \tag{32}
\end{align*}
$$

### 5.3. Viscoelastic stroma

With a viscoelastic stroma (model 3), we have four relaxation modes, are given in the short-wavelength limit by:

$$
\begin{align*}
& \omega_{1}^{\mathrm{ve}}=-\frac{\gamma_{\mathrm{i}}}{2 \eta} q-\frac{\mu}{\eta}+k-k_{0}+O\left(\frac{1}{q}\right) \\
& \omega_{2}^{\mathrm{ve}}=-\frac{\gamma_{\mathrm{a}}}{2 \eta} q+k \mathrm{e}^{-H / l}-k_{0}+O\left(\frac{1}{q}\right) \\
& \omega_{3}^{\mathrm{ve}}=-2 \frac{\mu}{\xi} q-\frac{\left(\eta+\eta_{\mathrm{s}}\right) \mu}{\eta \eta_{\mathrm{s}}}+O\left(\frac{1}{q}\right) \\
& \omega_{4}^{\mathrm{ve}}=-\frac{\mu}{\eta_{\mathrm{s}}}+\frac{2 \mu^{2}}{\gamma_{\mathrm{i}} \eta_{\mathrm{s}}} \frac{1}{q}+O\left(\frac{1}{q^{2}}\right), \tag{33}
\end{align*}
$$

and in the long-wavelength limit by:

$$
\begin{aligned}
\omega_{1}^{\mathrm{ve}}= & -\frac{36 \mu}{\eta} \frac{1}{H^{3} L^{3}} \frac{1}{q^{6}}-\frac{18 \mu}{5 \eta} \frac{2(H-L)^{2}-H L}{H^{3} L^{3}} \frac{1}{q^{4}}+O\left(\frac{1}{q^{2}}\right) \\
\omega_{2}^{\mathrm{ve}}= & -\frac{\mu}{4 \eta} \frac{1}{H L} \frac{1}{q^{2}} \\
& -\left(\frac{k \mathrm{e}^{-H / l}-k_{0}}{2}+\frac{\mu}{\eta} \frac{10\left(H^{2}+L^{2}\right)+3 H L}{24 H L}+\frac{\mu}{L \xi}+\frac{\mu}{\eta_{\mathrm{s}}}\right)+O\left(q^{2}\right) \\
\omega_{3}^{\mathrm{ve}}= & k \mathrm{e}^{-H / l}-k_{0}
\end{aligned}
$$

$$
\begin{align*}
& -\left(k \mathrm{e}^{-H / l}-k_{0}\right)\left(2\left(k \mathrm{e}^{-H / l}-k_{0}\right) \frac{\eta}{\mu} \frac{L}{H}+\frac{2 \eta}{\xi H}+\frac{2 \eta L}{\eta_{\mathrm{s}} H}+1\right) H^{2} q^{2} \\
& +O\left(q^{4}\right) \\
\omega_{4}^{\mathrm{ve}}= & -\frac{L^{2}\left[3 H \gamma_{\mathrm{a}}+2 L\left(\gamma_{\mathrm{a}}+\gamma_{\mathrm{i}}\right)\right]}{6 \eta_{\mathrm{s}}} q^{4}+\omega_{4}^{\mathrm{ve}, 6} q^{6}+O\left(q^{8}\right) . \tag{34}
\end{align*}
$$

Here, $\omega_{4}^{\mathrm{ve}, 6}$ has the exact same expression as $\omega_{2}^{\mathrm{v}, 6}$ discussed above in the case of a viscous stroma. In particular, when $\gamma_{\mathrm{a}}=0$, it has the expression given by equation (32).

### 5.4. Coupling to nutrient diffusion

When coupling to nutrient diffusion is included, the asymptotic expressions to next-to-leading order are very long. Here, we therefore only summarize the expressions to leading order. For all three choices of the stroma rheology, the expressions of the relaxation modes in the short-wavelength limit are identical to those presented above respectively for models $1-3$. This is because these expressions are not dependent on cell division to this order, since the relaxation toward the flat state in this limit is fast and therefore controlled by relaxation mechanics only. For one of the four modes of the viscoelastic model, the limit corresponds to the inverse viscoelastic relaxation time of the stroma and has therefore also the same expression here. This is also the case to leading order for the expressions in the long-wavelength limit whenever the relaxation rate diverges when $q$ goes to zero, for similar reasons. So, the expressions are changed in this limit only for one relaxation mode when the stroma is elastic, the two relaxation modes when it is viscous, and two of the four relaxation modes when it is viscoelastic. The full expressions are very long, and we give here only one example, that of the mode proportional to $q^{4}$ for both the viscous and viscoelastic rheologies. To leading order, and in the simplified case where $v_{\text {off }}=0$, this mode reads:

$$
\begin{align*}
\omega_{2}^{\mathrm{v} / \mathrm{ve}}= & -\frac{L^{2}}{6 \eta_{\mathrm{s}}}\left\{\left(3 H \gamma_{\mathrm{a}}+2 L\left(\gamma_{\mathrm{a}}+\gamma_{\mathrm{i}}\right)\right)\right. \\
& \left.-(3 H+2 L)\left[\gamma_{\mathrm{a}} A+16 H \kappa_{1} \eta \bar{\rho}_{0} B\right]\right\} q^{4}+O\left(q^{6}\right) \tag{35}
\end{align*}
$$

with $A$ and $B$ dimensionless expressions given by:

$$
\begin{align*}
A= & \frac{\sinh ^{2}(\alpha H)}{-\frac{D_{\mathrm{s}}}{D}+\frac{D_{\mathrm{s}}}{D \alpha H} \cosh (\alpha H) \sinh (\alpha H)+\frac{d}{H} \sinh ^{2}(\alpha H)} \\
B= & \frac{\cosh (\alpha H / 2) \sinh ^{3}(\alpha H / 2)[\cosh (\alpha H)-\sinh (\alpha H) /(\alpha H)]}{\alpha d[\cosh (2 \alpha H)-1]+\frac{D_{\mathrm{s}}}{D}[\sinh (2 \alpha H)-2 \alpha H]} \\
& \times \frac{1}{\left\{\cosh (\alpha H)+\alpha_{1} d \sinh (\alpha H)\right\}} . \tag{36}
\end{align*}
$$

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