Active Tension Network model of epithelial mechanics

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It is now widely recognized that mechanical interactions between cells play a crucial role in epithelial morphogenesis, yet understanding the mechanisms through which stress and deformation affect cell behavior remains an open problem due to the complexity inherent in the mechanical behavior of cells and the difficulty of direct measurement of forces within tissues. Theoretical models can help by focusing experimental studies and by providing the framework for interpreting measurements. To that end, “vertex models” have introduced an approximation of epithelial cell mechanics based on a polygonal tiling representation of planar tissue. Here we formulate and analyze an Active Tension Network (ATN) model, which is based on the same polygonal representation of epithelial tissue geometry, but in addition i) assumes that mechanical balance is dominated by cortical tension and ii) introduces tension dependent local remodeling of the cortex, representing the active nature of cytoskeletal mechanics. The tension-dominance assumption has immediate implications for the geometry of cells, which we demonstrate to hold in certain types of Drosophila epithelial tissues. We demonstrate that stationary configurations of an ATN form a manifold with one degree of freedom per cell, corresponding to “isogonal” - i.e. angle preserving - deformations of cells, which dominate the dynamic response to perturbations. We show that isogonal modes account for ~ 90% of experimentally observed deformation of cells during the process of ventral furrow formation in Drosophila. Other interesting properties of our model include the exponential screening of mechanical stress and a negative Poisson ratio response to external uniaxial stress. We also provide a new approach to the problem of inferring local cortical tensions from the observed geometry of epithelial cells in a tissue.

I. INTRODUCTION

Mechanics of growth and cellular rearrangements plays an important role in morphogenesis as both processes are central to defining the shape of developing tissues. As such, it has become a subject of intense study aiming to characterize specific mechanical processes involved in cell and tissue-wide dynamics [1–4], uncover the regulatory mechanisms [5], and identify if and how the mechanical state of the cell feeds back onto the larger developmental program [6–9]. Yet at the present, these questions remain largely unanswered due to the difficulty of measuring mechanical stress in live tissues and the challenge of identifying the relevant sub-cellular degrees of freedom needed to model the cell’s mechanical state.

Many developmental processes involve two-dimensional epithelial layers, making it essential to understand cell mechanics in such systems. In its simplest form, an epithelial tissue is a monolayer of apico-basally polarized cells tightly connected to their lateral neighbors [10]. Viewed from the apical side, cells tesselate the plane, forming a polygonal packing reminiscent of a soap foam. Unlike passive foams, interfacial tension is not a simple material property, but rather derives from the cortical actin-myosin network [11] [12] localized as a planar ring just inside the cell’s lateral surface [13]. Each cell’s cortical cytoskeleton is linked to those of the neighboring cells via adherens junctions [14]. The equilibrium geometry of cells is determined by the balance of cytoskeletal forces [5] [15] within the tissue. However, unlike passive materials, cells actively regulate such forces through mechanotransduction and internal remodeling, resulting in an intrinsically time-dependent stress-strain constitutive relation and controllable plasticity [16] [17], which can drive rearrangement of cells. Elucidation of the manner in which cellular activity manifests in collective properties of the tissue is critical to understanding morphogenesis.

Here we formulate a phenomenological model of an epithelial tissue as a two dimensional Active Tension Network (ATN), which in addition to cytoskeletal elasticity describes cytoskeletal re-arrangement through myosin activity and the recruitment of myosin into cytoskeletal fibers, thus capturing the plastic response of cells to external stress. We shall demonstrate that the assumption that mechanical equilibrium of cells is dominated by tension has testable consequences for cell and tissue morphology, allowing immediate tests of this hypothesis. We show that Active Tension Networks have a number...
of interesting mechanical properties, which include “screening” that (exponentially) localizes transient perturbations. Furthermore, an ATN’s ground state is degenerate: a consequence of the fact that “isogonal” - i.e. angle preserving - perturbations of cell geometry also preserve tension balance. These isogonal (zero) modes dominate ATN fluctuations and result in unusual behaviors in response to external perturbations. For example, we demonstrate that an ATN generates a negative Poisson ratio in response to a uniaxial stress. We also provide a new local “Mechanical Inverse” \[18\] [19] algorithm for inferring cytoskeletal tension - under the ATN approximation - from images of epithelial tissue. Finally, we shall demonstrate that dynamics of the initial stage of Drosophila Ventral Furrow formation is well described by the ATN model.

II. RESULTS

A. Formulation of the Active Tension Net Model

Epithelial cell monolayers form approximate twodimensional polygonal tilings, that are conveniently parameterized by the set of vertex coordinates \( \{r_i\} \). The mechanical state of the tissue is often described using a generalized `Vertex Model` [2] [8] [20] which defines the mechanical energy of a cell array (given by vertex positions \( \{r_i\} \) connected by edges defined by the array’s topology) as

\[
E = \sum_{<i,j>} \frac{\kappa_{ij}}{2} (r_{ij} - \ell_{ij})^2 + \sum_{\alpha} \frac{\kappa_{\alpha}}{2} (A_\alpha - \bar{A}_\alpha)^2
\]

(1)

which incorporates the cortical cytoskeleton contributions from each interface \( i \)- \( j \)- elastic energy stored by deformation of the bundle’s length, \( r_{ij} \), relative to its intrinsic length, \( l_{ij} \), as well as the mechanical energy associated with cell area, \( A_\alpha \), deformation relative to the intrinsic area \( \bar{A}_\alpha \). Anticipating the heterogeneity of cells, Eq. (1) allows for the variation of intrinsic parameters from cell to cell and interface to interface. However, it is useful to further generalize the description by defining mechanical energy in its differential form [18]

\[
dE[\{r_i\}] = \sum_{<i,j>} T_{ij} dr_{ij} + \sum_{\alpha} p_\alpha dA_\alpha
\]

(2)

Here tension \( T_{ij} \) defines the change in mechanical energy in response to the change of edge length by \( dr_{ij} \) and ‘pressure’ (or more precisely, radial stress in cylindrical coordinates) \( p_\alpha \) defines the response to the change in area by \( dA_\alpha \). The force acting on a vertex is simply the projection of the above energy differential along the corresponding vertex displacement - i.e. \( F_i = -\partial r_i E \).

Equation (2) is more general than (1): the mechanical degrees of freedom \( \{T_{ij}\} \) and \( \{p_\alpha\} \) provide the means to describe the full time dependent behavior of a heterogeneous cell array, beyond the constitutive relations implied by Eq. (1). Instead of considering this model in its full generality, we will make the simplifying assumption that the contribution of ‘pressure’ to mechanical balance can be neglected in comparison to tension. This is tantamount to the assumption that the magnitude of typical pressure differentials across cell interfaces satisfies \( \Delta p << \bar{T}/\bar{r} \), where \( \bar{T} \) and \( \bar{r} \) are the characteristic scales of tension and length of an interface respectively. This implies that the interfacial curvature \( \Delta p/\bar{T} \) - as defined by the Young-Laplace law [18] [21] - is small compared to cellular length scales and thus this assumption is appropriate for any epithelial cell array with little to no observable bond curvature. As such, we set \( p_\alpha = p_0 \) and convert the sum over cell areas to a boundary condition on the change of total tissue area, \( p_0 \sum dA_\alpha \). In this limit, the only forces within the bulk of the cell array are interfacial tensions due to cortical acto-myosin and the pressure only enforces conservation of the total area of the cell array, preventing its collapse under the action of internal tension. Alternatively, we will be considering finite patches of tissue with specified normal stresses on the boundary (that also prevent collapse), as a boundary condition. We shall refer to the corresponding structures as ‘Tension Nets’ and investigate their properties in some detail.

Dynamics of vertex positions within a tension net is assumed to be relaxational

\[
\nu \frac{d}{dt} r_i = -\partial r_i E = \sum_{\{j\}} T_{ij} \dot{r}_j
\]

(3)

where \( \{j\} \) denotes the set of all vertices connected to vertex \( i \) and \( \nu \) represents the effective friction between apical cytoskeleton and its substrate [22]; it sets the timescale of mechanical relaxation, assumed to be fast relative to morphogenetic time scales. We adopt the constitutive relation for tension corresponding to the cortical contribution to mechanical energy given in Eq. (1)

\[
T_{ij} = \kappa (r_{ij} - \ell_{ij})
\]

(4)

where for simplicity we assumed homogeneous cytoskeletal stiffness, \( \kappa_{ij} = \kappa \), effectively setting the
FIG. 1. Expected dependence of the local contractility rate of the cortical acto-myosin filament on the mechanical load, \( W(x) \) - hereafter referred to as the "walking kernel". The generic features are the zero crossing at \( x = 1 \) which separates myosin activity into a regime of walking, \( W(x) < 0 \), and slipping, \( W(x) > 0 \), and the positive slope, \( W'(x = 1) > 0 \) - i.e. we slip above the stall force. The dynamics close to the fixed point is immune to the exact functional form (which are cell-specific) and will only measure the aforementioned slope - depicted as a dashed blue line.

scale of tension. However, as already mentioned above, acto-myosin bundles are not simple passive elastic elements, but can dynamically remodel in response to external stimuli [23]. In the simplest form this remodeling can be described by letting the intrinsic length of each intercellular edge \( \ell_{ij} \) evolve dynamically on a time scale slow compared to the mechanical relaxation of the tissue described by Eq. (3). Specifically:

\[
\frac{d}{dt} \ell_{ij} = \ell_{ij} W \left( \frac{T_{ij}}{m_{ij} T_s} \right)
\]

where \( W \left( \frac{T_{ij}}{m_{ij} T_s} \right) \) describes the dependence of the local contractility rate of the cortical acto-myosin filament on the mechanical load \( T_{ij} \) that it carries. The generic features of \( W \) are known from single-molecule experiments [24, 25]: each myosin will walk in a polarized direction, contracting the actin bundle, unless the load per myosin, \( T_{ij}/m_{ij} \), reaches the “stall force” level \( T_s \). Above this critical value, the filament simply elongates as each motor slips backwards [24]. We note that in assuming the load carried by each myosin motor scales inversely proportional with the total number of motors, we have implicitly assumed that motors are non-interacting which is only valid for low densities [27].

Given a specified myosin distribution on interfaces, Eqs. (3 - 5) define the dynamics of an active tension net. The fixed point of these equations is then reached when i) tensions balance at all vertices and ii) all edges are at their stall force, set by the local myosin level. Alas, arbitrarily specified myosin levels will lead to a frustrated system where these conditions cannot be satisfied. Indeed not all distributions of tensions under fixed topology will admit a set of angles that balance in the plane. However, in reality myosin levels are not fixed and are known to themselves respond to cytoskeletal tension through mechanotransduction [9, 28]. Here we shall propose a particular form of mechanical feedback on myosin, that will ensure convergence to a balanced state. Specifically, we assume that myosin is locally recruited into acto-myosin fibers under positive strain rate of the intrinsic length:

\[
\frac{d}{dt} m_{ij} = \mu m_{ij} \ell_{ij} \frac{d \ell_{ij}}{dt} = \mu m_{ij} W \left( \frac{T_{ij}}{m_{ij} T_s} \right)
\]

with \( \mu \) parameterizing the speed of myosin recruitment; myosin redistribution occurs on morphogenetic timescales and thus the postulated feedback is assumed to occur slow relative to both mechanical relaxation and acto-myosin contractility. While presently we do not have direct evidence for this specific form of mechanical feedback on local myosin concentrations, it is generally consistent with experimental observations [9, 28].

B. Static properties of Tension Nets

The force balance condition of a static tension net defines equilibrium geometry through Eq. (7)

\[
 F_i = \sum_{(j)} T_{ij} \hat{r}_{ji} = 0
\]

This immediately defines a relationship, for the ratio of tensions of any pair of adjacent edges in terms of angles at their shared vertex (depicted in Fig. 2(a)).

\[
 \frac{T_{ij}}{T_{il}} = \frac{\hat{r}_{il} \wedge \hat{r}_{ik}}{\hat{r}_{ik} \wedge \hat{r}_{ij}}
\]

Since the product of such ratios computed for any closed loop of edges has to be equal to unity, a consistent global assignment of tensions \( \{T_{ij}\} \) is only possible if the polygonal array satisfies the following
FIG. 2. (a) Force balance relates tensions on adjacent edges and cell geometry. Projections of $T_{ij}$ and $T_{ik}$ onto the dotted line must balance, providing a relation between tensions and angles at equilibrium. (b) Consistent assignment of tensions on edges surrounding the cell is possible only if the compatibility characteristic $\chi$, defined by Eq. (9), is equal to unity, implying a constraint on lattice angles adjoining the cell. (c) Comparison of the PDF of the measured $\log(\chi)$'s (blue) with the control distribution (red) defined by permuting angles, shown here for two Drosophila epithelial tissues: i) embryonic ventral ectoderm and ii) third instar imaginal wing disc. In the former case, cell geometry is significantly closer than random to satisfying compatibility constraints on every cell. In the latter case, enrichment of nearly compatible cells is very weak. A table summarizing the results for the four analyzed tissues (see text) is shown below.

A useful geometric way of understanding the constraints on the equilibrium geometry of tension nets is based on the fact that any balanced set of tensions $\{T_{ij}\}$ defines a triangulation of the tension plane with triangles $\{T_{ij}^+, T_{ik}^+, T_{ij}^-\}$ defined for triads of edges that meet at a vertex $i$ with the dual tension vector $T_{ij}^* = \hat{z} \wedge \hat{r}_{ij}T_{ij}$ being an edge tension vector rotated in the plane by $\pi/2$. Each triangular plaquette is then ‘dual’ to the original vertex and the vertices of the aforementioned triangulation are dual to the original cells. An example of such a static tension net and its corresponding dual graph is shown in Fig. 3(a).

To count the number of degrees of freedom that define balanced tension configurations we note that a triangulation is completely specified by the positions of its vertices, $Q_{\alpha}^*$, the number of which equals $c$ - the number of polygonal cells - so that triangulation is specified by $2c$ independent degrees of freedom. Tensions are given by differences of dual vertex positions - i.e., $T_{ij}^* = T_{\alpha ij}^* = Q_{\alpha i}^* - Q_{\alpha j}^*$ where $\alpha$, $\beta$ denote the cells that share edge $ij$. As such, the dual graph is an irrotational decomposition of the original force diagram. The naive count of $e = 3c$ ($e$ being the number of edges) tension parameters is reconciled with the correct result by noting that the sides of a triangulation tensions must satisfy the local planarity condition. Internal angles of the triangles around

| Tissue       | Ventral Furrow | Pupal Notum | Lateral Ectoderm | Wing Disc |
|--------------|---------------|------------|-----------------|-----------|
| $\sigma_{data}/\sigma_{null}$ | 0.53          | 0.57       | 0.72            | 0.98      |

compatibility constraint $\chi_\alpha$ for each cell $\alpha$

$$\chi_\alpha = \prod_{i \in \mathcal{V}(\alpha)} \frac{\hat{r}_{i,i+1} \wedge \hat{r}_{\alpha_{i,i}}}{\hat{r}_{i,i-1} \wedge \hat{r}_{\alpha_{i,i}}} = 1$$

(9)

$i$ labels the vertices of cell $\alpha$, denoted as $\mathcal{V}(\alpha)$, in a clockwise fashion; $\hat{r}_{i,i+1}$ are the unit vectors that point from vertex $i$ to $i+1$, and $\hat{r}_{\alpha_{i,i}}$ are the unit vectors that point along the external edge of vertex $i$, relative to cell $\alpha$. A diagram of the construction is shown in Fig. 2(b). This compatibility constraint can be understood as the geometric consequence of demanding that a polygonal array to be balanced by edge tension alone which requires one geometric constraint per cell, compensating for the absence of pressure differentials necessary to balance an arbitrary array. 

Interestingly, the compatibility constraint provides us with a simple quantitative assay to assess the validity of static tension net approximation for real epithelial tissues. To that end we examine snapshots of cell arrays calculating the value of $\chi_\alpha$ for each cell and compare the resultant distribution to a suitable empirical “null” - i.e. a distribution constructed from a fictitious cell array with the equivalent angle distribution as measured from the data. Any cell array approximating a tension net would generate a distribution of $\chi_\alpha$, clustering significantly closer to 1 than the randomized null distribution as correlations imposed by the compatibility constraint between angles of a given cell are lost in the latter. As shown in Fig. 2(c), three out of four measured Drosophila tissues (fly embryo at the stage just before gastrulation at the ventral site [29], the embryonic lateral ectoderm [30] and the pupal notum [31], but not the 3rd instar wing imaginal disc [32]) deviate significantly from the null, in strong support of the static tension net approximation. Tissue data for ventral ectoderm and imaginal wing disc was kindly provided by Eric Wieschaus and Ken Irvine respectively.
each dual vertex must sum to $2\pi$, which imposes $c$ constraints on tensions, that are the dual of the compatibility constraints on the geometry of the original cell array. The existence of these constraints implies that an arbitrary distribution of myosin concentrations would not allow mechanical equilibration and thus motivates our conjectured mechanical feedback on myosin dynamics. The existence of a dual triangulation for equilibrium tension nets also provides a robust way of inferring tensions from experimentally observed cell array geometries, improving on the previously proposed “Mechanical Inverse” method [18, 19].

C. Variational approach to inferring tension from the geometry of a Tension Net.

![Physical Lattice Tension Triangulation](image)

**FIG. 3.** (a) Graphical example of a static tension net, shown in black, and its corresponding tension triangulation or dual graph, shown in blue. (b) Cartoon illustrating the variational inverse. Algorithm projects observed tissue geometry onto the ‘closest’ tension triangulation. Blue is the better fit of the two shown.

Provided the lattice obeys the compatibility constraint globally, the force balance condition defines a local mechanical inference method based on “propagating” Eq. (8) for ratios of tensions, along adjacent edges. This local method is convenient insofar as it allows inference independent of boundary conditions. In practice, however, as seen in Fig. 2(c), the compatibility constraint is at best only approximately satisfied. Thus the direct use of Eq. (8) would result in an accumulation of errors as geometric factors are multiplied together. To circumvent this problem we define a more general variational method which finds the best fit tension graph - i.e. position of the vertices of the corresponding triangulation - to the observed epithelial geometry by minimizing the (pseudo-) energy functional defined by

$$
\Omega \left[ \left\{ Q_\alpha^a \right\}, \Lambda \left\{ \hat{r}_{ij} \right\} \right] = \frac{1}{2} \sum_{\langle \alpha, \beta \rangle} \left[ (Q_\alpha^a - Q_\beta^b) \cdot \hat{r}_{\alpha\beta} \right]^2 - \frac{\Lambda}{2} \sum_{\langle \alpha, \beta \rangle} (Q_\alpha^a - Q_\beta^b)^2
$$

(10)

where $\hat{r}_{\alpha\beta}$ is the unit vector along the common edge of neighboring cells $\alpha$ and $\beta$. We constrain the variance of tension $T_{\alpha\beta}$ to be equal to one via Lagrange multiplier $\Lambda$ to preclude the trivial solution. Variation of the above functional with respect to dual vertices returns

$$
\frac{\delta \Omega}{\delta Q_\alpha^a} = \sum_{\{ \beta \}_\alpha} \left[ \hat{r}_{\alpha\beta} \hat{r}_{\alpha\beta}^b - \Lambda \delta^{ab} \right] \left[ Q_\alpha^b - Q_\beta^b \right]
$$

(11)

where $\{ \beta \}_\alpha$ denotes the set of all cells adjacent to cell $\alpha$. $\Lambda$ is chosen to be the smallest value that ensures the matrix defined by Eq. (11) has a non-trivial null space; it measures the deviation of the epithelial geometry from a true static tension net insofar that it is a necessary global perturbation to the orthogonality condition between an edge and its dual conjugate. Fig. 3(b) illustrates the action of this algorithm: minimization of $\Omega$ amounts to minimizing the overlap between all edges and their conjugate duals.

Equations (10,11) reduce the tension inference problem to convex minimization subject to quadratic constraints and thus can be numerically solved using interior point methods standard to Quadratically Constrained Quadratic Programming (QCQP) [35]. The benefit of the proposed variational “Mechanical Inverse” method is that the output is a true static tension net - the algorithm projects the observed lattice onto the closest static tension net and extracts tension parameters from the projection. Provided the tissue snapshot can be thought of as a static tension net with superimposed fluctuations, representing real dynamical fluctuations plus measurement errors, the variational inverse algorithm should provide a more robust measurement of equilibrium parameters as compared to the matrix inversion of force balance equations done on instantaneous tissue geometry [18, 19].

D. Multiplicity of equilibrium Tension Net geometries.

Next we observe that the number of degrees of freedom for equilibrium tension net geometries,
given by at $2v - c = 3c$ ($v$ being the number of vertices of the cell array), is larger than the $2c$ degrees of freedom for the dual triangulations of the tension plane. Hence, a given set of tensions must correspond to multiple possible polygonal arrays: specifically, to a manifold of nets with one degree of freedom per cell. To sort this out we first note that our construction of the dual triangulation generalizes the standard passage from the Voronoi lattice to its Delaunay dual triangulation. Conversely, given a triangulation we can construct a dual polygonal lattice by defining the circumcircle center for each triangle and drawing a Voronoi lattice based on these centroids. Yet, such a lattice is not the unique dual of the tension triangulation. As long as none of the vertex angles are perturbed, we can freely “inflate” or “deflate” lattice cells, as illustrated in Fig. 4(a), without disturbing mechanical equilibrium and thus the underlying tension-triangularization. The compatibility condition satisfied by equilibrium nets is essential for allowing such “isogonal” - i.e. angle preserving - dilation modes to exist.

This mathematical observation has interesting physical implications, as it suggests that “isogonal” deformations should dominate observed fluctuations of tension nets close to mechanical equilibrium, acting as easily excitable “soft modes” of the cellular lattice. Moreover, we expect that the isogonal modes are fundamental to ATN dynamics on time scales longer than mechanical equilibration, but short compared to the redistribution of myosin. Because tension net equilibrium (at static cortical myosin) does not specify a unique cell array geometry, after any transient perturbation from equilibrium a cell array is not constrained to relax to the original configuration, but instead moves to a different point on the c-dimensional manifold of equilibrium lattice geometries. Transient perturbations take a cell array out of equilibrium, but because the equilibrium state is a manifold rather than a point, the system does not necessarily return to the same state, resulting in an ‘isogonal’ transformation.

This is achieved by introducing Lagrange multipliers $Q_\alpha$ for each cell in our original energy functional defined by Eq. (1). Interestingly, equilibrium values for Lagrange multipliers are equivalent to a $\pi/2$ rotation of our tension triangulation $\{Q_\alpha\}$ defined above, modulo translations. Full dynamical equations for edge vectors can be derived analogously to Eq. (3), however we will only explore dynamics of small perturbations $\delta r_{\alpha\beta}$ near equilibrium. In all equations that follow, time is rescaled $t \rightarrow \frac{\kappa}{\nu} t$ to reduce the appearance of unnecessary constants. The equations of motion are

$$\frac{d}{dt} \delta r_{\alpha\beta} = -u_{\alpha\beta}\delta \hat{r}_{\alpha\beta} - \hat{r}_{\alpha\beta} \delta u_{\alpha\beta} + \delta Q_{\beta\alpha}$$  

where $u_{\alpha\beta} \equiv \kappa^{-1} T_{\alpha\beta}$ and $\delta Q_{\beta\alpha} \equiv \delta Q_{\alpha} - \delta Q_{\beta}$. Lagrange multipliers are determined by imposing the constraint outlined by Eq. (12)

$$\sum_{\{\beta\}_{\alpha}} \delta Q_{\beta\alpha} = \sum_{\{\beta\}_{\alpha}} [u_{\alpha\beta}\delta \hat{r}_{\alpha\beta} + \hat{r}_{\alpha\beta} \delta u_{\alpha\beta}]$$  

Equation (14) can be thought of as Poisson’s equation for $Q_\alpha$ defined over our dual triangulation, sourced by the out-of-equilibrium force summed around each cellular plaquette. It is convenient to project Eq. (13) into transverse and longitudinal components, defined by

$$\delta r_{\alpha\beta} = \delta r_{\alpha\beta} \hat{r}_{\alpha\beta} + \delta \theta_{\alpha\beta} r_{\alpha\beta} [\hat{z} \land \hat{r}_{\alpha\beta}]$$  

FIG. 4. (a) Cartoon illustrating the isogonal, i.e. angle preserving, breathing mode of a cell in a tension net. (b) A schematic diagram of expected ATN dynamics and the c-dimensional manifold of equilibrium lattice geometries.
leaving us with

\[
\frac{d}{dt} \delta r_{\alpha\beta} = -\delta u_{\alpha\beta} + \hat{r}_{\alpha\beta} \cdot \delta Q_{\beta\alpha} \tag{16}
\]

\[
r_{\alpha\beta} \frac{d}{dt} \delta \theta_{\alpha\beta} = -u_{\alpha\beta} \delta \theta_{\alpha\beta} + \hat{r}_{\alpha\beta} \wedge \delta Q_{\beta\alpha} \tag{17}
\]

The dynamics of small perturbations in intrinsic length is found by expanding Eq. (5) about the fixed point

\[
\frac{d}{dt} \delta \ell_{\alpha\beta} = q_{\alpha\beta} [\delta u_{\alpha\beta} - \delta m_{\alpha\beta}] \tag{18}
\]

where

\[
q_{\alpha\beta} \equiv \frac{\nu f_{\alpha\beta}}{T_{\alpha\beta}} W'(1) \tag{19}
\]

Tension dynamics is easily obtained via the constitutive relation defined in Eq. (4).

\[
\frac{d}{dt} \delta u_{\alpha\beta} = -(1 + q_{\alpha\beta}) \delta u_{\alpha\beta} + \hat{r}_{\alpha\beta} \cdot \delta Q_{\beta\alpha} + q_{\alpha\beta} \delta m_{\alpha\beta} \tag{20}
\]

Lastly, the myosin dynamics is governed by

\[
\frac{d}{dt} \delta m_{\alpha\beta} = \omega (\delta u_{\alpha\beta} - \delta m_{\alpha\beta}) \tag{21}
\]

where myosin has been rescaled to have units of interfacial deformation: \(\delta m_{\alpha\beta} \rightarrow T_{\alpha\beta}^* \delta m_{\alpha\beta} \) and \(\omega \equiv \mu \kappa^{-1} W'(1)\).

Isogonal modes correspond to \(\delta \theta = \delta u = 0\) (and thus \(\delta Q = 0\)) which is realized by \(\delta \ell_{\alpha\beta} = \delta r_{\alpha\beta}\), provided \(\sum_{\beta} \delta r_{\alpha\beta} = 0\). The latter constraint is satisfied for

\[
\delta r_{\alpha\beta\gamma} = \hat{r}_{\alpha\beta} T_{\alpha \beta} \Theta_{\gamma} - \hat{r}_{\beta\gamma} T_{\beta \gamma} \Theta_{\alpha} - \hat{r}_{\gamma\alpha} T_{\gamma \alpha} \Theta_{\beta} \tag{22}
\]

where \(\delta r_{\alpha\beta\gamma}\) denotes displacement of vertex at which adjacent cells \(\alpha, \beta, \gamma\) meet and \(S_{\alpha\beta\gamma}\) denotes the area of said vertex’s dual triangular plaquette. Thus, isogonal deformations are parameterized by \(\{\Theta_{\alpha}\}\) and have no restoring force. Tensions \(T_{\alpha\beta}\) appear as coefficients because their ratios capture the implicit geometric constraints within tension nets central to the structure of the isogonal modes. (Note for example that \(\delta r_{\alpha\beta\gamma} = 0 \) for \(\Theta_{\alpha} = \Theta_{\beta} = \Theta_{\gamma}\)).

Equations (14, 16, 17, 20, 21) define the dynamics of fluctuations for ATNs near equilibrium. As the structure of these equations is quite complex, before presenting their full analysis we explore the more transparent case of a 1D linear chain before presenting their full analysis.

1. One-dimensional active tension cable.

In the limit of a one-dimensional uniform cable, \(q_{\alpha\beta} = q\), Eqs. (16, 20, 21) reduce to

\[
\frac{d}{dt} \delta r_i = \delta u_i - \delta u_{i-1} \tag{23}
\]

\[
\frac{d}{dt} \delta u_i = \nabla^2 \delta u_i - q (\delta u_i - \delta m_i) \tag{24}
\]

\[
\frac{d}{dt} \delta m_i = \omega (\delta u_i - \delta m_i) \tag{25}
\]

where \(\nabla^2 \delta u_i \equiv u_{i+1} + u_{i-1} - 2u_i\). Equations (24, 25) form a closed set which couples the dynamics of tension and myosin perturbations along the cable. Myosin does not appear in Eq. (23) and thus doesn’t couple to tissue geometry directly. We consider the limit that \(\omega \rightarrow 0\) and \(\delta m \rightarrow 0\). Equation (24) is then recognized as the discrete form of a damped diffusion equation; a local perturbation of tension will diffuse through the linear array while cytoskeletal remodeling dampens it to the stall condition over a time scale \(q^{-1}\). From this and Eq. (23), we obtain the asymptotic change in length (in the continuum limit) of each actin bundle along the cable due to a perturbation of unit amplitude at the origin

\[
\Delta r(x) = e^{-\sqrt{q} |x|} - \frac{2}{\sqrt{q}} \delta (x) \tag{26}
\]

The entire process nets no change in tensions asymptotically, but locally remodels fiber lengths over distances of order \(q^{-1/2}\), explicitly showing geometric plasticity. This is the 1D analog of the aforementioned isogonal mode. Relaxing the \(\omega = 0\) constraint will only change the dynamics of \(u\), opening up an acoustic branch that allows for the global rescaling of myosin and thus tension along the cable. However, as stated earlier, \(\delta m\) does not appear in Eq. (23) and thus plastic deformation will still occur, albeit now with a non-exponential profile (see S.I. for full analysis).

2. General two-dimensional case.

We now return to the general case of a 2D ATN. The equations of motion previously derived can be compactly written as the evolution of a 4\(c\) dimensional vector

\[
\frac{d}{dt} \begin{pmatrix} \delta r_{\alpha\beta} \\ \delta u_{\alpha\beta} \\ \delta m_{\alpha\beta} \end{pmatrix} = H_{\alpha\beta\gamma\sigma} \begin{pmatrix} \delta r_{\gamma\sigma} \\ \delta u_{\gamma\sigma} \\ \delta m_{\gamma\sigma} \end{pmatrix} \tag{27}
\]
In Eq. (22), a general isogonal transformation is defined by a set of parameters \( \{ \Theta_n \} \) that specify the amplitudes of all \( \phi^\alpha \) eigenmodes. Conversely, the isogonal component of an arbitrary perturbation is extracted by projecting the initial state vector \( v \equiv (\delta r, \delta u, \delta \theta, \delta m)^T \) onto the \( \phi^\alpha \) eigenmode, \( \Theta_n = \sum_n \psi^\alpha_n v_n \), where \( \psi^\alpha \) is the associated left eigenvector of \( H \). It is defined by the condition \( \sum_n \psi^\alpha_n \phi^\nu_n = \delta^\alpha\nu \) where \( \nu \) indexes the set of all eigenmodes. As numerically demonstrated in the S.I., components along vertex and tension perturbations of \( \psi^\alpha \) are found to be spatially extended within a length scale \( q^{-1/2} \), centered about cell \( \alpha \). This is in direct analogy to the 1D cable, wherein length deformations are excited by tension perturbations within an exponentially localized patch of size \( q^{-1/2} \).

Furthering the analogy to the 1D cable, we analyze the dynamics of the reduced system between \( \delta u, \delta \theta \), and \( \delta m \). The reduced matrix is manifestly symmetric in our chosen basis, and as we show in S.I., its eigenvalues are real and negative ensuring the system relaxes back to the same underlying dual graph. Fig. 5 illustrates the eigenvalue spectrum computed in the perturbation analysis of two cases: i) a regular hexagonal ATN state and ii) a highly disordered polygonal tiling state generated numerically as a random Voronoi lattice. For simplicity of presentation in Fig. 5, myosin dynamics is quenched by setting \( \omega = 0 \). Restoring myosin dynamics opens an acoustic branch that allows for global rescaling of tensions and for the dilation of the underlying triangulation, as found in the 1D cable limit. Perturbations in tension are again damped via cytoskeletal activity on the timescale set by \( q^{-1} \), as evidenced by the scaling of their eigenvalues with \( q \), shown in Fig. 5. These considerations reinforce the picture gleaned from both our graph-theoretic count and the 1D toy model - perturbations off the equilibrium manifold are damped by internal remodeling of the cytoskeleton, returning the system back to the same tension triangulation, but subsequently translating the system isogonally.

**F. ATNs subject to external forces**

We now study the response of an ATN to a small external force \( F \). The initial response is governed by linearized equations

\[
\frac{d}{dt} v = Hv + F
\]

and can be conveniently expressed by projecting onto the normal modes via \( c^\nu = \sum_n \psi^\nu_n v_n \) in terms of which

\[
\frac{d}{dt} c^\nu = \lambda c^\nu + \sum_n \psi^\nu_n F_n
\]
FIG. 6. (a) Negative Poisson ratio response. Diagrams of a passive \( q = 0 \) and active \( q > 0 \) network subjected to uniaxial tensile stress (red arrows). The blue box represents the initial state of the tissue. In response to the applied external force, the passive network shrinks along the orthogonal direction while the active network expands. (b) Distribution of \( \Theta \) (see Eq. (28)) after re-equilibration in response to the uniaxial external force: the approximately parabolic profile implies excitation of a global dilation mode of the tissue. (c) Poisson ratio \( \sigma \) as a function of activity parameter \( q \) and tissue size \( L_{sys} \) (measured for a range of \( q \) and \( L_{sys} \) values) depends only on \( q^{1/2} L_{sys} \). As external perturbations are screened within a length scale of \( q^{-1/2} \), Poisson ratio approaches zero when \( q^{1/2} L_{sys} \) exceeds one.

For isogonal modes \( \nu = \alpha \) the eigenvalue is zero, \( \lambda_\alpha = 0 \), which implies secular growth of corresponding deformations with time, \( c^\alpha(t) = t \sum_n \psi^\alpha_n F_n \), the growth rate being determined by the overlap of the corresponding left eigenvector with the external force field, projected onto the longitudinal component of each bond. The latter means that external forces are ‘screened’ within length scale discussed above - plastic deformation will be limited to a region of size \( q^{-1/2} \). Of course this growth of deformation is not expected to continue indefinitely and is cut-off on the time scale of myosin redistribution, governed by Eq. (6), which will terminate the ‘slipping flow’ of acto-myosin bundles and thus re-equilibrate the tissue in the presence of the external force. The plastic ‘isogonal’ deformation remains.

This raises an interesting question: how do isogonal modes change macroscopic mechanical properties of the epithelium in comparison to traditional passive materials? We focus on our model’s Poisson ratio \( \sigma \), defined as the negative of the ratio of transverse to longitudinal strain in response to uniaxial stress applied on the boundary \[36\]. Passive networks generically have a positive Poisson ratio - they compress along the axis orthogonal to the applied tensile loads. Auxetic foams (materials with \( \sigma < 0 \)) require concave cell configurations \[37\] and thus negative interfacial tensions to maintain force balance.

Interestingly, we generically recover \( \sigma < 0 \) for non-zero activity while still maintaining convexity of the underlying network. This is mediated by a global tissue dilation through the excitation of local isogonal modes via the external uniaxial force. For short times, isogonal modes roughly grow linearly with rate predicted by Eq. (31). Under uniaxial stress, these rates are patterned roughly parabolically - shown in Fig. 6(b) - resulting in an overall tissue dilation. The anisotropic distribution simply implies \( |\sigma| < 1 \). At long times, isogonal deformations are adiabatically quenched as myosin redistributes to triangulate the new boundary conditions. An important corollary to this picture is that \( \sigma \) should strongly depend upon the local contractility rate of the acto-myosin cytoskeleton; if the screening length \( q^{-1/2} \) is on the order of the system size then the perturbation on the boundary will propagate the entire interior of the tissue and thus globally excite isogonal deformations. Conversely, if the screening length is much smaller than the tissue then most of the plastic deformation will be limited to a small layer around the stressed boundary and none along the orthogonal axis. This behavior was observed numerically for randomly generated Voronoi lattices, as shown in Fig. 6(d). Upon removal of the external force, the tissue was found to relax approximately back to the initial tension-triangulation and cell configuration. Interestingly, negative Poisson ratio has been observed experimentally for embryonic amphibian epithelia \[35\].

G. Ventral Furrow formation in Drosophila embryo

In the beginning of the gastrulation process in \textit{Drosophila}, embryo cells along the ventral midline constrict their apical surfaces, initiating the formation of a furrow that subsequently internalizes the
future mesoderm [29], as shown in Fig. 7(a). This apical constriction was shown to be driven by pulsed contractions of a medial acto-myosin network (located on the apical cell surface) that connects to the adherens junction-anchored cortical cytoskeleton [39, 40]. The process has been described as a “ratchet” [39] where medial myosin pulses cause transient constrictions, that are subsequently stabilized by the retracted cytoskeletal cortex. This phenomenon is readily interpretable in terms of our ATN model, which is a reasonable approximation because as shown in Fig. 2(c), embryonic epithelial cells appear to satisfy the geometric compatibility constraint as defined by Eq. (9). We note that medial myosin pool exists in addition to the junctional myosin associated with the adherens junction-anchored cytoskeleton that is modeled by the ATN. If we assume that the junctional myosin concentrations are relatively static over the timescale of medial myosin pulsing, the ATN model predicts that any transient perturbation of mechanical balance due to medial myosin contractions would leave behind an isogonal deformation of the cell array, as it returns to mechanical balance dominated by cortical tensions that remain unchanged. Hence we predict that cell deformation during the early stages of ventral furrow formation should be well described by motion along an isogonal manifold.

This prediction was tested using time-lapse microscopy data on the early stage of Ventral Furrow formation in the Drosophila embryo [39, 40]. The initial time point of each movie was fit to the closest possible tension net, using the variational approach defined by Eqs. (10, 11). Deformations of the cell array at subsequent time points were used to define the best fit amplitudes of isogonal modes. Specifically, Eq. (22) is a rectangular (2v by c) linear system of equations defining vertex displacements corresponding to an arbitrary isogonal transformation \{\Theta_\alpha\}. Conversely, the best fit (in the sense of least square error) \{\Theta_\alpha\} is given by a pseudo-inverse of this rectangular matrix. We found, as shown in Fig. 7(b), that thus defined isogonal modes accounted for about 90% of the total variance of the dynamic vertex displacement field, which clearly indicates that apical deformation of cells during ventral furrow formation is well approximated by an isogonal transformation. Thus, the cell array appears to behave much like a transiently perturbed ATN, flowing along the isogonal manifold which comprises the set of its (mechanical) equilibrium states. The latter, in turn, suggests that cortical-myosin levels do not significantly change during this time despite medial-myosin spiking. The results not only suggest that an ATN model is suitable for describing tissue behavior, but also provide a simpler set of degrees of freedom that suitably describe the dynamics. The spatial distribution of final \{\Theta_\alpha\} is shown in Fig. 7(c): It resembles parabolic cylinder straddling the ventral midline. The parabolic profile of isogonal mode amplitudes corresponds to anisotropic constriction of cells with the long axis oriented along the anterior-posterior direction [29].

### III. DISCUSSION

In this study, we proposed a quasistatic tension-dominated active model of epithelial tissue mechanics. There are two main assumptions on which this approximation rests: intercellular forces are dominated by cortical tensions held in the underlying actin network and that these tensions predominately balance each other across the tissue. Taken together, these assumptions make a falsifiable, quantitative prediction about the geometry of cells in static tension nets via our compatibility constraint. This was subsequently tested against four different Drosophila epithelia. While perfect agreement was
neither found nor expected, the fact that three out of the four epithelia were found to cluster significantly closer to a static tension net as opposed to their empirically constructed “nulls” supports our original Ansatz. The formulated variational inference of interfacial tension should allow further and more direct tests our model once suitable experimental measurements of cortical tension became available.

Our study centers on the exploration of tissue-scale phenomena concomitant with internal cell remodeling. Specifically, our simple model, including only the effects of acto-myosin contractility and a generic load-dependent myosin walking rate, exhibited non-trivial, floppy ‘isogonal modes’ that are expected to dominate the dynamics asymptotically. This predicts local cellular plasticity excitable by both internal perturbations and external forces that decouples instantaneous stress and strain. This suggests a striking picture of tissue morphogenesis; we envision tissues operating in this limit to evolve their shape adiabatically, either by perturbing intercellular junctions to move isogonally, as shown to be the case for Drosophila ventral furrow formation, or via modulating cytoskeletal chemistry to excite movement off the isogonal manifold (see 11). The existence of such zero modes makes quantitative predictions on macroscopic tissue behavior immediately amenable to experimental verification. For example, any such tissue should exhibit global auxetic behavior in response to uniaxial stress.

Isogonal modes can be thought of as the discretized degrees of freedom associated to the conformal symmetry of the continuum description. The elastic energy associated to displacement field \( u_i \) with vanishing bulk modulus is

\[
E = \frac{1}{2} \int d^2r \left[ \partial_i u_k + \partial_k u_i - \delta_{ik} \partial_l u_l \right]^2
\]

Assuming relaxational dynamics - i.e. \( \ddot{u}_i = \frac{\delta E}{\delta u_i} \) - the equation of motion for field \( u_i \) is found to be \( u_i = -\partial^2 u_i \). Any solution of the Cauchy-Riemann equations can be added to \( u_i \) with no generation of additional internal stresses. That is to say, any conformal transformation of our equilibrium displacement field is also a valid ground state.

In conclusion, we expect that generalization of the ATN model and application of the proposed mechanical inference will further advance understanding of the interplay between cellular biophysics and tissue morphogenesis by making clear testable predictions that can be subsequently verified.

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