Topological defects organize collective shape oscillations in biological tissues

Collective synchrony in confluent, pulsatile epithelia
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Collective oscillations are ubiquitous in living systems, ranging from intracellular biochemical cycles to tissue-scale pulsations and rhythmic deformations [1, 2]. Such oscillations emerge from interacting units that continuously consume and dissipate energy locally. Active matter offers a natural theoretical framework to describe such phenomena, as it captures how local energy injection and interactions give rise to large-scale spatiotemporal organization [3]. In this context, biological tissues subject to oscillatory deformation can be viewed as dense active matter in which phase coherence, wave propagation, and defect dynamics emerge as collective properties.

In their recent work, Tang et al. present compelling results from experiments on confluent monolayers of Madin–Darby Canine Kidney (MDCK) epithelial cells, a well-established model system for studying collective epithelial mechanics *in vitro*. Cells are cultured to confluence on flat substrates, forming a continuous two-dimensional epithelial sheet in which every cell is mechanically coupled to its neighbors. Under these conditions, individual MDCK cells exhibit spontaneous oscillations in shape, that we refer to as *pulsations*. As the tissue is densely packed, these local oscillatory deformations cannot relax independently; instead, they exhibit collective oscillations throughout the monolayer.

By marking the nuclei of cells with the fluorescent NLS-GFP protein, the authors reconstruct the local velocity field, which provides a spatial map of collective motion across the entire field of view. By computing the divergence of this velocity field, they identify dilatational modes corresponding to local cycles of expansion and contraction, a direct mechanical signature of cellular pulsations. From the temporal signal of these modes at each spatial point, they extract an effective phase variable, enabling them to quantify synchronization, phase coherence, and the emergence of topological defects across the tissue.

A central experimental finding is that the degree of global synchrony, quantified through spatiotemporal phase correlations, exhibits a non-monotonic dependence on cell density. At low densities, oscillations are largely incoherent due to weak mechanical coupling. As density increases, temporal coherence strengthens, giving rise to extended regions of phase

alignment and sustained oscillatory order. At even higher densities, global synchrony deteriorates: phase patterns become fragmented, and topological defects in the phase field emerge spontaneously. This striking density dependence points to a subtle interplay between local activity, mechanical coupling, and collective organization in biological tissues [Fig. 1].

To rationalize these observations, the authors introduce a continuum description in which the local cell density $\rho(\mathbf{r}, t)$ is coupled to the complex order parameter $G(\mathbf{r}, t) = A(\mathbf{r}, t)e^{i\theta(\mathbf{r},t)}$ that effectively describes the shape oscillation of nearby cells:

$$\begin{aligned} \partial_t \rho &= \alpha \nabla^2 (\rho - \rho_0 - \epsilon A \cos\theta) \ , \\ \partial_t \theta &= \Gamma \left[\nabla^2 \theta + 2(\nabla \ln A) \cdot (\nabla \theta) \right] - A\epsilon \sin\theta (\rho - \rho_0 - A\epsilon \cos\theta) + \Omega \ , \\ \partial_t A &= \Gamma \left[\nabla^2 A - A(\nabla\theta)^2 \right] + 2\chi A(\rho/\rho_0 - A^2) \ , \end{aligned} \tag{1}$$

where Ω is the bare pulsation frequency, (α, Γ) are mobility parameters, ρ_0 is the baseline density, and (ϵ, χ) are mechanochemical coupling constants. This minimal, yet non-trivial model captures how local oscillators interact through the tissue: the phase $\theta(\mathbf{r}, t)$, which embodies the periodic deformation of cells, is modulated by the amplitude $A(\mathbf{r}, t)$, which quantifies the degree of shape synchronization, and the density $\rho(\mathbf{r}, t)$. In this description, the breakdown of synchrony is associated with the emergence and proliferation of topological defects in the phase profile $\theta(\mathbf{r}, t)$, which act as sources of disorder and disrupt long-range temporal coherence.

Beyond reproducing experimental trends, this model highlights the role of defects as central organizing elements in biological tissues subject to active deformation. By correlating defect density with loss of synchrony in normal and cancerous cell lines, Tang et al. suggest that defect-mediated dynamics may provide a unifying physical mechanism linking tissue mechanics, collective rhythms, and biological functions. In fact, their study places epithelial pulsations within the broader class of defect-controlled states of active matter [4], opening the door to systematic comparisons between various biological and synthetic oscillatory systems.

The theoretical analysis resonates strongly with a recently proposed hydrodynamic theory of pulsating active liquids, where oscillatory degrees of freedom are coupled to a conserved density field [5, 6], in line with models of actively deformable particles [7–11]. Specifically, the dynamics in Eq. (1) reduces to the continuum model of Refs. [5, 6] in the regime where the complex amplitude field $A(\mathbf{r}, t)$ is constant in space and time. This regime entails the emergence of propagating waves in the profiles of phase $\theta(\mathbf{r}, t)$ and density $\rho(\mathbf{r}, t)$ whose coarsening results from interactions between defects in the contraction profile.

A key theme emerging from these works is the central role of defects in the study of collective dynamics of active liquids; namely, how defect-based diagnostics lead to distinguishing between coherent oscillatory states and disordered regimes, and help rationalize the mechanisms underlying the spatiotemporal organization of deformation waves. Moreover, these studies highlight how shape oscillations in dense biological tissues can be understood as resulting from the mechanochemical coupling between the local density and some degrees of freedom at the intracellular level. Beyond epithelial tissues, this approach is likely relevant to a broader class of living and synthetic systems that exhibit rhythmic activity. By combining experiments, continuum modeling, and defect-based analysis, a general framework to capture the nonequilibrium physics of collective shape oscillations begins to emerge.

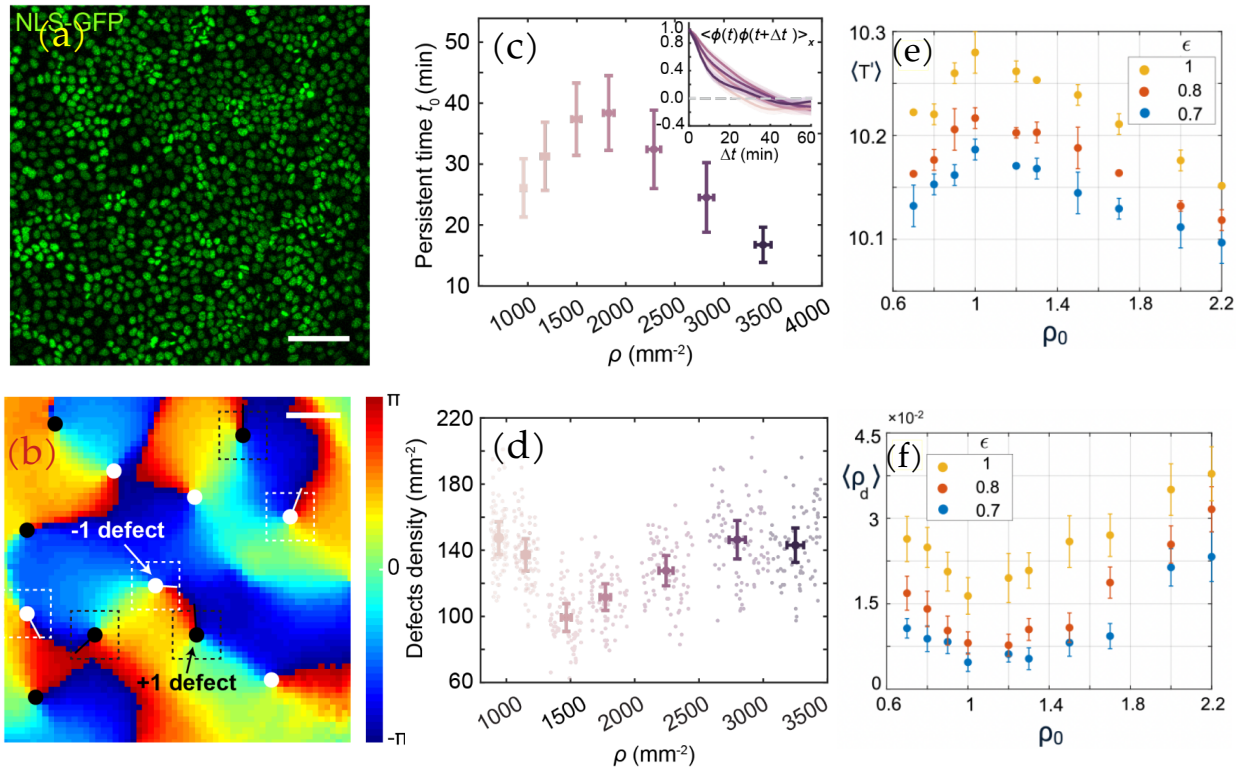

Figure 1: **Collective oscillations and topological defects in biological tissues.** (a) NLS-GFP labeled MDCK cell nuclei on a flat surface. (b) Corresponding map of the deformation phase ϕ constructed from the divergence of the local velocity field. Topological defects with charges ± 1 are highlighted in white and black circles. (c) Temporal autocorrelation of ϕ (inset) and the corresponding persistence time t_0 for different cell densities ρ; t_0 is the time when the auto-correlation reaches zero, see dashed line in inset. (d) Non-monotonic dependence of the density of phase defects as a function of the cell density ρ. The minimum of the defects density in (d) roughly corresponds to the cell density range at which the persistence time is maximal in (c). (e) Non-dimensionalised averaged period of oscillations $\langle T'\rangle$, and (f) average defects density $\langle\rho_{\rm d}\rangle$ for different total densities ρ_0, as evaluated in numerical simulations of the continuum model [Eq. (1)]. The minimum of $\rho_{\rm d}$ and the maximum of $\langle T'\rangle$ are found at comparable values of ρ_0, in line with the experimental results in (c-d). Scale bars in (a,b): 50 μm. Figures adapted from the original article.

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