Inflationary Embryology

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***Short Abstract* — Soft tissues can build up residual stresses as they grow if their growth rate contains spatio-temporal variations due to local fluctuations in cell division rate. These stresses in turn can feed back on the local growth resulting in nontrivial growth dynamics. We model the growth of epithelial sheets subject to local noise and mechanical feedbacks, and study the density correlations across the tissue. We find that generically these show power law scaling.**

***Keywords* — epithelial growth, morpho-elasticity, target metric, mechanical feedback**

I. Background

Growth of epithelial tissues often involves a level of stochasticity due to noise in cell division rates [1]. Local fluctuations in growth rate can lead to uneven accumulation of mass, which in turn can cause mechanical stresses to build up. It is been known that such stresses can affect cell growth and division rates via the Hippo pathway [2,3]. For example, areas with high density (high compression) are expected to show a decreased growth rate, while areas with low cell density should show increased growth. How strong this stress response is and how much it affects growth in normal conditions are not entirely known.

Experimentally, one can look at the density profile and correlations at different time points, or study how the shape of tagged clones evolves in time. Then, from the theoretical point of view, the question becomes, given a growing tissue with local noise in growth rate and a specific mechanical feedback, what is the time evolution of the density profile, and what can we predict about the shape of clones undergoing growth? Answering these questions can help us better understand the growth dynamics and possible stress response mechanisms underlying the development of epithelial tissues.

II. Model

We model the epithelium as a continuum, elastic sheet undergoing noisy, exponential growth. The challenge is that a non-uniform growth can lead to "incompatible" configurations that cannot be embedded in $\mathbb{R}^3$ [4,5]. Thus, the tissue deforms into a stressed configuration. Tackling the growth incompatibility is in general not an easy task. To make the problem tractable, we work in the target metric formalism [5], and linearize about the average growth rate. We consider both isotropic and anisotropic growth. Anisotropic growth can occur due to oriented cell divisions [6-8], which in turn can be due to stress anisotropy. In each of these two cases, we study the time evolution of density-density correlation functions in the presence of two biologically sensible stress feedbacks. We also look at initially circular clones undergoing non-uniform growth, and study the clone shape statistics.

III. Conclusion

We find that the initial fluctuations in the tissue are correlated on an intrinsic length scale. These fluctuations can then be advected over the tissue as the tissue is dilated, leading to a non-trivial power-law behavior for the density-density correlators at long times. These results are interestingly reminiscent of inflationary cosmology where quantum fluctuations in the early universe are believed to have caused the formation of large-scale structures [9]. Our model also predicts specific clone shape statistics for isotropic and anisotropic growths. By comparing our predictions with experimental findings, we could constrain the underlying mechanisms of mechanical feedback on growth in epithelia.

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