Growing microbial colonies are unstable 'active' fluids

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How do growing bacterial colonies get their shapes? In this talk, I will describe our work showing how colony morphogenesis—the process by which a growing multicellular colony develops its shape—can be understood using the tools and analytic approaches of rheology. Using experiments in transparent 3D granular hydrogel matrices, we show that dense colonies of four different species of bacteria generically become morphologically unstable and roughen as they consume nutrients and grow beyond a critical size—eventually adopting a characteristic branched, broccoli-like morphology independent of variations in the cell type and environmental conditions (an example is shown in the Figure[1] below). We elucidate the onset of the instability using linear stability analysis and numerical simulations of a continuum model that treats the colony as an "active fluid" whose dynamics are driven by nutrient-dependent cellular growth. We find that when all dimensions of the colony substantially exceed the nutrient penetration length, nutrient-limited growth drives a 3D morphological instability that recapitulates essential features of the experimental observations. Moreover, we show that our "active fluid" approach can also describe experimental observations of the shapes of mixed, multi-species bacterial colonies. Our work thus provides a framework to predict and control the organization of growing colonies—as well as other forms of growing active matter, such as tumors and engineered living materials—in 3D environments. It also generates new questions for us to consider as rheologists: for example, what are the limits of traditional rheological models in describing living systems that consume energy to move and grow, and are therefore inherently out of equilibrium?

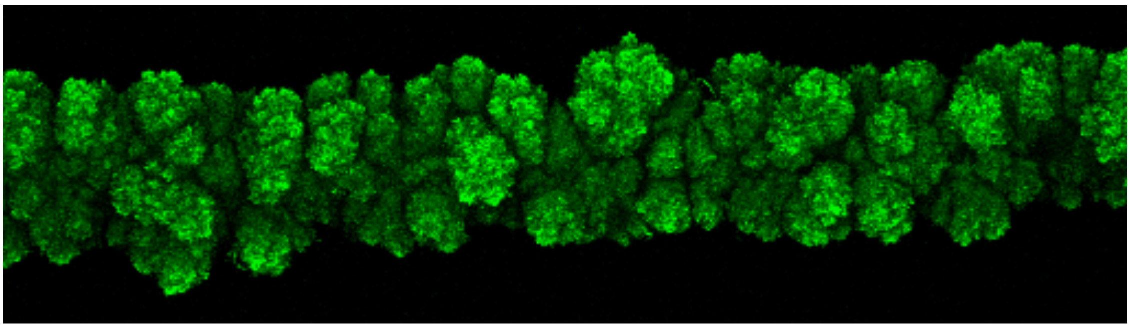

Figure: Confocal micrograph of a colony of *E. coli,* showing the characteristic "broccoli"-like shape that it grows into. The vertical size of the image spans ~500 μm.

[1] A. Martínez-Calvo, *et al.*, *PNAS.* **119,** e2208019119 (2022).