Onset of 3D tissue morphogenesis near integer topological defects

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Distortions or imperfections of ideal patterns, often called defects, are responsible for the selection and steady-state evolution of patterns. Defects are found in several biological systems and they participate in key processes for tissue homeostasis, such as cell extrusion. However, our understanding of the role of defects in biological systems remains still in its infancy [1,2]. Here, we built on a physical description for defects in active polar fluids [3] to study the onset of 3D reshaping of cell monolayers under strong 2D confinement. Our physical approach adds two types of active forces, corresponding to nematic-like cell-cell interactions (active stresses) and polar-like cell-substrate interactions (active traction forces). For sufficiently small confinements, we find a second-order bifurcation between unmoving aster defects to spinning spiral defects. Asters and spirals result in distinct mechanical environments, depending on the confinement geometry and material characteristics. The experimental cell velocity and cell orientation maps fixed the sign of both active forces, and the shape of spirals provided a direct way to measure the flow-alignment coefficient in cell monolayers, which currently remains unknown. Based on these results, asters render compressive stresses at the defect core, resulting in 2D density accumulation and conditioning 3D migration.

[1] T. B. Saw, et al., *Nature*, **544**, 212 (2017)

[2] K. Kawaguchi, et al., *Nature*, **545**, 327 (2017)

[3] K. Kruse, et al., *Phys. Rev. Lett.*, **92**, 078101 (2004)