Configurational fingerprints of multicellular living systems

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Cells cooperate as groups to achieve structure and function at the tissue level, during which specific material characteristics emerge. Analogous to phase transitions in classical physics, transformations in the material characteristics of multicellular assemblies are essential for a variety of vital processes including morphogenesis, wound healing, and cancer. In this work, we develop configurational fingerprints of particulate and multicellular assemblies and extract volumetric and shear order parameters based on this fingerprint to quantify the system disorder. Theoretically, these two parameters form a complete and unique pair of signatures for the structural disorder of a multicellular system. The evolution of these two order parameters offers a robust and experimentally accessible way to map the phase transitions in expanding cell monolayers and during embryogenesis and invasion of epithelial spheroids.

phase transition | jamming | order parameter | cell mechanics | multicellular system

Cells interact and cooperate at length scales far above individuals (1, 2); these long-ranged interactions help determine tissue-level material characteristics. The ability to tune these material characteristics is important for many multicellular physiological and pathological processes including embryogenesis (3–5), cancer invasion (6, 7), and wound healing (8). In these vital processes in living systems (9–11), cells bear many of

order parameters are defined solely based on static images and do not rely on dynamic measurements. Using this framework, we characterize the changes that occur during a variety of order–disorder transitions in two dimensions (2D) and three dimensions (3D), including jamming transition of thermal systems and simulated confluent cell monolayers, maturation of a 2D cell monolayer, extending *Drosophila* germband epithelium, and human epithelial spheroids in 3D.

In thermal systems, the energy competition between isotropic (volumetric) and isochoric (shear) deformation identifies three distinct phases (i.e., gas, liquid, and solid). Gas can barely resist volumetric or shear deformation while solid resists both. In between, liquid is often considered as resistant only to volumetric deformation. Theoretically, the isotropic and isochoric invariants of deformation are a pair of mutually independent and complete variables that can fully quantify the local deformation. Here, we demonstrate how to calculate these for a 2D system; this can be extended to 3D as well (details in *SI Appendix*). In 2D, three noncolinear adjacent cells form a triangle. Assuming N triangles can be formed by linking adjacent cells, the nth triangle ($n = 1, 2, \ldots, N$) in current configuration can be expressed as a matrix $\boldsymbol{T}_n = \begin{bmatrix} X_{n1} - X_{n0} & X_{n2} - X_{n0} \\ Y_{n1} - Y_{n0} & Y_{n2} - Y_{n0} \end{bmatrix}$ (Fig. 1*A*), where X_{nm} and Y_{nm} ($m = 0, 1, 2$) are Cartesian coordinates of the mth vertice of the nth triangle. This segmentation