M2 internship and PhD thesis

Cohesion and fluidity of an epithelial tissue: how active cell mechanics preserve diffusion in a dense, disordered system

Laboratory :
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Context and motivation. Epithelial tissues must maintain organ integrity while continuously remodeling during morphogenesis, wound healing, and disease progression. At high cell density, tissues are often described as mechanically arrested, disordered, solid-like materials, and a large body of work interprets them within the framework of glassy and jamming physics. In this picture, cells are trapped by their neighbors (the "cage effect"), which should lead to subdiffusive dynamics and strongly slowed rearrangements, as in thermal glass-formers near the glass transition. Yet tissues do remain fluid over long timescales: cells exchange neighbors and eventually diffuse over distances much larger than their size, with transport that is often much closer to normal diffusion than what a passive glassy system would give. This tension between cohesion (solid-like at short times) and fluidity (liquid-like at long times) is the central question of this project. A plausible explanation is that active, non-equilibrium mechanisms intrinsic to cells (shape changes, self-propulsion, polarity dynamics, cell division and extrusion) continuously fluidize the tissue. However, these mechanisms are rarely compared on equal footing, and in particular the role of the coupling between cell geometry and cell motility remains poorly understood.

Objectives. Combining numerical simulations and analytical calculations, the objectives of this internship/PhD project are:

1. Characterize cell diffusion in dense active systems. Quantify the single-cell dynamics (mean-squared displacement, effective diffusion coefficient, caging signatures, non-Gaussianity of displacements) as a function of density, activity and mechanical parameters.
2. Compare models of active cells in which the magnitude and orientation of motility are coupled to the cell's own shape and/or to the shape and motility of its neighbors (e.g. polarity aligned with the cell's long axis, motility modulated by area or perimeter, alignment with neighbors). The aim is to identify which couplings are sufficient to suppress caging and restore diffusion.
3. Characterize spatial dynamical heterogeneity and determine whether it emerges spontaneously at the scale of a cluster of cells, through correlated displacements, mobile and immobile regions, and a characteristic dynamical length scale.
4. Compare homogeneous and heterogeneous cell populations, for instance mixtures of cells differing in motility, stiffness or target shape. We will ask whether a minority of fluid cells can fluidize a jammed majority, and under what conditions.

Required skills: the candidate should have a strong inclination for theory (especially statistical physics and stochastic processes) and numerical simulations.

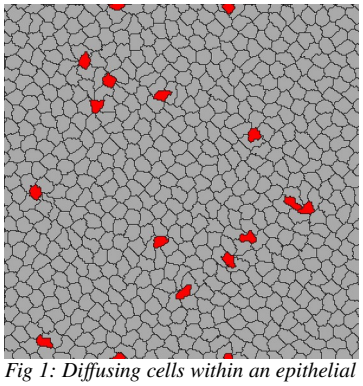


Fig 1: Diffusing cells within an epithelial tissue.