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Epithelial gap closure governed by forces and geometry.

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The closure of gaps within epithelia is crucial to maintain the integrity and the homeostasis of the tissue during wound healing or cell extrusion processes. Cells mediate gap closure through either the assembly of multicellular actin-based contractile cables (purse-string contraction) or the protrusive activity of border cells into the gap (cell crawling). I will present experimental data and numerical modeling that show how these mechanisms can mutually interact to promote efficient epithelial gap closure and how mechanical constraints can regulate these mechanisms. I will first present how geometrical constraints dictate mechanisms of epithelial gap closure. We determine the importance of tissue shape during closure and the role of curvature of cell boundaries in this process. An essential difference between the two closure mechanisms is that cell crawling always pulls the edge of the tissue forward (i.e. towards the gap) while purse string pulls the edge forward or backwards depending on the local geometry. Our study demonstrates how the interplay between these two mechanisms is crucial for closing gaps and wounds, which naturally come in arbitrary shapes. Then I will focus on epithelial closure mechanism during cell extrusion. Within confluent cell layers, cellular motions coupled between neighbors are tightly regulated by the packing density of the epithelium inducing drastic changes in the dynamics of these tissues. I will show how cell density and tissue mechanics regulate the extrusion of cells within a confluent epithelial cell sheet, simultaneously measuring collective movements and traction forces. Epithelial packing and collective cell dynamics dictate the modes of cellular extrusions from lamellipodia crawling of the neighboring cells at low densities to coordinated actin-based contractile purse-string mechanism at higher density.