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## Bottom-up mechanobiology: from cell sheets to organoids

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Epithelial sheets form specialized 3D structures suited to their physiological roles, such as branched alveoli in the lungs, tubes in the kidney, and villi in the intestine. To generate and maintain these structures, epithelia must undergo complex 3D deformations across length and time scales. How epithelial shape arises from active stresses, viscoelasticity and luminal pressure remains poorly understood. I will present different approaches to study the mechanobiology of epithelial shape from the bottom up. I will discuss new technologies to design epithelia of arbitrary size and geometry and to subject them to controlled mechanical deformations in 3D. I will show that monolayers exhibit superelastic behavior when stretch is applied and that they readily buckle when compressed. We use this phenomenology and a 3D vertex model to rationally direct spontaneous pattern formation, and hence engineer tissue folding. I will also present our recent advances to understand the mechanobiology of intestinal organoids. We show that these organoids exhibit a non-monotonic stress distribution that defines mechanical and functional compartments. Finally, I will discuss how intestinal mechanobiology is derailed in patient-derived colorectal cancer organoids.

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