MONTANA STATE UNIVERSITY
College of ENGINEERING

Gastrointestinal Organoid Structure and Transport

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PhD Dissertation Defense
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ABSTRACT

Organoids are three-dimensional (3D) self-assembled, mammalian tissue cultures derived from stem cells that differentiate to contain multiple cell types, which are spatially organized within the 3D structure and capable of recapitulating the function of a particular organ. Organoids offer a variety of existing and potential applications in medicine and biotechnology, including drug formulation testing, regenerative medicine and microbiome research. Despite their value, knowledge of how organoid structure impacts dynamics, mechanics, and transport is lacking. This is particularly true for gastrointestinal organoids, which are composed of a monolayer-thick epithelial sheet wrapped into a closed spherical shape. The topologically-closed shell suppresses liquid advection into or out of the luminal space, which leads to the buildup of cellular and metabolic waste, results in periodic shell rupture, and ultimately limits experimentation. Here, we present experimental results on human gastric organoids (HGOs) to support the hypothesis that gut organoid rupture is osmotically-driven and can be mitigated by limiting the buildup of osmotic pressure in the organoid. Furthermore, we present a millifluidic device which we use to directly circumvent transport limitations by establishing internal liquid flow through the lumen of human intestinal organoids (HIOs). In the process, we used a combination of time-lapse microscopy, image analysis, modeling, and fluidics fabrication techniques to develop an understanding of organoid.

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