
Mechanical Stability of Multicellular Assemblies

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Abstract

Cell intercalation –or T1 transition– is a crucial event in morphogenetic processus where cells exchange positions by remodeling their cell-cell and cellsubstrate adhesions. It allows a dynamic spatial redistribution of cells while keeping their integrity and collective cohesiveness as a tissue. Most of the experiments performed to assess this process are done in vivo where mechanical readouts are indirectly retrieved from image analysis. Therefore, a complete understanding of cell intercalation is still lacking. To address this gap, we designed a novel in vitro assay to simplify the system by making a compromise: reducing the biological relevance but allowing the imaging of specific molecular pathways and the quantitative measurement of forces involved. Practically, assemblies of four cells –cell quadruplets– were arranged in vitro to mimic the "minimal tissue pavement" that exists in vivo, i.e. the most basic structure that makes possible the T1 transition. To this end, a variety of extracellular matrix (ECM) architectures were micropatterned on treated glass coverslips. Subsequently, those patterns were seeded with Madin-Darby Canine Kidney (MDCK) cells, which self-organized into cell quadruplets, owing to the optimization of the geometrical boundary conditions of the patterns. With such minimalistic system, in vitro cell intercalation events were recorded in two different patterns, although with a rare frequency. Thus, this approach allows the morphological characterization and the mechanical assessment of cell quadruplets' dynamics on different micropatterns, over their lifetime and during the T1 transition.

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