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Towards a single-cell-based model of early development in ruminants

Embryonic losses and, after birth, the formation of chronic diseases of metabolic origins such as obesity, diabetes, arterial hypertension, have been observed as critical in early ruminant (sheep, cow) development.

In order to understand the possible mechanisms leading to such failures, the mechanisms controlling two developmental phases, the growth of the blastocyst (a hollow sphere of cells) during late blastula formation as well as early trophoblast development needs to be understood. The trophoblast is the first epithelium that appears at the beginning of embryogenesis in mammals. It forms the wall of the blastocyst and helps for implantation in the uterine wall. During early development of the trophoblast, a temporal window of 15 days from the blastocyst stage, the trophoblast floats in the uterine liquid, and undergoes an extremely fast growth and elongation. This period of early morphogenesis is fundamental for a normal development of the embryo. We established a process chain to quantitatively analyze the two developmental phases by experiments, analysis of images from the embryos of different stages, and mathematical modeling. We analyze confocal images to infer the cellular organization into the tissue sheet, and determine the distribution of cell size and cell shapes prior and during the embryo shape transition. Based on the results of this analysis, we set up a mathematical single-cell-based model. Our model cells are parametrized by measurable biophysical and cell biological quantities. They can migrate, grow and divide, and interact with other cells and extracellular matrix by forces. In the first step we considered a representative section of the developing embryo and studied different mechanisms to explain the deformation. The model permits predictions of several manipulations of cells and embryo that are currently experimentally tested.