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Physically-based modeling of the trophoblast tissue morphogenesis



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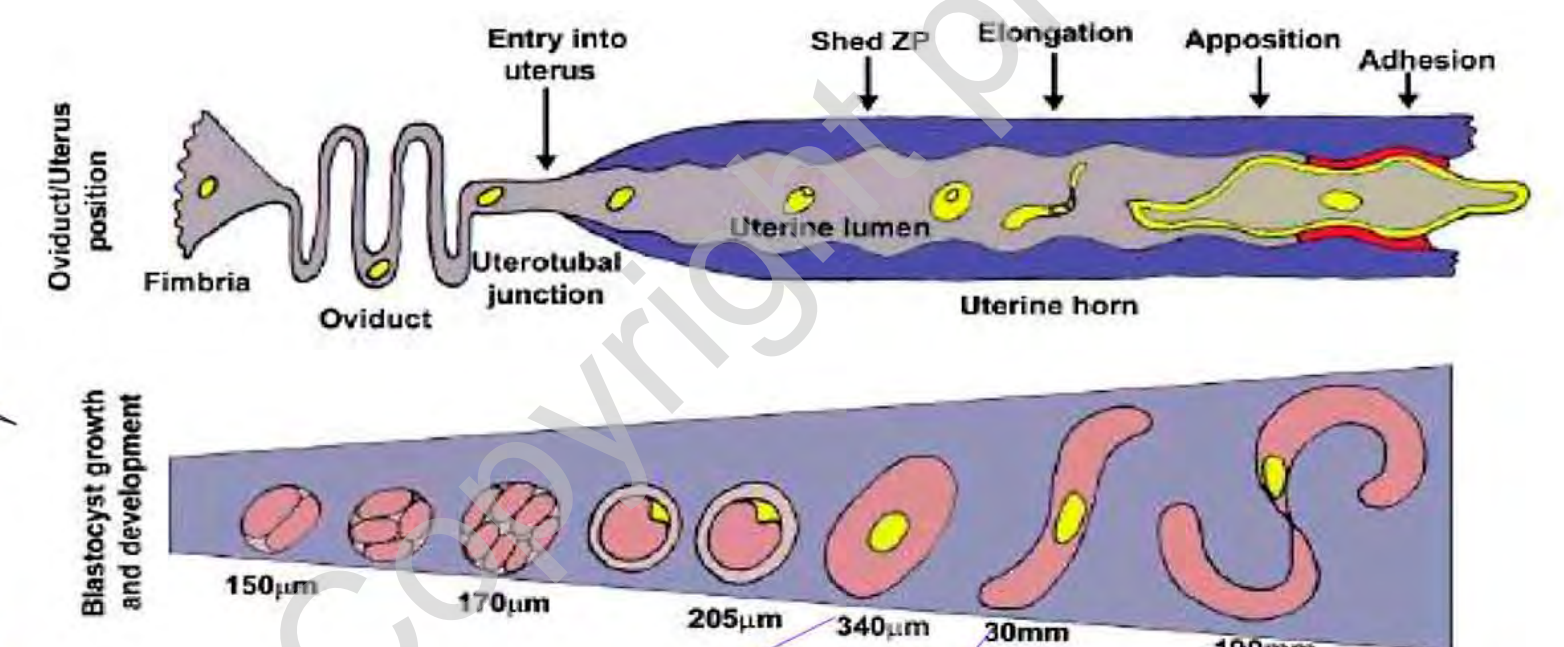
Aim:

Our purpose is to develop a mathematical model which can explain the essential mechanisms underlying the bovine trophoblast morphogenesis and can thereby contribute to our understanding of regulation in early embryo development. We are particularly interested in how molecular events and physical constraints interact to control the transition of spherical blastula to an elongated cigar-shaped trophoblast.

The trophoblast

- ✓ The first epithelial tissue which appears during animal embryogenesis
- ✓ The original tissue of the placenta
- ✓ Trophic tissue: Get oxygen and nutrients for the embryo before uterus embedding
- ✓ Rapid growth: From one cell (almost 30 micrometer) to about one million of cells (almost 20 centimeters) in a period of 21 days
- ✓ Undergoes a remarkable shape change from spherical to tubular to filamentous shape

The trophoblast Development Process



How are the embryo stages of development distributed?

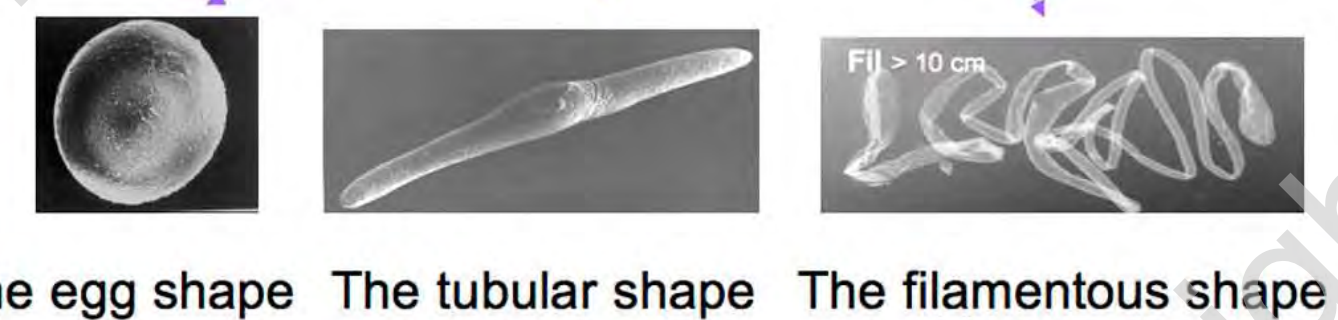
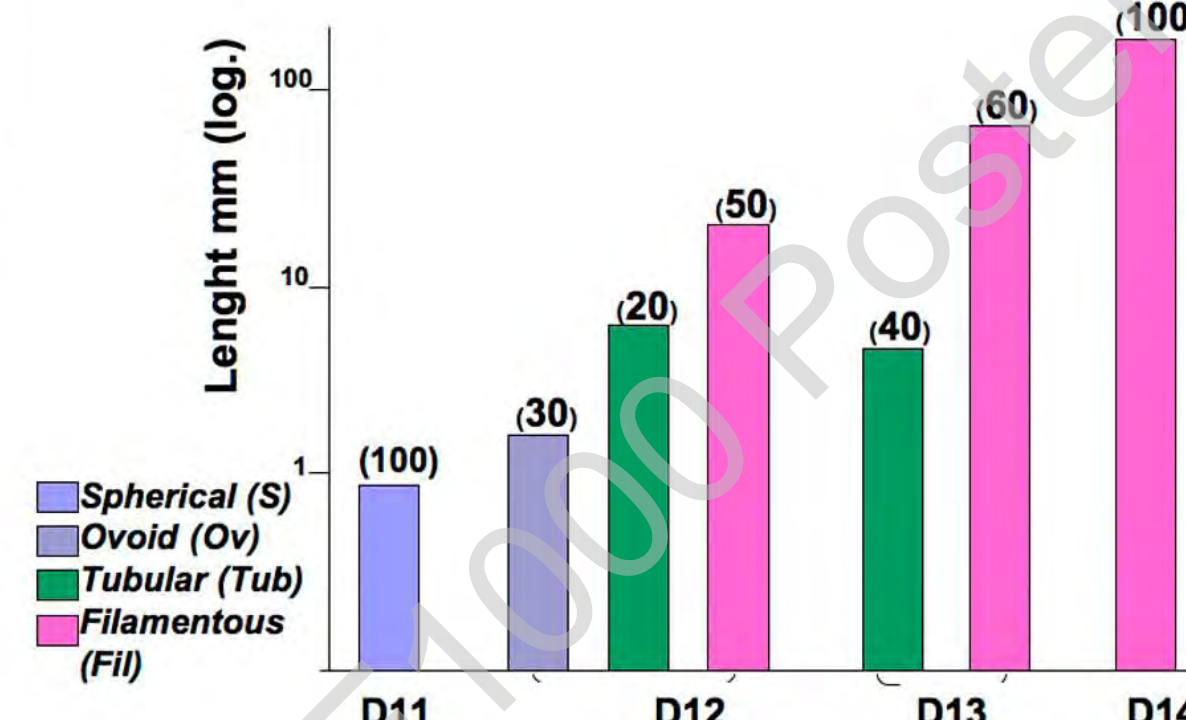
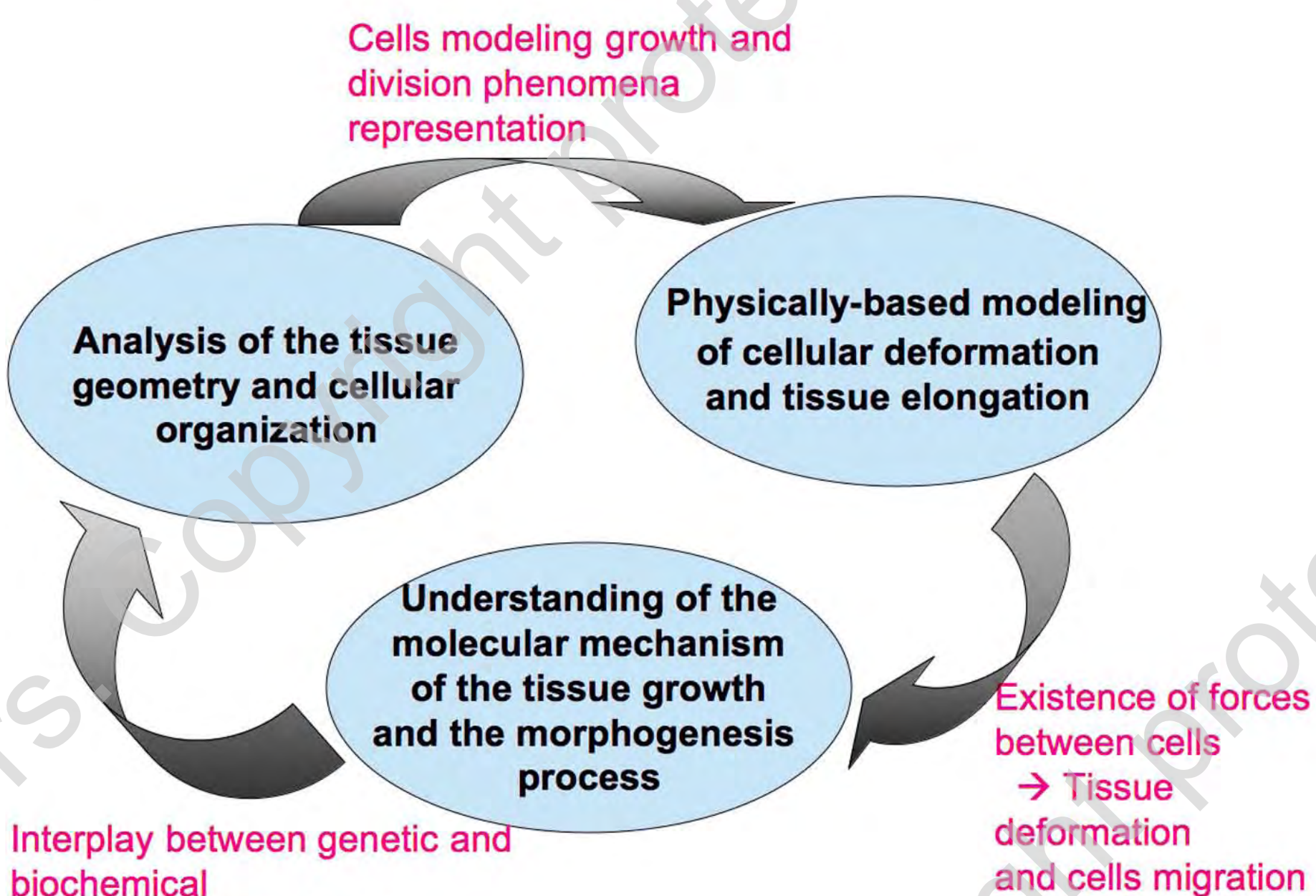


Image analysis: Morphological & textural analysis

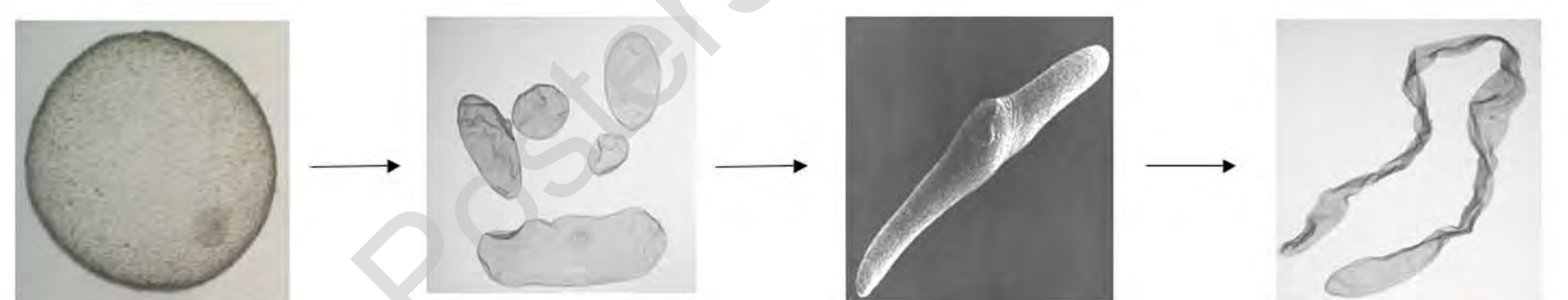


Interplay between genetic and biochemical elements on one hand and physical constraints in shape formation

Existence of forces between cells → Tissue deformation and cells migration

Modeling & simulations

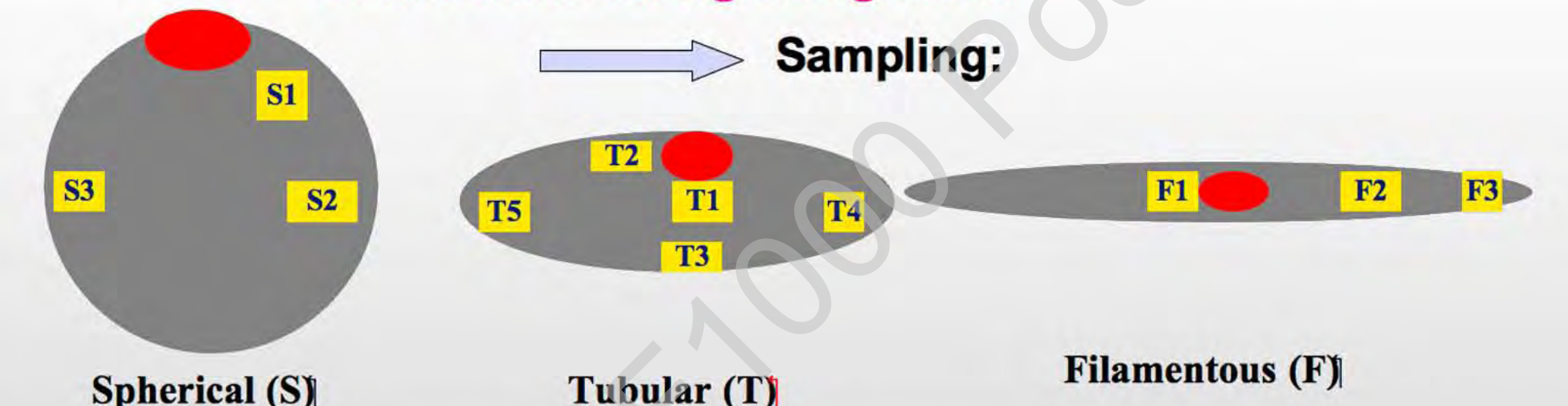
$$\underbrace{\Gamma_{cm} v_i}_{\text{friction with the environment}} + \underbrace{\sum_{innj} \Gamma_{ij} (v_i - v_j)}_{\text{friction between cells}} = \underbrace{f_i(t)}_{\text{random motion}} + \underbrace{\sum_{innj} F_{ij}}_{\text{rep-attract. forces}}$$



First preliminary simulations of the trophoblast at different stages of development based on C++ programming and using the force-based model. The asymmetry is due to the hypothesis of a preferred direction in cells division and movement.

Collaborations: François Graner, Michel Guillomot, Ignacio Ramis-Conde, Alain Trubuil

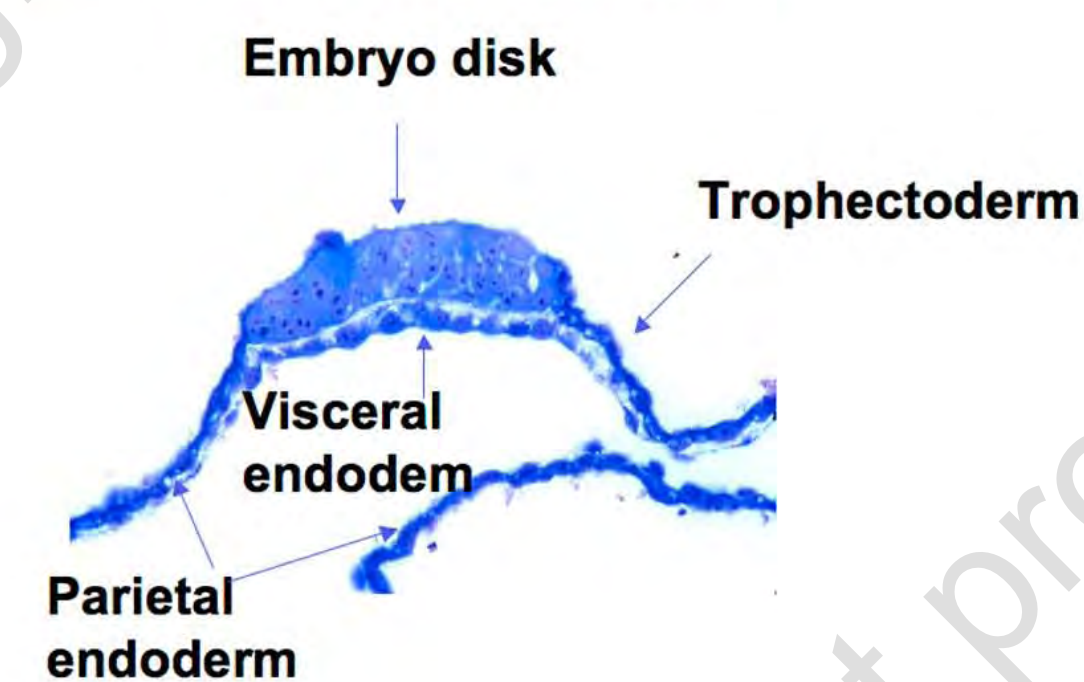
Do the trophoblast cells have a specific shape or direction during elongation?



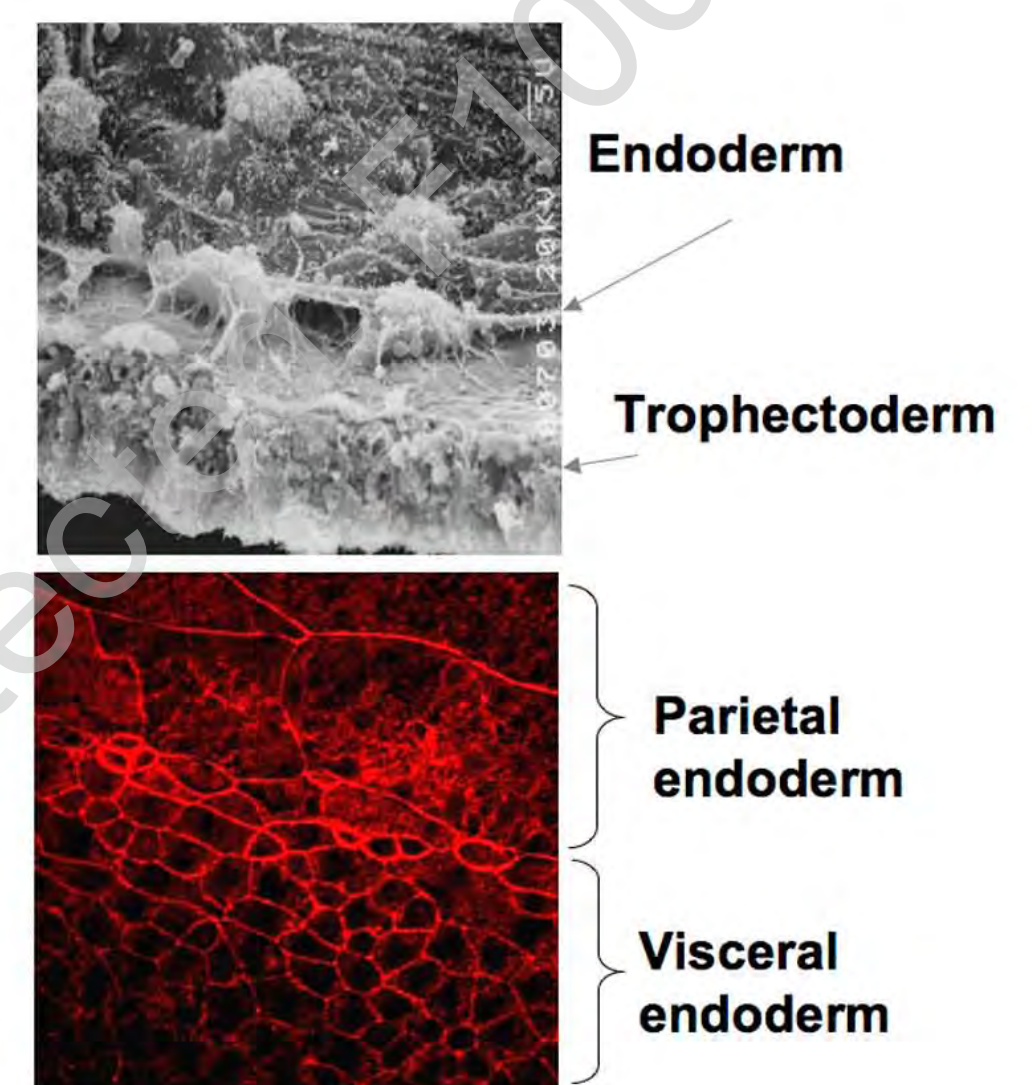
Results:

1. Cells size within a sample changes a lot & most of cells look like hexagon
2. Cells orientation is random
3. Although, the tissue has an elongated shape, trophoblast cells organization is very isotropic

Transverse section through the embryonic area of an ovoid conceptus



The trophoblast is a mononucleated epithelial tissue and the endoderm is a plurinucleated one



Bovine embryos