Tissue Development and Morphogenesis Modeling: A Case Study for Bovine Trophoblast Growth

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The project aim

Understand the development of

the trophoblast : a special tissue in animal embryogenesis

The Trophoblast

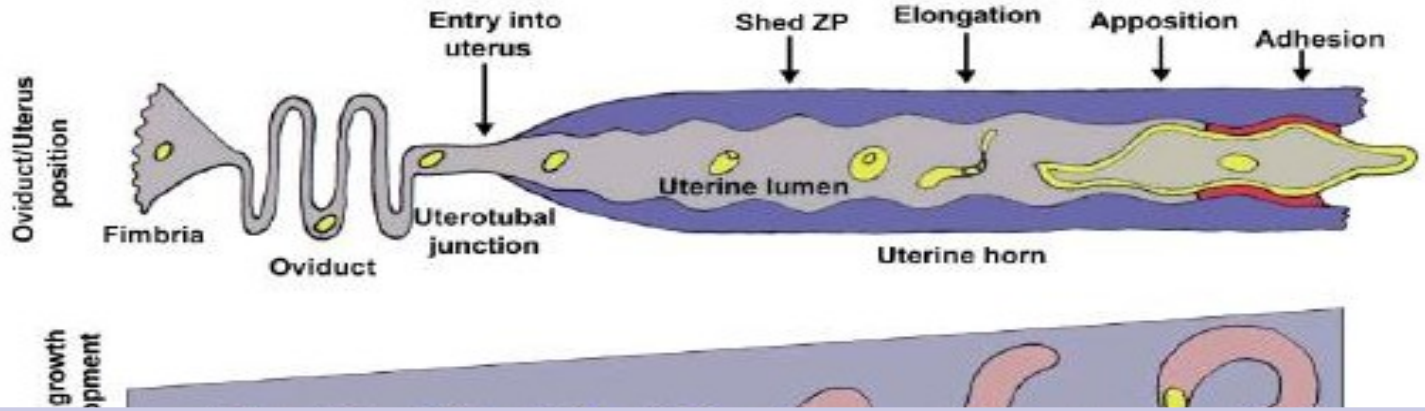
1) The first epithelial tissue which appears during animal embryogenesis

2) The original tissue of the placenta

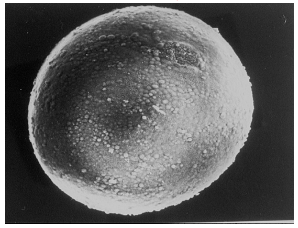
3) Trophic tissue: Get oxygen and nutriments for the embryo before it embeded into the uterus

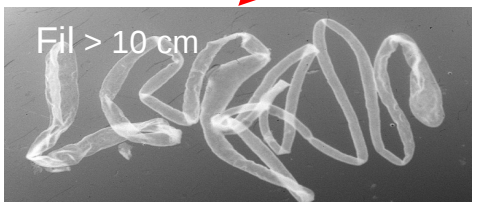
4) Rapid growth: From one cell (almost 30 micrometer) to about one million of cells (almost 20 centimeters) in a period of 21 days

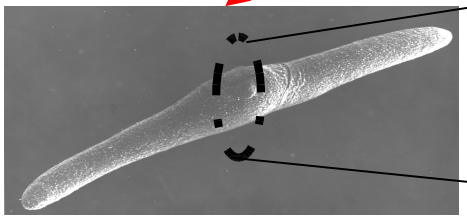
5) The development of the trophoblast is very similar to that of the tumor. First, they develop very fast, and after a fast growth phase, they need to implant into a mother tissue to survive and to develop

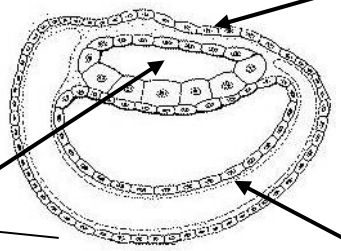


How do physical forces interplay with the molecular elements to regulate the development process?

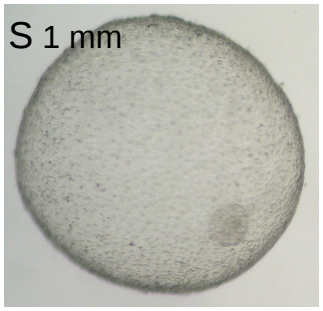


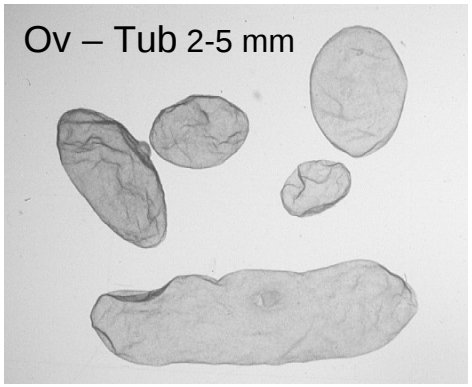


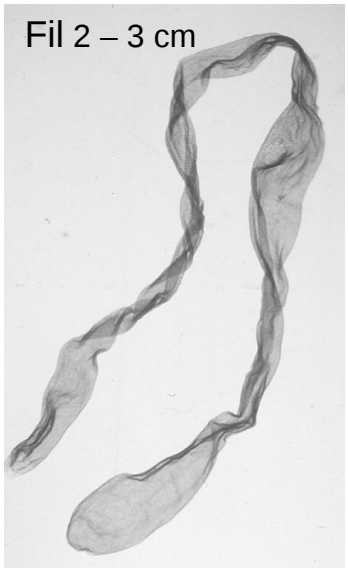


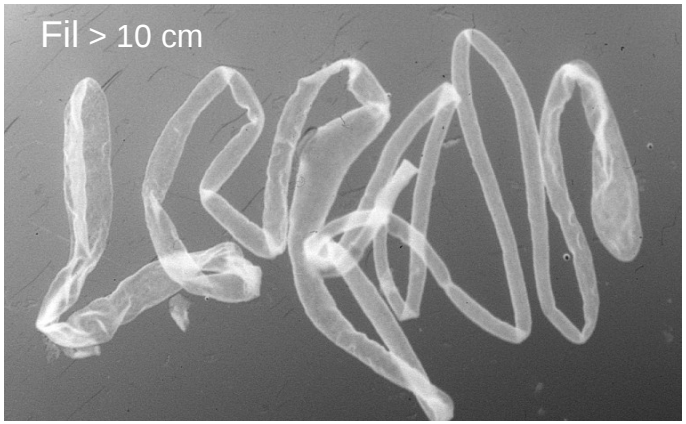


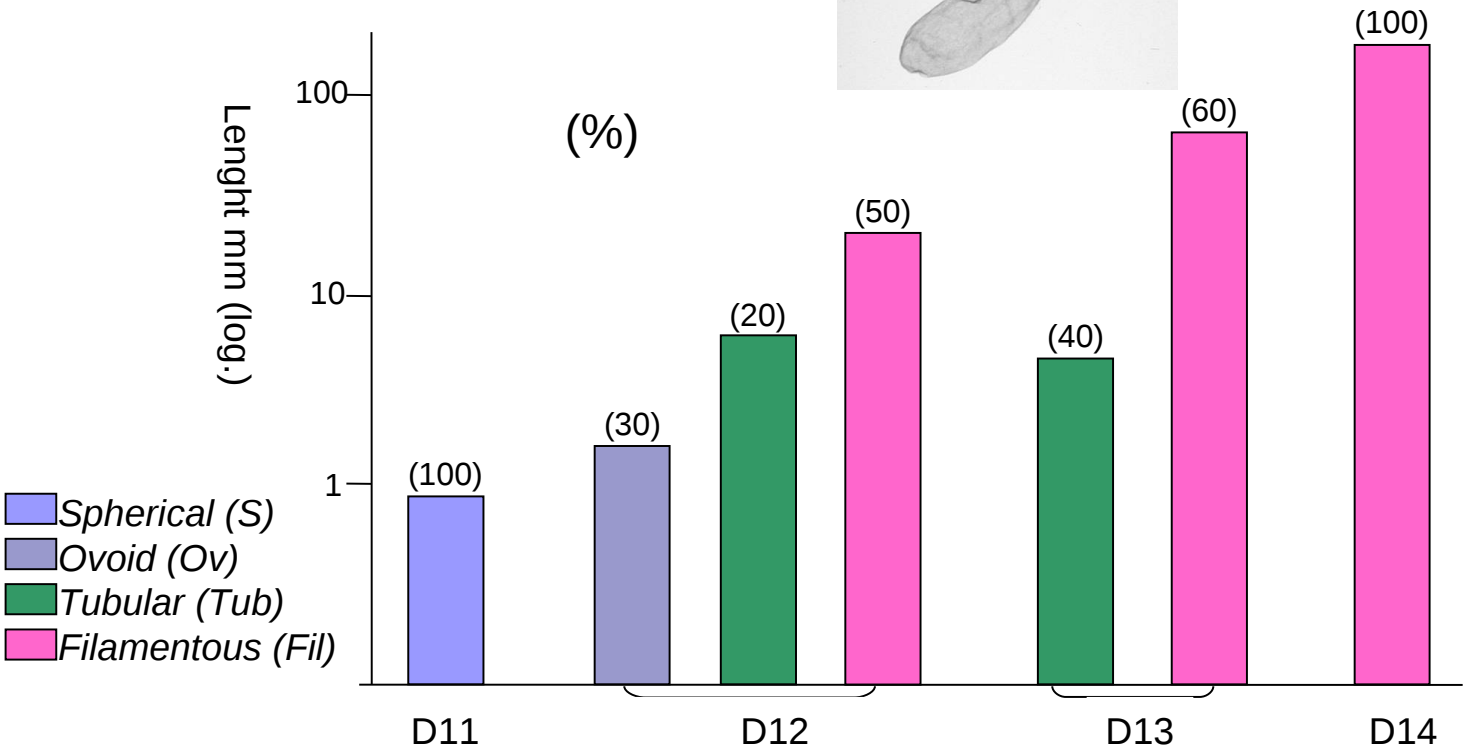
Elongation stages of the ovine conceptus (Days 11 – 14)



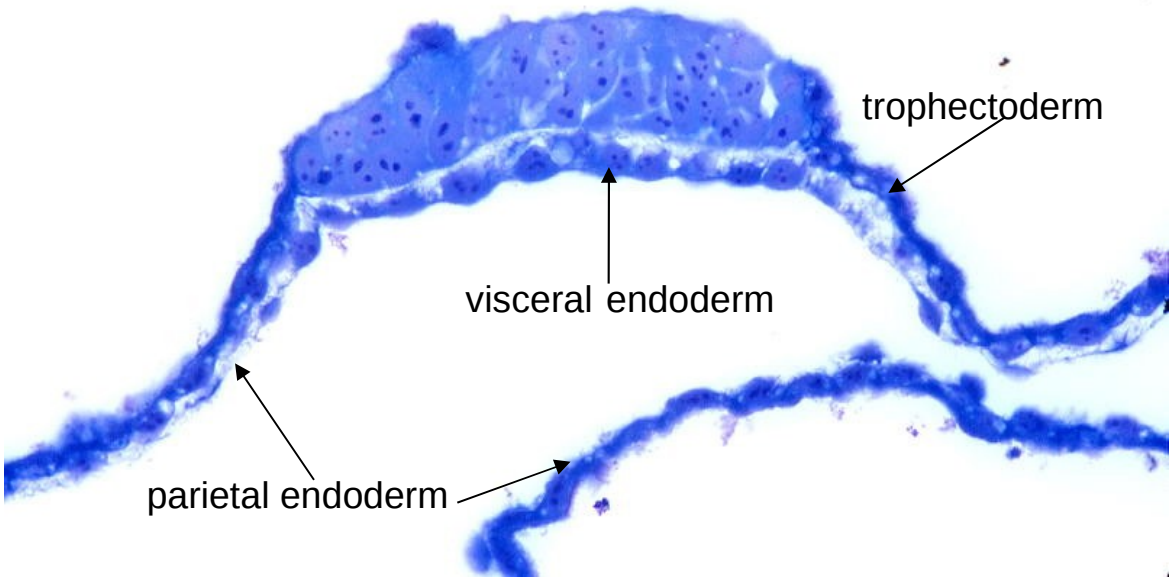






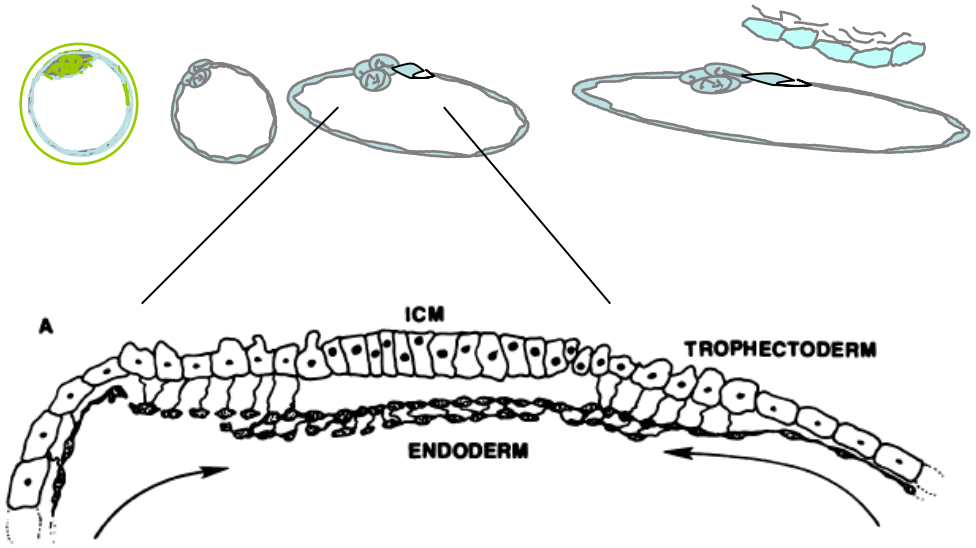


The conceptus and the endoderm differentiation



Transverse section through the embryonic area of an ovoid conceptus

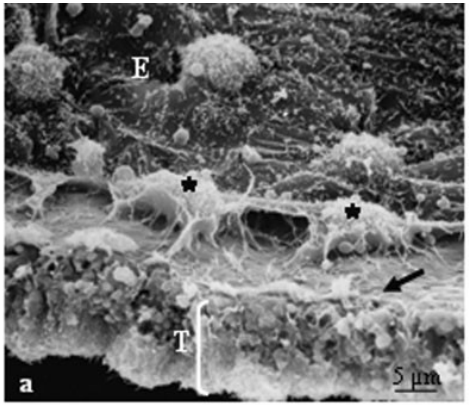
ov tub fil



4 shapes: S, O, T, F

S: 150 µm, 250-300 cells
O: 5-10 mm, 3-5000 cells
T: 5-10 cm, > 10^4 cells
F: 15-30 cm, > 10^6 cells

S to F transition within 2 weeks



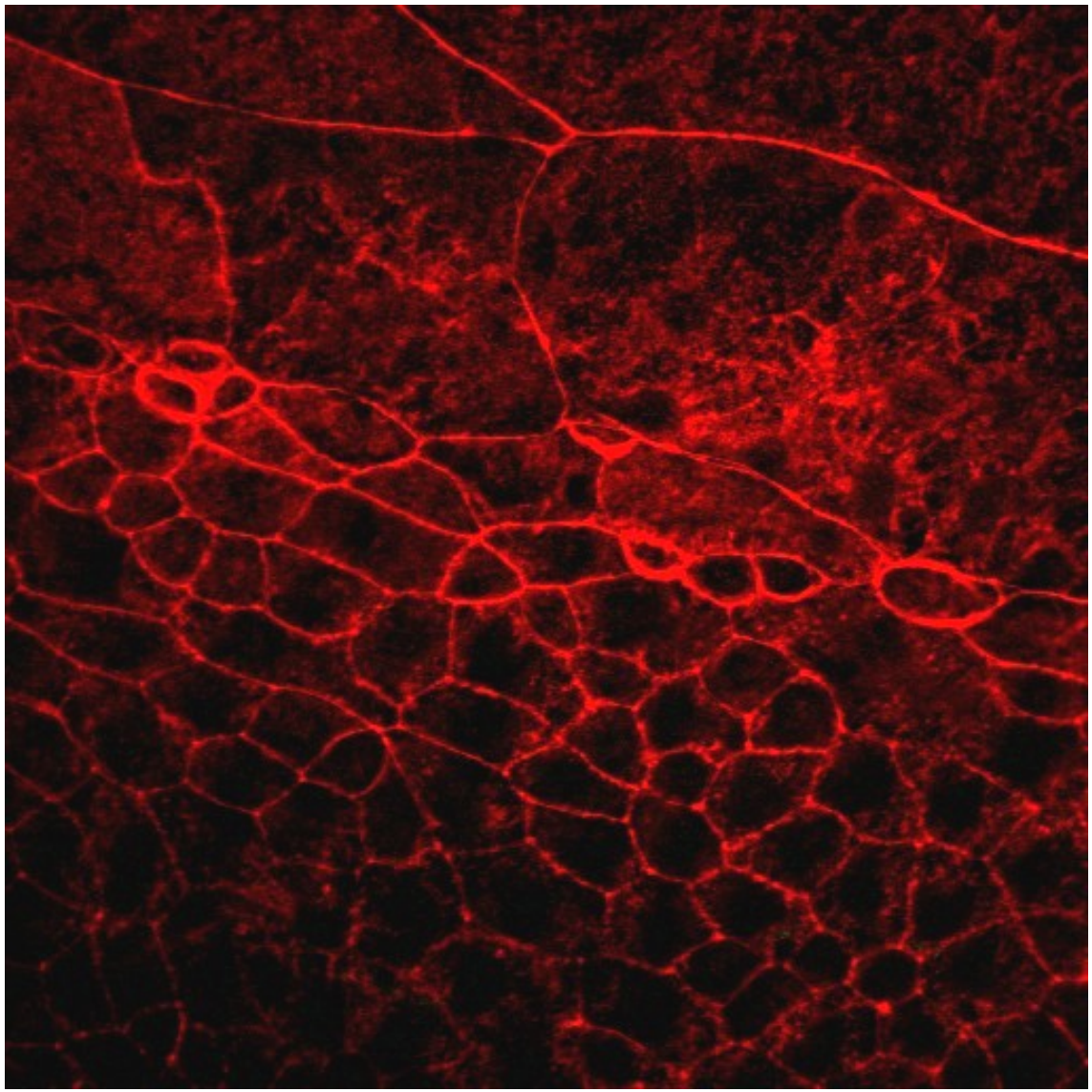
E

T

2 cell layers: T and E
= 2 epithelia
2 cell morphologies
2 cell shapes
2 cell sizes

Endoderm

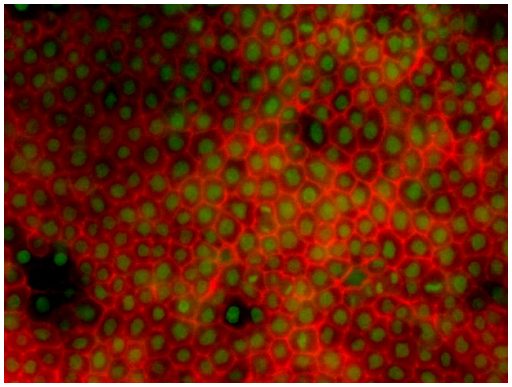
Inner face of the Embryonic area



parietal endoderm

visceral endoderm

Actin stained by rhodamin-conjugated Phalloïdin

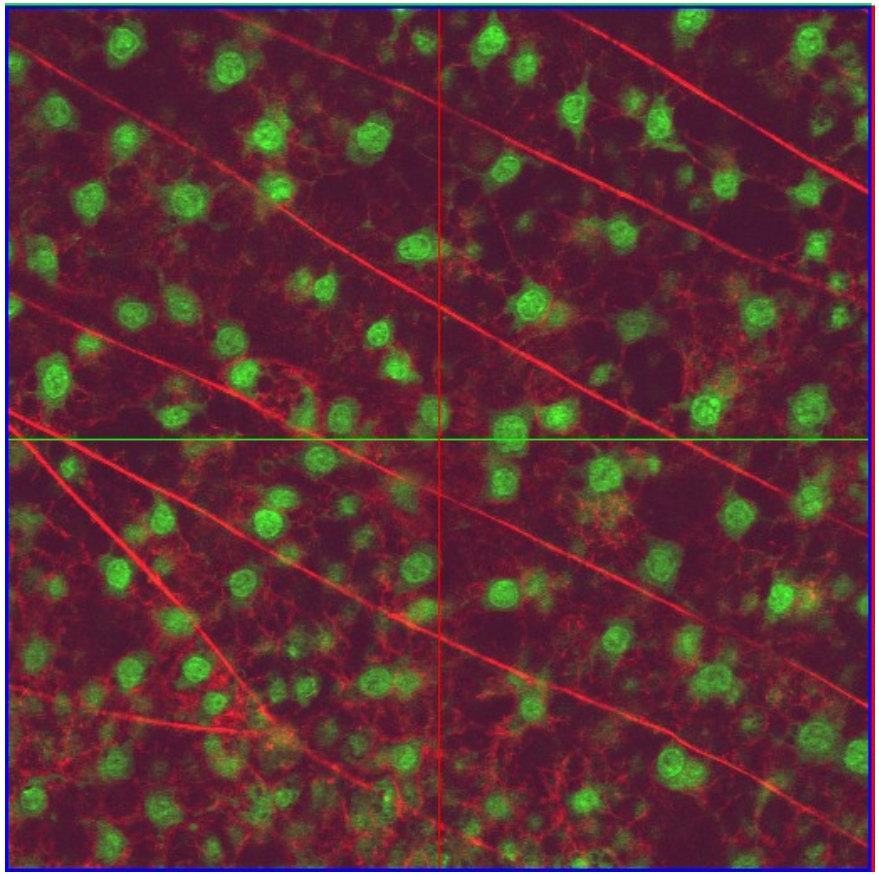


Endoderm: marked anisotropy at T and F stages and at specific places within the tissue

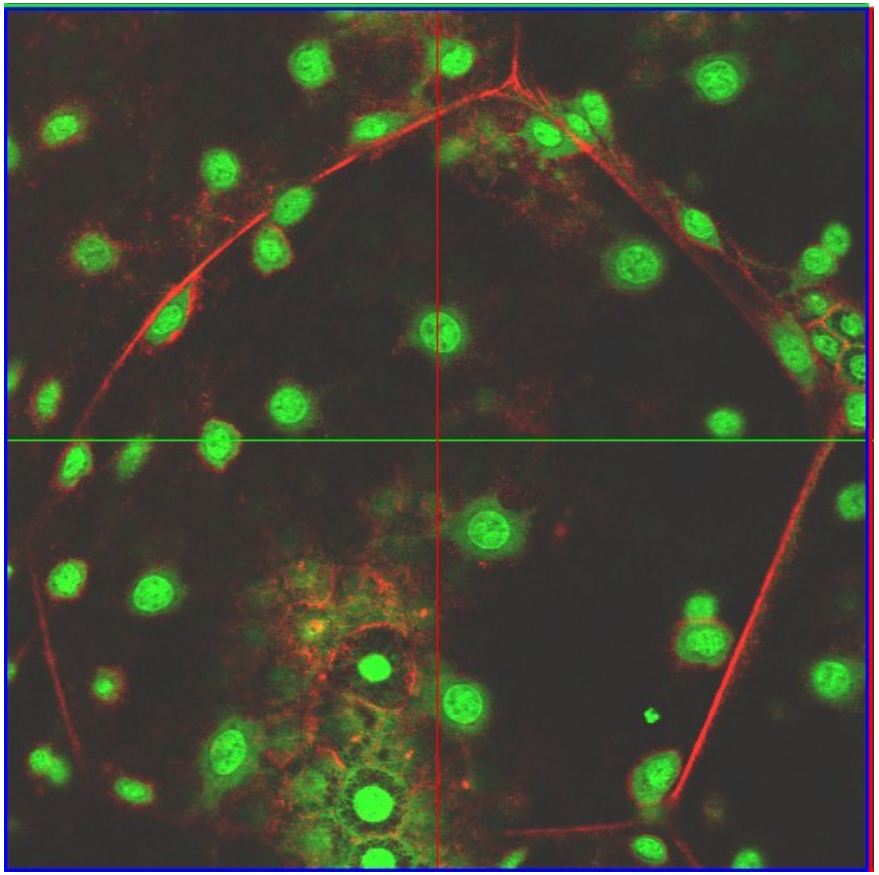
Trophectoderm

Parietal endoderm

Middle part of the conceptus



Tip of the conceptus



Actin: rhodamin-phalloidin

Nuclei: YOPRO

Parietal endoderm segregates from the visceral endoderm and forms a specific structure.

Parietal endoderm cells:

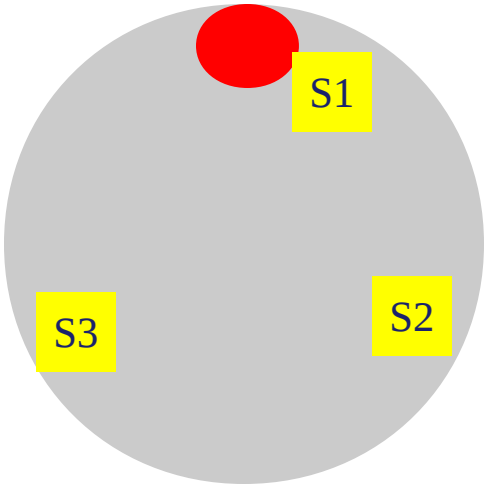
- Become plurinucleated but retain an epithelial phenotype
- Elongate parallel to the long axis of the conceptus
- Have specific functions (secrete the ECM components)

1) Do the transformations of the parietal endoderm drive the elongation process of the conceptus?

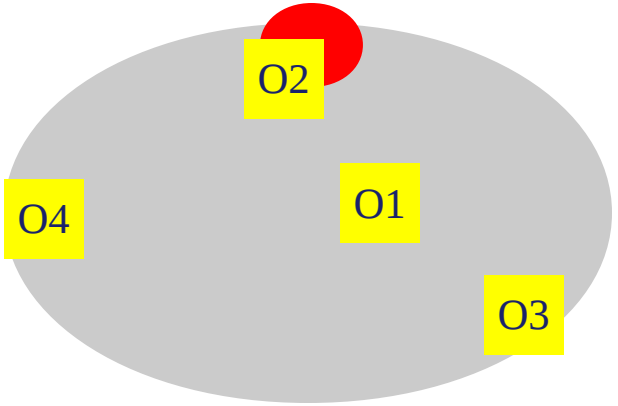
2) Do the trophoblast cells have a specific shape or direction during elongation?

3) Does the cells plan of division lead to the elongation process?

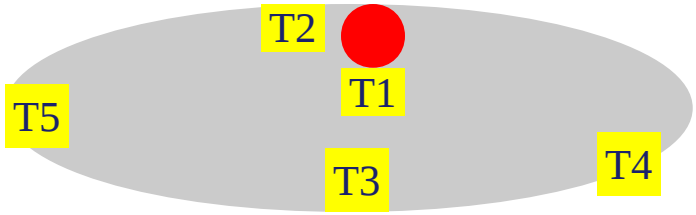
Sampling



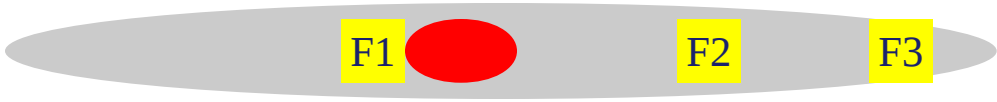
Spherical (S)



Ovoïd (O)

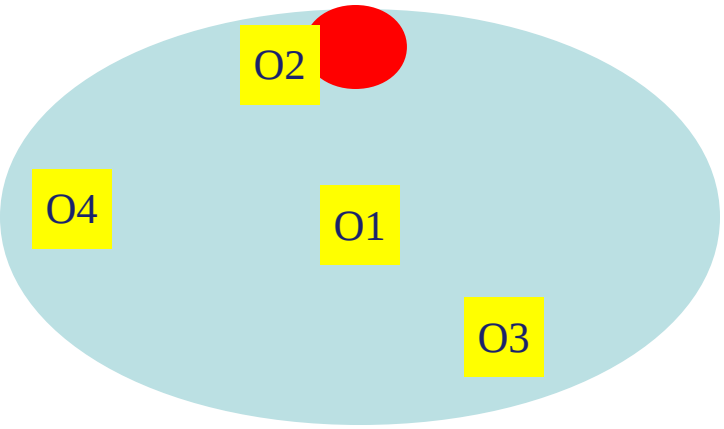


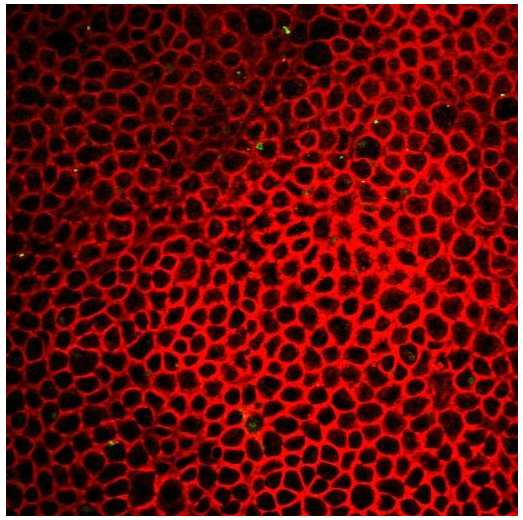
Tubular (T)

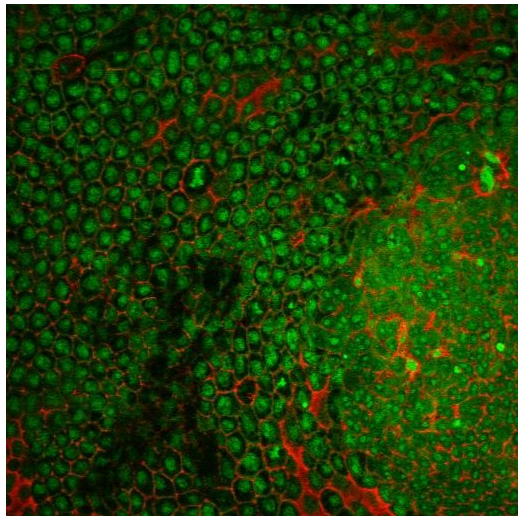


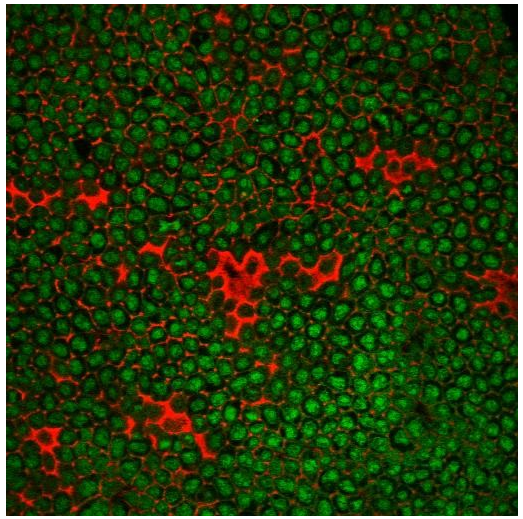
Filamentous (F)

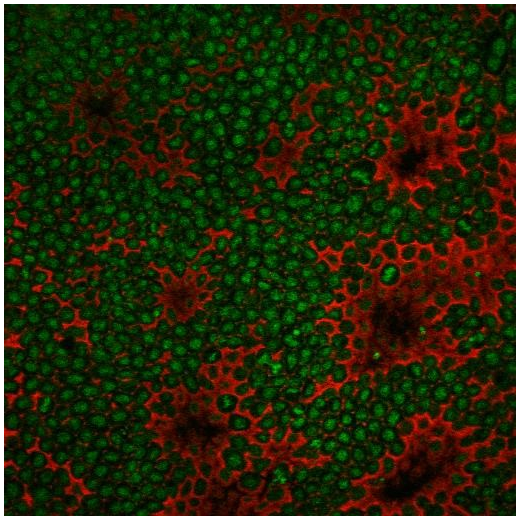
Ovoïde Stage







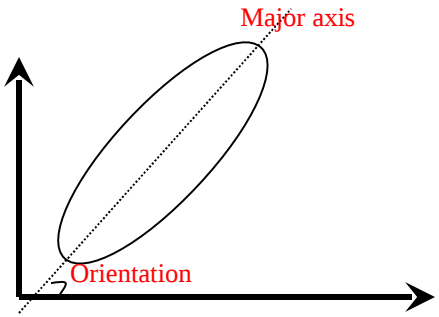


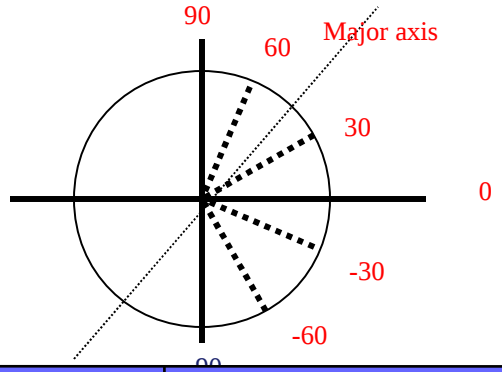


1) O1: 14/03/07, Scaling: 0.63 micron, 22ALa, Slice: 5
2) O2: 06/04/07, Scaling: 0.63 micron, L21b, Slice: 20
3) O3: 06/04/07, Scaling: 0.63 micron, L21d, Slice: 21
4) O4: 06/04/07, Scaling: 0.63 micron, L22a, Slice: 25

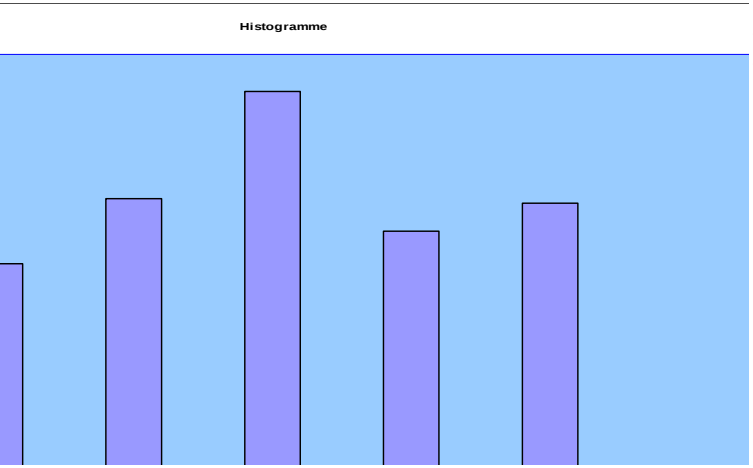
Morphological analysis of cells

Descriptors**:** Position, surface, Perimeter, major axis, minor axis, Orientation, Elongation, Convexity, Nbr of neighbors



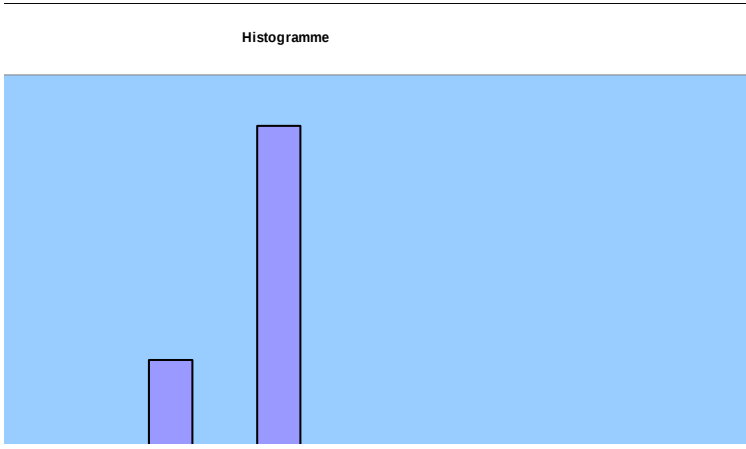


	Surface	Elongation	Convexity	Perimeter	Major axis	Minor axis
Mean	156.58250	0.567502	0.952026	47.7810328	15.9478439	12.7667
Median	152.013	0.579052	0.953202	47.2315	15.6976	12.6232
Standard Deviation	39.923763	0.137412	0.014693	6.48602637	2.24018252	1.78159



Distribution of cells orientation

Distribution of cell neighbours



Conclusions

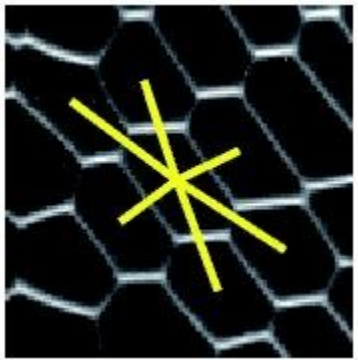
1) Cells size within a sample changes a lot

2) The mean value of cells size is relatively stable from a position to another and from a stage of development to another

3) Cells orientation is random

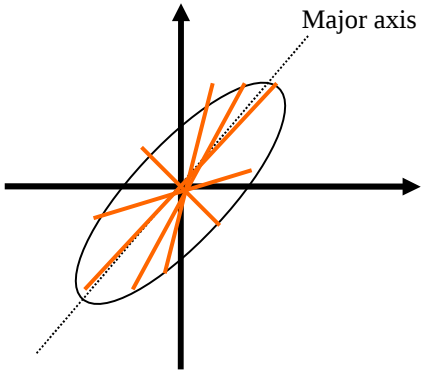
4) Most cells have 5, 6, or 7 neighbors

Texture analysis of cells
(F. Graner, I. Bonnet, Institut Curie, Paris)

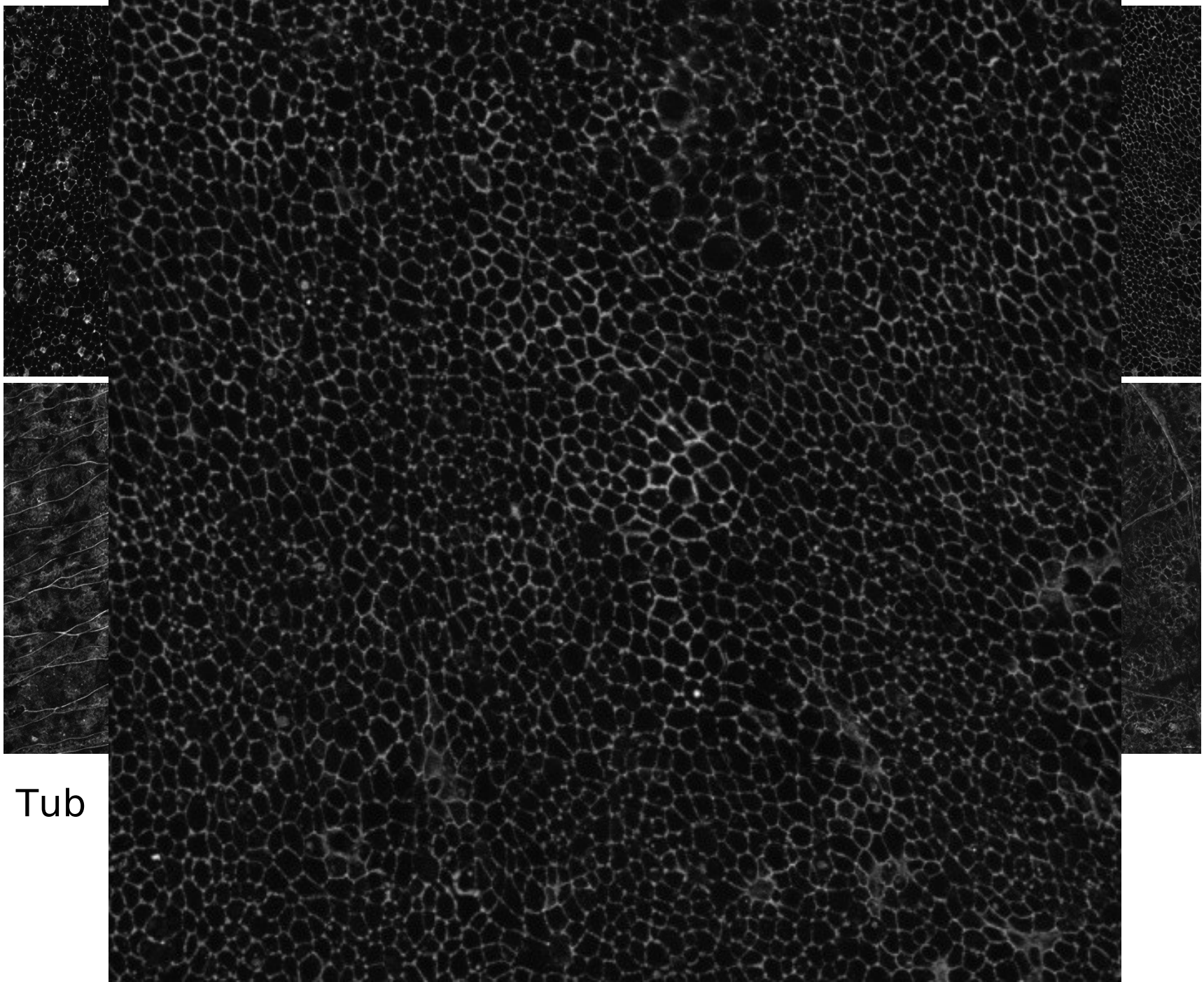


The tissue pattern anisotropy is given by:

$$\alpha = 1 - \frac{\lambda_2}{\lambda_1}$$



S1	S2	S3	O1	O2	O3	O4	T1	T2	T3	T4	T5	F1	F2	F3
0.09	0.02	0.12	0.04	0.13	0.03	0.08	0.04	0.07	0.18	0.06	0.09	0.2	0.14	0.08



Tub

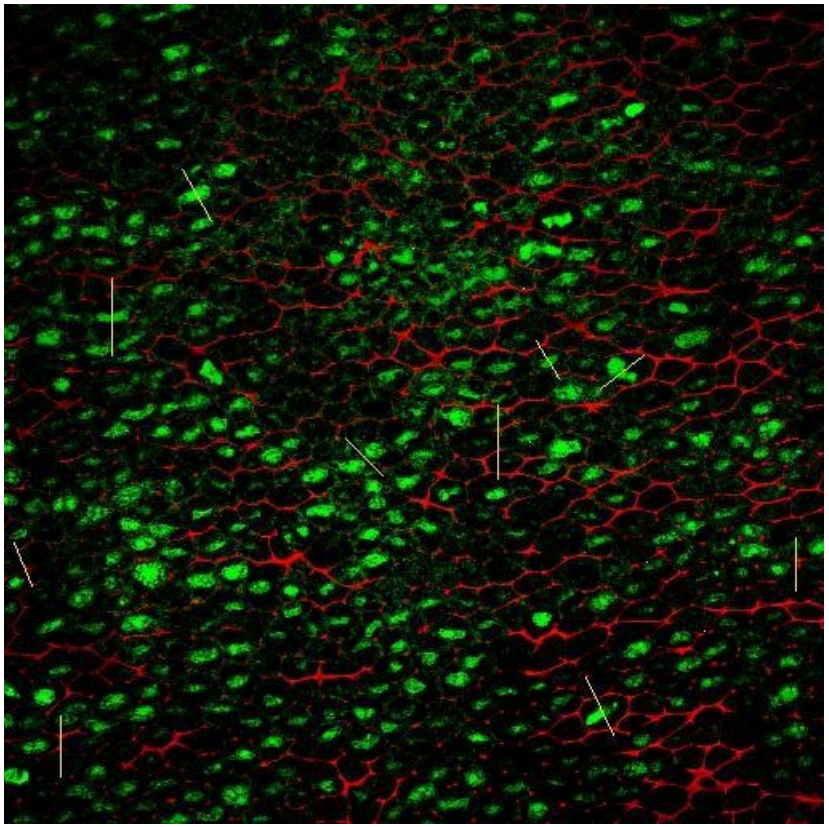
Conclusions

1) Although, the tissue has an elongated shape, cells organization is very isotropic. The same tools have been applied on the Drosophila tissue, and they found that the cellular organization of Drosophila tissue is very anisotropic.

2) The analysis show that the trophoblast elongation is not at all due to cells geometrical deformation or to cells stretching as the case for the drosophila.

3) We think that elongation might be the consequence of cell addition associated with peculiar plans of cell division or intercalation.

Plans of division



Hypothesis

The elongating parietal endoderm cells might exert a mechanical tension onto the proliferating trophoblast and drive it along the elongation axis, this probably added to the existence of specific plans of division.

Force-based model

- Cell is not subject to external forces, then it undergoes a random walk

Langevin equation:

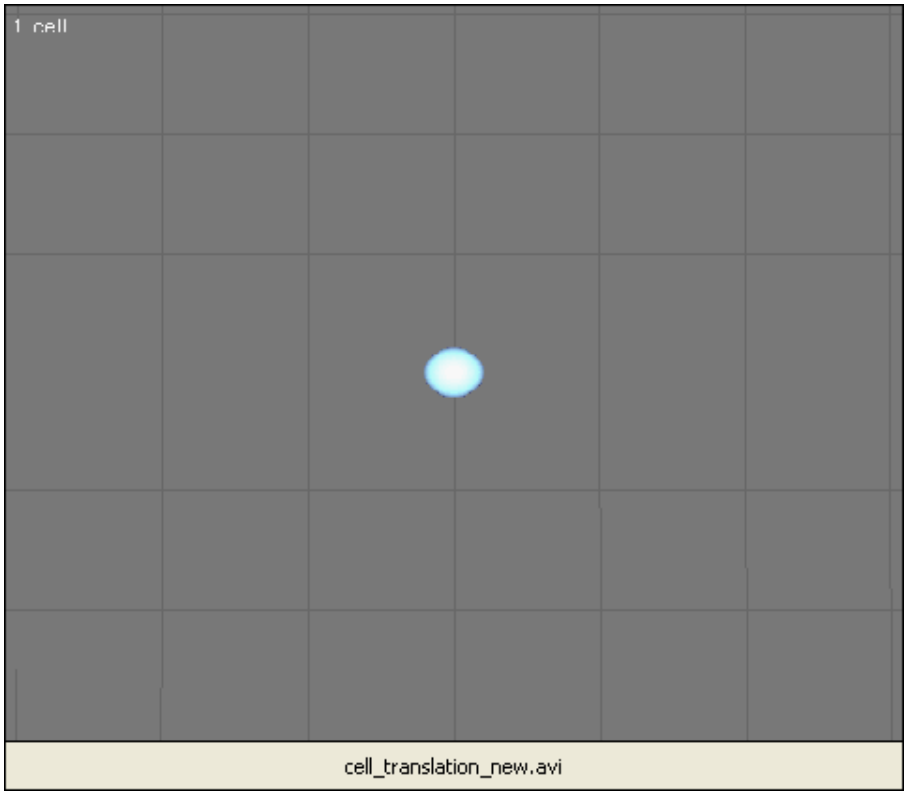
$$\frac{\partial p_i}{\partial t} = M \frac{\partial v_i}{\partial t} = f_i(t)$$

- Interaction with external environment and cells neighbours

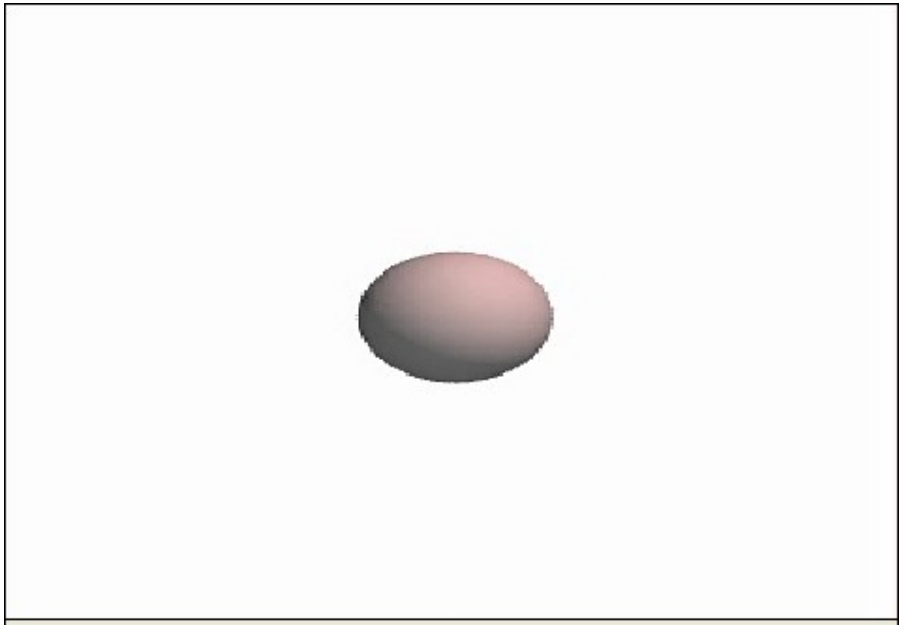
Equation of motion:

$$\Gamma_{cm} v_i + \sum_{innj} \Gamma_{ij} (v_i - v_j) = f_i(t) + \sum_{innj} F_{ij}$$

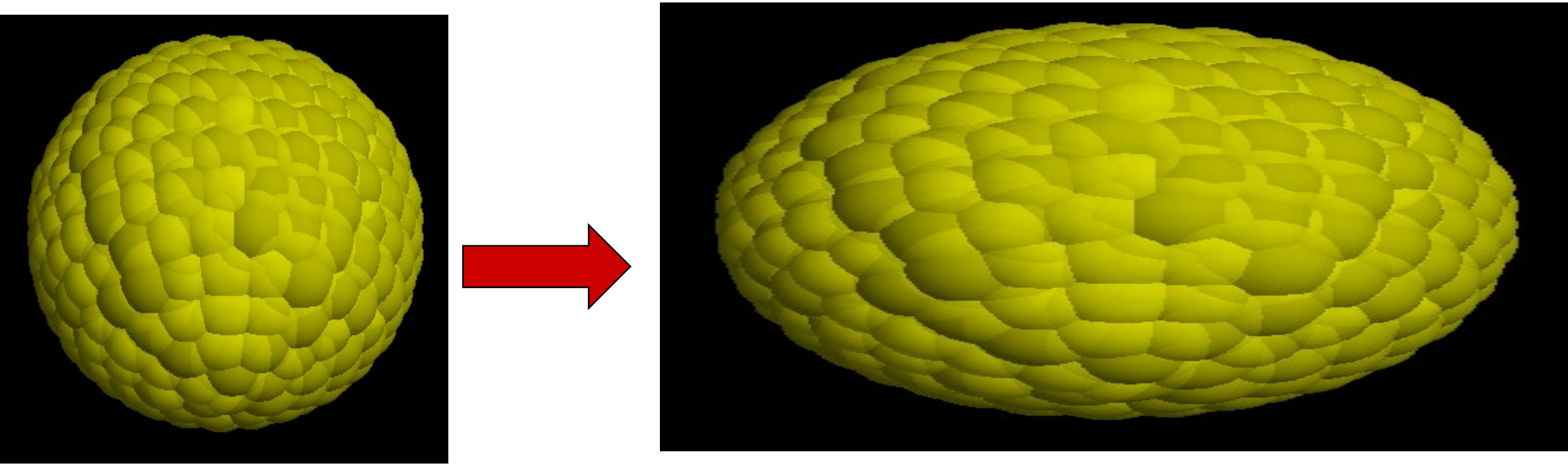
Cell migration



Cells growth and cells division



Simulation



Thanks

- Many thanks to Michel Guillomot and Severine Degrelle who provide us with images from the confocal microscopy in INRA, BDR.

- Thanks to Christophe Richard who provides us with cow embryos in Bressonviliers farm.