In silico modelling of embryogenesis

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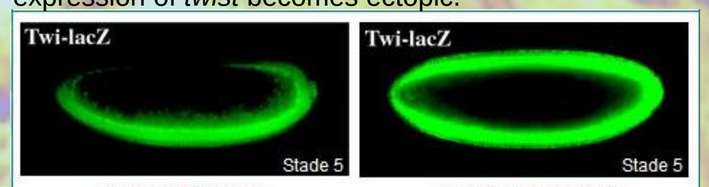
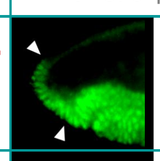
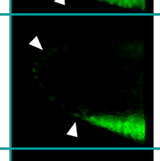
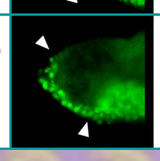
Context

Embryogenesis is an amazing choreography of highly regulated cells movements. The genetic programme drives these processes through the expression of developmental genes. But recent experiments of Emmanuel Farge's team have demonstrated that, in Drosophila Melanogaster, the mechanical constraints due to tissue deformation induces gene expression. Is this phenomenon an exception or a general mechanism of morphogenetic self regulation ? To address this second hypothesis, it is necessary to integrate the biomechanical behaviour of the tissue in response to specific active deformations through the whole embryo.

The *twist* gene is a master regulator of embryo morphogenesis. It is involved in active cell deformations and in anterior gut track formation.
In artificially deformed embryos, the (normally ventral) expression of *twist* becomes ectopic.

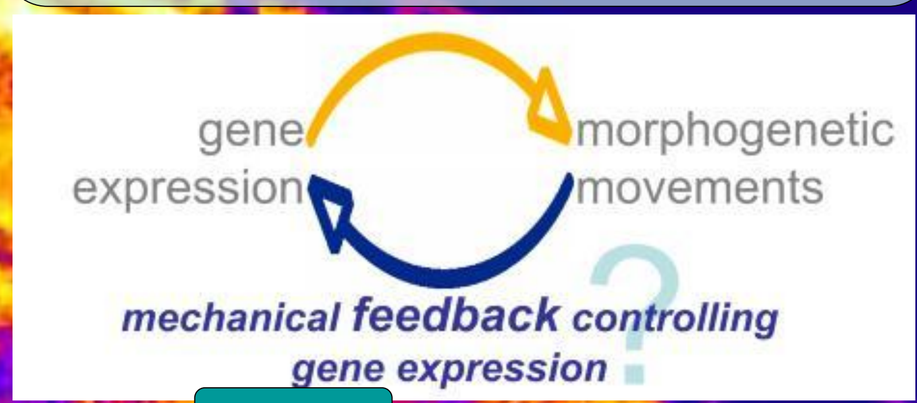


	Movements	*twist* expression	
Case 1 (Wild-type)	+ Native		+ Strong
Case 2 (BNT mutant)	- Genetically disrupted		- Low
Case 3 (BNT mutant)	+ Mechanically rescued		+ Strong

The anterior pole *twist* gene expression is lost in a mutant where morphogenetic movements are disrupted, and can be restored by an artificial compression with a needle. Farge E., Current Biology, 2003

The project

The research project consists in generating a biomechanical *in silico* multi-cellular model of the whole Drosophila embryo at earliest stages of development, including the active differential shape morphing of cells.

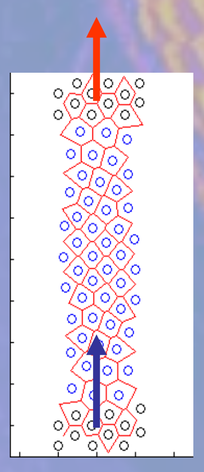


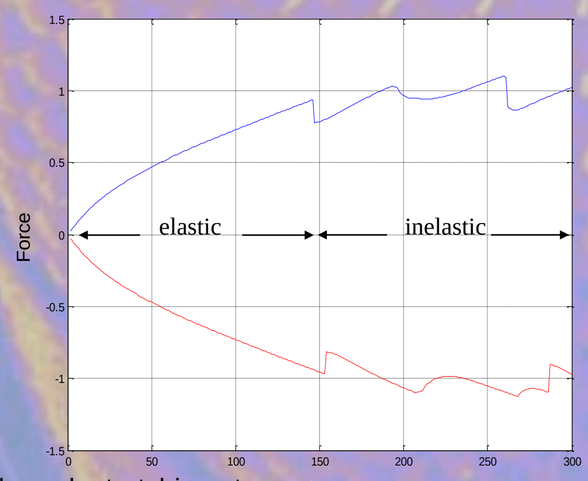
What for ?

-To investigate the rheology of an epithelium
-To mark out the active cell movements from the passive responsive ones
-To predict and quantify the correlation between gene expression and tissue deformations
-To suggest other possible mechanically driven processes
-To realize the first *in silico* embryo

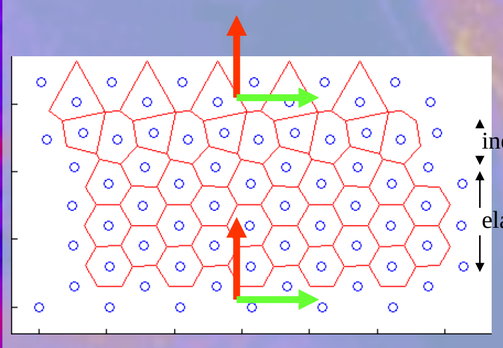
Rheological Studies

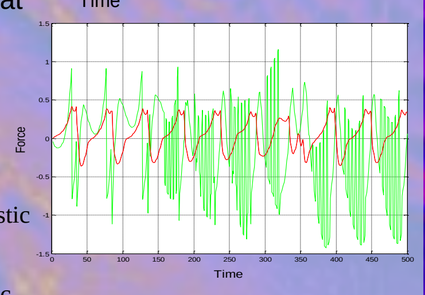
To investigate biomechanical properties of early Drosophila embryo, I first designed a simple model of cells in a two dimensional tissue. Its numerical simulation shows basic properties of an epithelium: elasticity at low deformation and inelasticity at strong deformation that leads to complex fluid behaviour at large time scale.

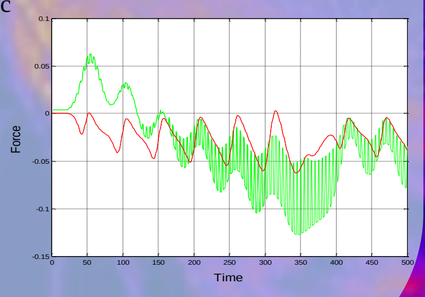




Visco-elastic properties through stretching at constant speed.

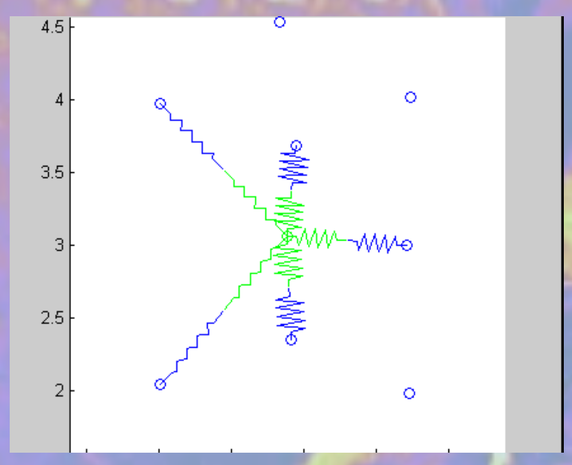






Visco-elastic properties through sheer stress at constant speed on a cylinder.

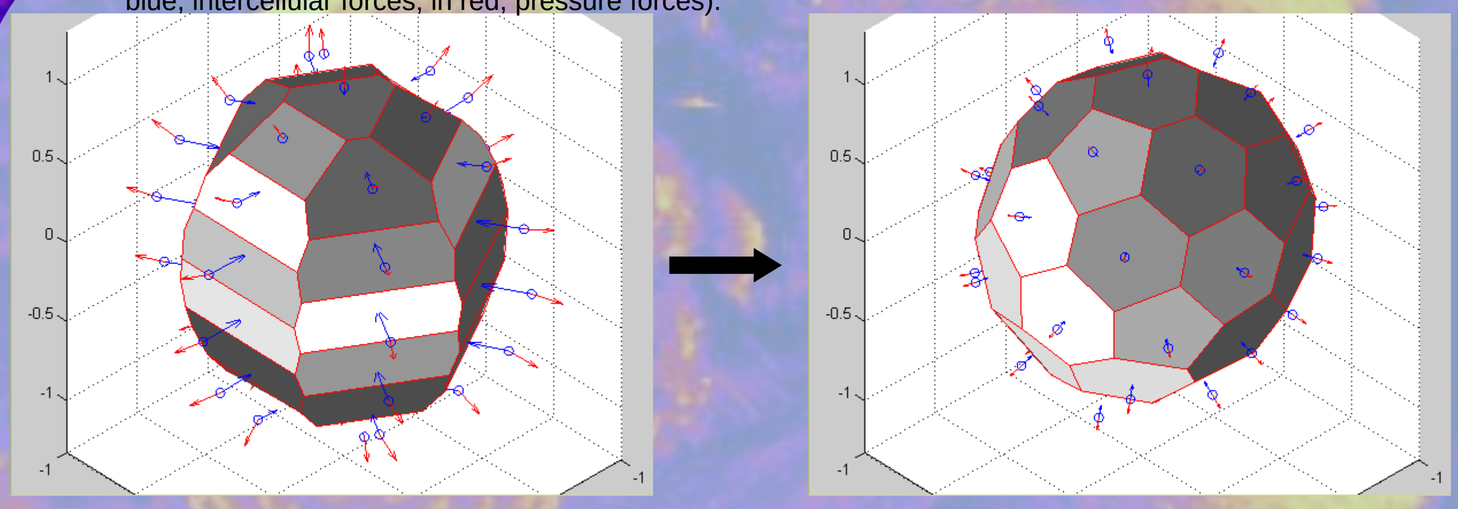
The Fluid Cell Model



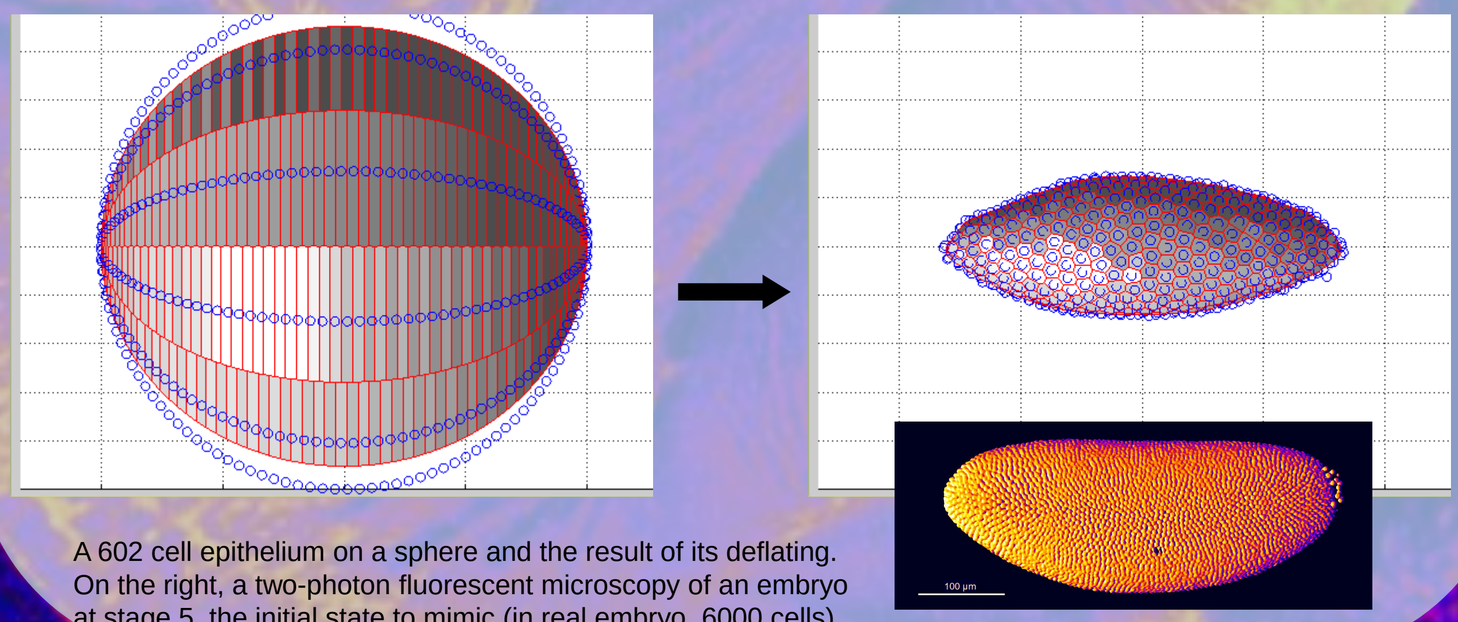
It consists in a centre of interaction and springs radiating from it in the direction of the centres of interaction of neighbour cells. The neighbours of a cell can change because of geometrical rules dealing with interface surface. Unlike previous attempts to model living tissues, this one favours the cell as the base element, and so sticks to living matter where cell is the unit bridging bio molecular processes and macroscopic behaviour.

The Making of an Embryo

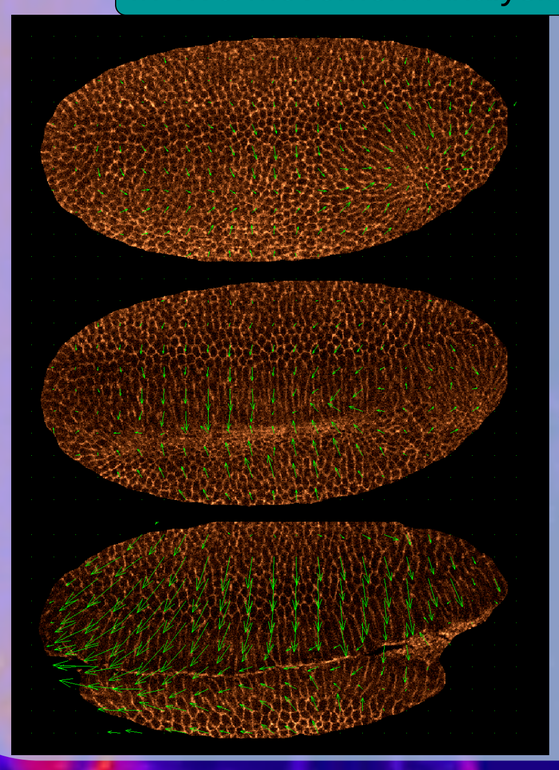
A 38 cell epithelium on a sphere and its relaxation at constant volume through surface reorganisation (in blue, intercellular forces; in red, pressure forces).



A 602 cell epithelium on a sphere and the result of its deflating. On the right, a two-photon fluorescent microscopy of an embryo at stage 5, the initial state to mimic (in real embryo, 6000 cells).



In vivo Movement Analysis



Whence making experimental science, one must confront with experimental data. Here three snapshots of a two-photon fluorescent microscopy film of a zoom of one of the first morphogenetic events, the invagination of the ventral furrow, and the measure of the displacement field visualised with green arrows. The film itself is an extraction of 2D slices tangent to the embryo surface from 3D stacks.

Next Steps

-Thickening of the tissue to model three dimensional cells;
-Implementation of the motors of the morphogenetic movements at the scale of the cells;
-*In silico* morphogenesis simulation;
-Comparison with *in vivo* morphogenesis and optimisation of model parameters;
-Understanding the mechano-genetic interplay and self-organisation.