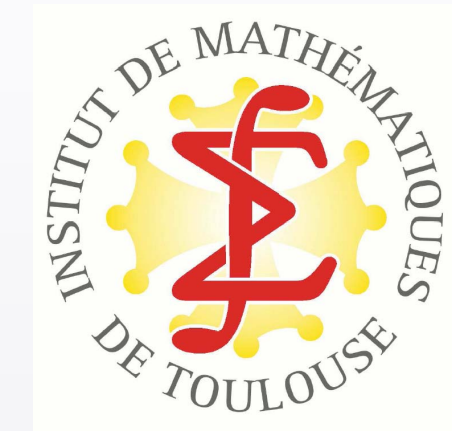# Mathematical modeling of embryo axis elongation
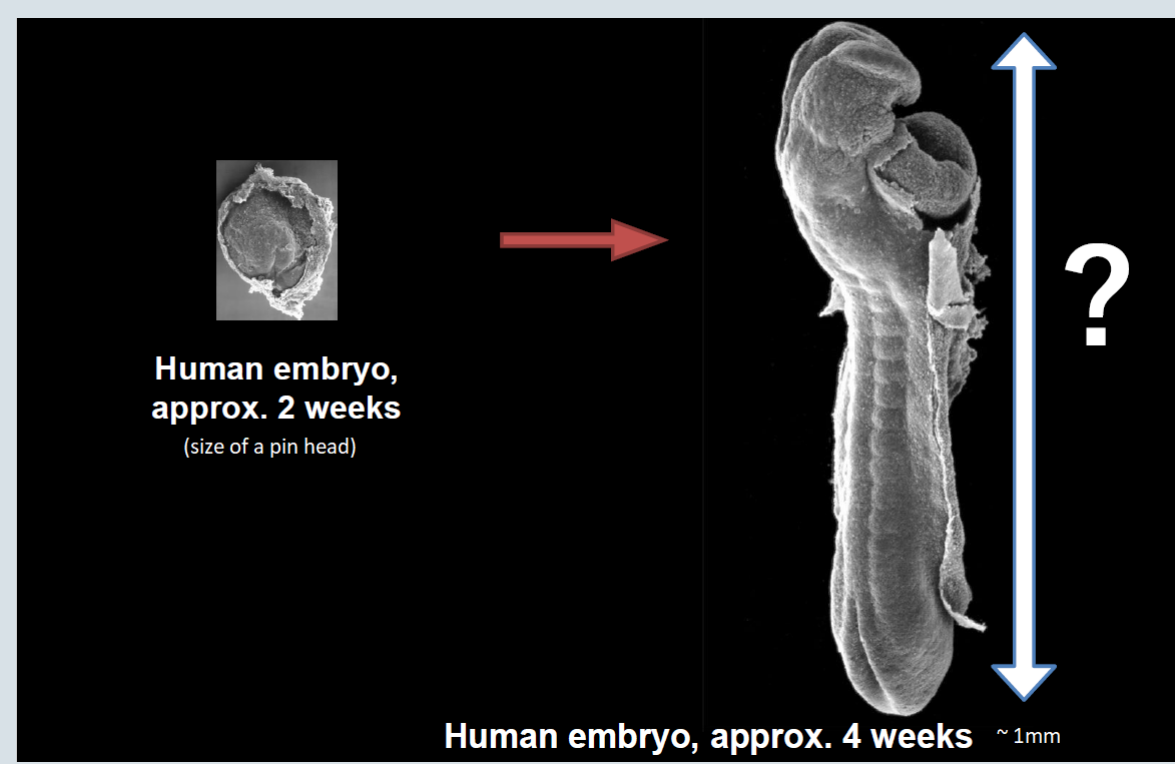
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Supervisors: Ariane Trescases (IMT) and Bertrand Bénazéraf (CBI)

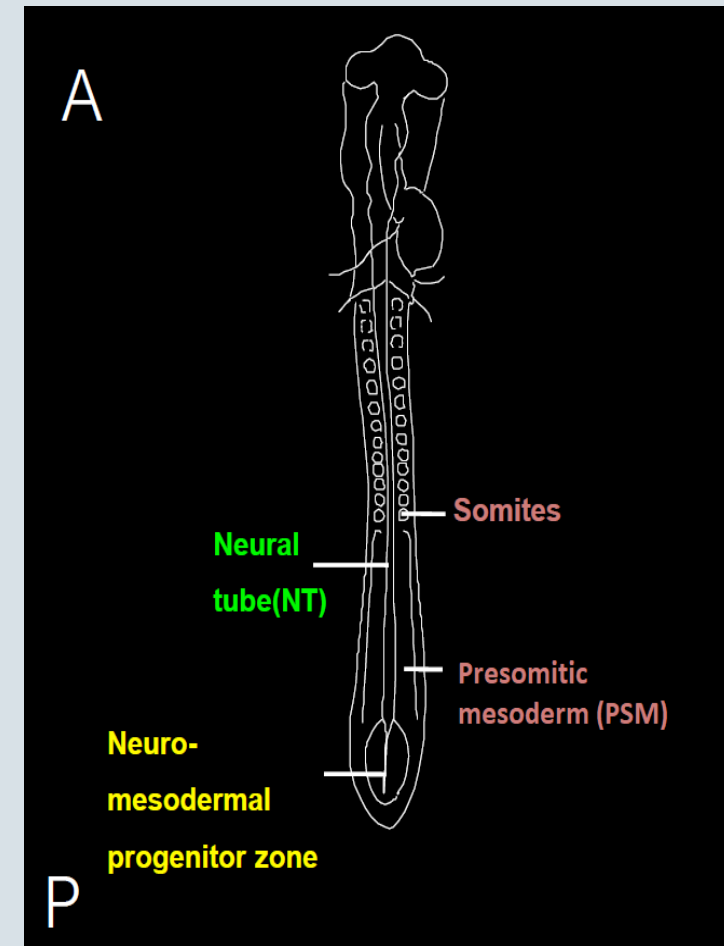## 1 – Introduction to the biological model

During embryonic development thousands of cells self-organize in a very precise and complex choreography to form the tissues and the future adult organs.

Human embryo development

Coordination between:

- Cellular proliferation
- Migration
- Adhesion
- Addition of new cells

Different tissues involved in bird development

How is this coordination contributing to the rise of mechanisms causing elongation?

2 – The viscous two species model

Consider the densities n_1 and n_2 of two cell populations in each tissue. Each tissue is endowed with a viscosity coefficient β_1 and β_2, a proliferation rate G_1 and G_2, a mechanical pressure $p_\epsilon = \epsilon \frac{n_1+n_2}{1-(n_1+n_2)}$, and a repulsion term $q_m = \frac{m}{m-1}((1+n_1 n_2)^{m-1}-1)$, and v_1, v_2 the velocities of each tissue which follow the Brinkman law:

$$\partial_t n_1 + \nabla \cdot (n_1 v_1) + \alpha \nabla \cdot (n_1 \nabla (\Delta n_1)) = n_1 G_1(p_1), \tag{1}$$

$$\partial_t n_2 + \nabla \cdot (n_2 v_2) + \alpha \nabla \cdot (n_2 \nabla (\Delta n_2)) = n_2 G_2(p_2), \tag{2}$$

$$p_1 = p_\epsilon(n_1+n_2) + n_2 q_m(n_1 n_2), \tag{3}$$

$$p_2 = p_\epsilon(n_1+n_2) + n_1 q_m(n_1 n_2), \tag{4}$$

$$-\beta_1 \Delta v_1 + v_1 = -\nabla p_1 \tag{5}$$

$$-\beta_2 \Delta v_2 + v_2 = -\nabla p_2 \tag{6}$$

with α a regularizing parameter (avoid bubble effect), ϵ and m parameters of the pressure laws.

3 – The free boundary problem: $\alpha \to 0$, $m \to \infty$, $\epsilon \to 0$

Objective: Computing the incompressible limit of the viscous two-species model when $\alpha \to 0$, $m \to \infty$, and $\epsilon \to 0$.

We formally determine this limit and find the following free-boundary problem:

$$\partial_t n_1^\infty + \nabla \cdot (n_1^\infty v_1^\infty) = n_1^\infty G_1(p_1^\infty), \tag{7}$$

$$\partial_t n_2^\infty + \nabla \cdot (n_2^\infty v_2^\infty) = n_2^\infty G_2(p_2^\infty), \tag{8}$$

$$p_1^\infty = p^\infty + n_2^\infty q^\infty, \tag{9}$$

$$p_2^\infty = p^\infty + n_1^\infty q^\infty, \tag{10}$$

$$-\beta_1 \Delta v_1^\infty + v_1^\infty = -\nabla p_1^\infty \tag{11}$$

$$-\beta_2 \Delta v_2^\infty + v_2^\infty = -\nabla p_2^\infty \tag{12}$$

Moreover we have the following relation

$$p^\infty(1-(n_1^\infty+n_2^\infty)) = 0,$$

the segregation property at the limit: $n_1^\infty n_2^\infty = 0$ and the complementary relation:

$$(p^\infty)^2 \left(n_1^\infty \nabla \cdot v_1^\infty + n_2^\infty \nabla \cdot v_2^\infty \right) = (p^\infty)^2 \left(n_1^\infty G_1(p_1^\infty) + n_2 G_2(p_2^\infty) \right)$$

We define the moving domain

$$\Omega(t) = \{x \mid p^\infty > 0\} = \{x \mid n_1^\infty + n_2^\infty = 1\} \text{ a.e.} \tag{13}$$

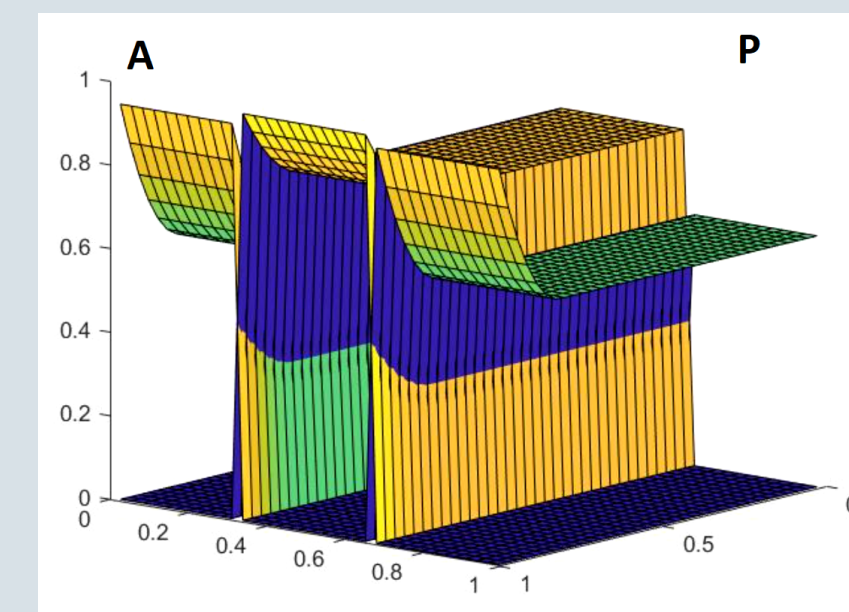Finally we get the velocities of the free boundaries and the continuity condition on the interface $\Gamma(t)$

$$V_{\partial\Omega_1(t)\cap\partial\Omega(t)} = v_1^\infty.\vec{v}, \quad V_{\partial\Omega_2(t)\cap\partial\Omega(t)} = v_2^\infty.\vec{v}, \quad \text{and} \quad v_1^\infty.\vec{\mu} = v_2^\infty.\vec{\mu} \quad \text{on } \Gamma(t)$$

with $\vec{v}$ the outward normal vector to the boundary and $\vec{\mu}$ that of the interface.
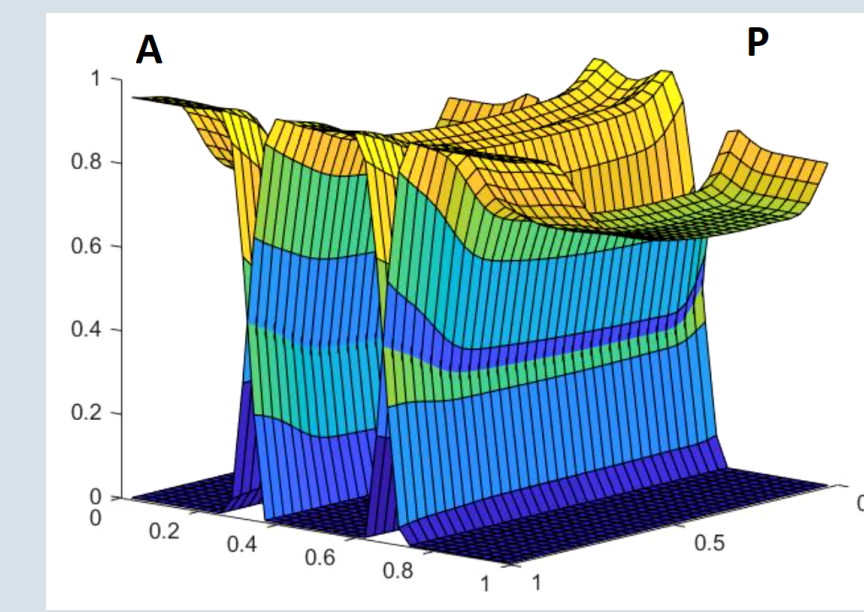
4 – Numerical Simulations

We use a 2D finite volume scheme to simulate the evolution of the densities, and the flux in each tissue:
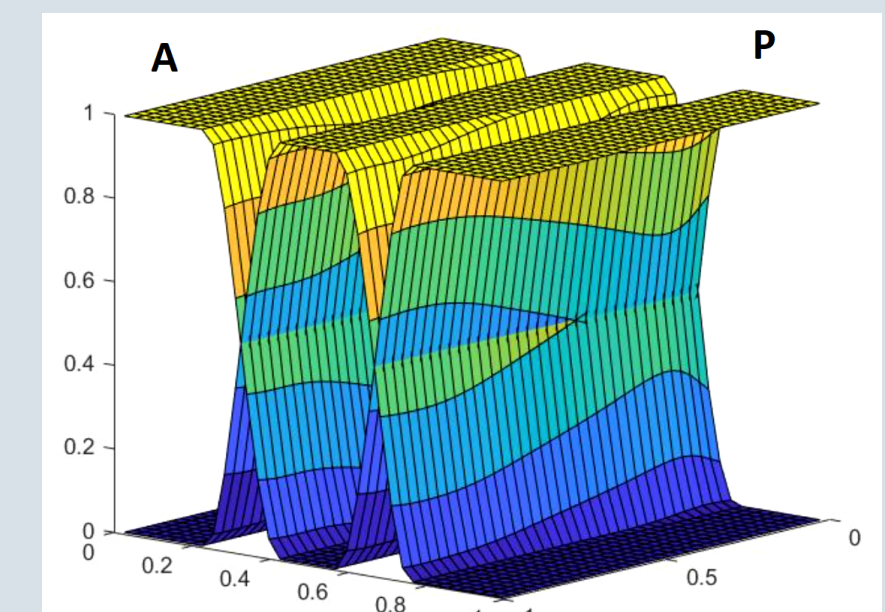
Density profile:
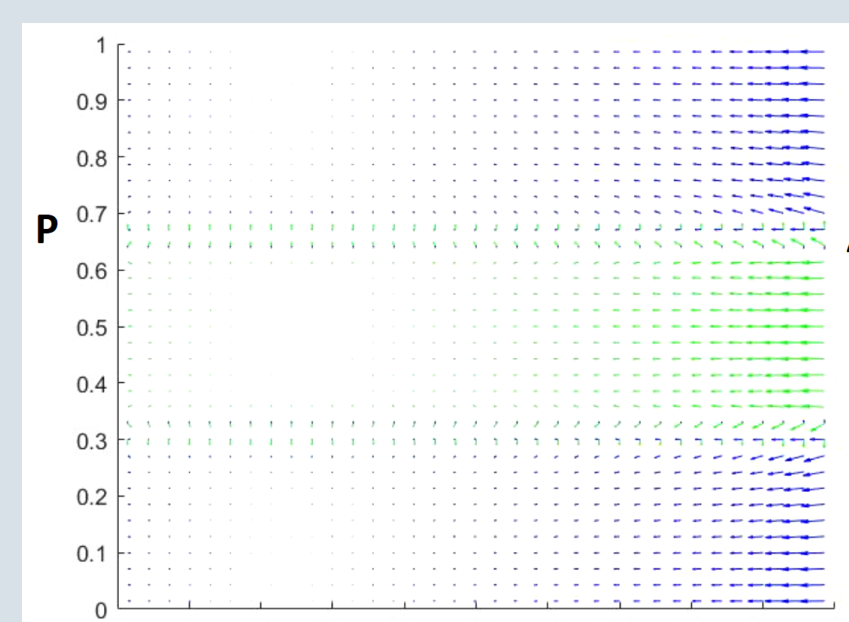

0h of development.
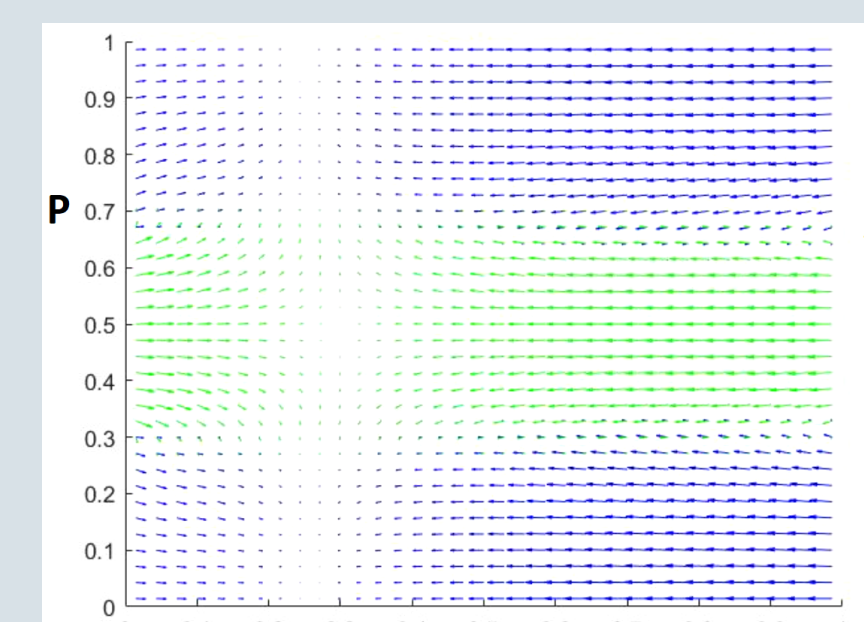

After 10min of development.
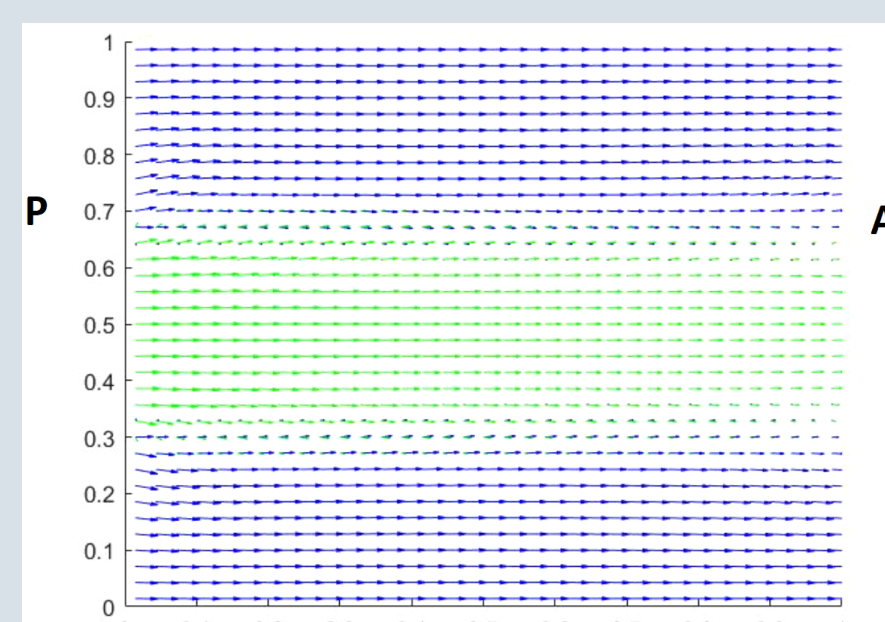

After 1h of development.

Flux profile:

0h of development.

After 10min of development.

After 1h of development.

Main challenges: Blow up of the pressure when the density is close to its maximum value, strict CFL conditions, calibrating the model parameters to fit the biological data...

5 – Conclusion and perspectives

Experimentally: Ongoing work with B. Bénazéraf

Objective: Validate the model and generate new biological hypotheses

Varying the model parameters such as: proliferation rates, viscosity coefficients, incoming flux from the progenitor zone (boundary conditions) allows us to generate new biological hypotheses and analyse:

- Sliding between the tissues
- Differential growth

To validate the new hypotheses of the model i will harvest quail eggs and:

- Inhibit proliferation
- Control the incoming flux from the progenitor zone
- Track cells using live imaging to compare with in silico experiments

Mathematically: Ongoing work with S. Hecht, P. Degond, A. Trescases

Objective: Prove rigorously the limit to the free boundary problem - in the spirit of [4] (one species)

- New difficulty: two-species [1], without considering the velocity as a gradient
- Achieved: Well posedness of the limit system in a case test (one species, homogeneous Dirichlet boundary conditions)
- Extend previous result to more general boundary conditions, for two-species
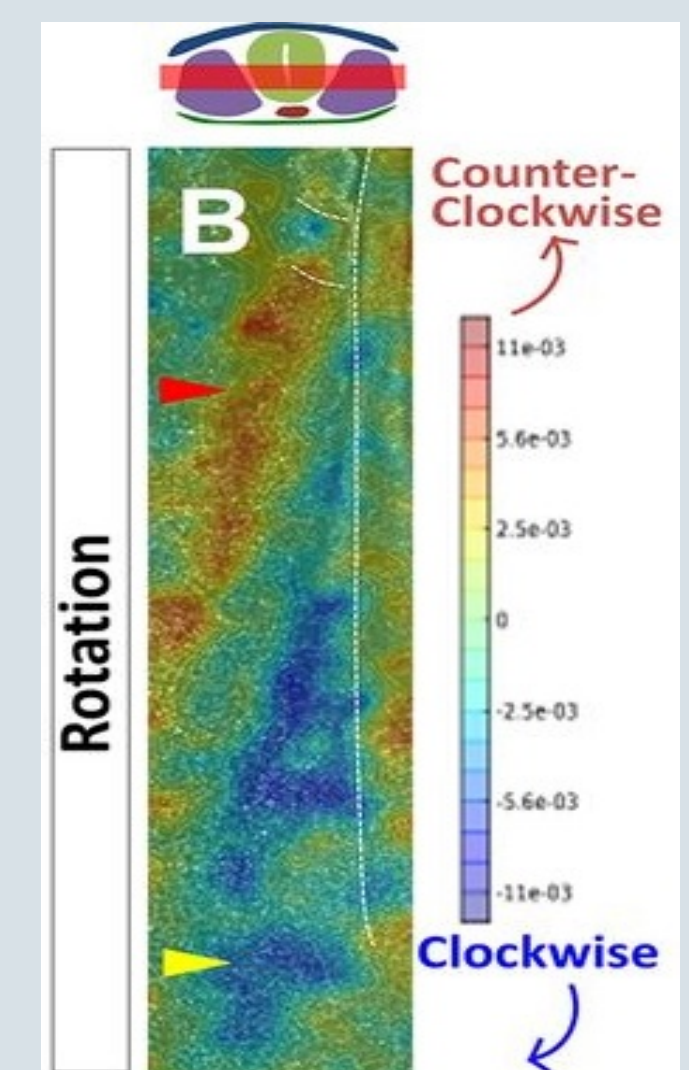
Rotational movement of cells observed in bird embryos. [3]

6 – References

1. T. Debiec and M. Schmidtechen *Incompressible limit for a two-species tumour model with coupling through Brinkman's law in one dimension* (2019).
2. A. Chertock, P. Degond, S. Hecht, and J-P. Vincent *Incompressible limit of a continuum model of tissue growth with segregation for two cell populations* (2018).
3. B. Bénazéraf, M. Beaupeux and M. Tchernookov *Multi-scale quantification of tissue behavior during amniote embryo axis elongation* (2017)
4. B. Perthame and N. Vauchelet *Incompressible limit of mechanical model of tumor growth with viscosity.* (2014)