Physics of embryonic cavity formation by hydro-osmotic coarsening

Mathieu Le Verge--Serandour[1] & Hervé Turlier[1]

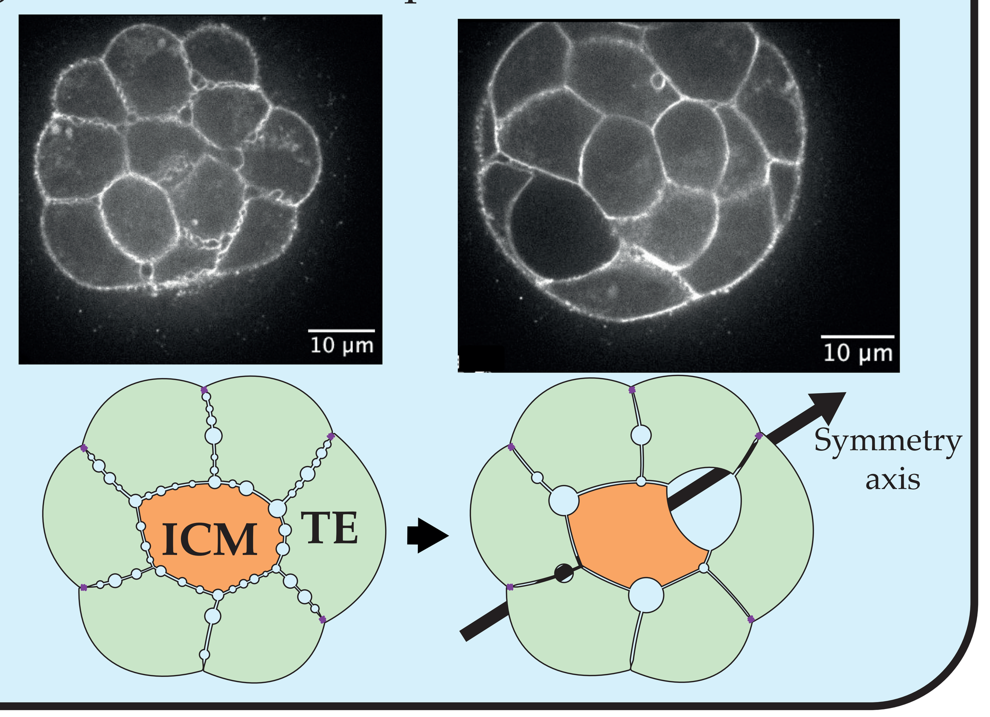
1. Center for Interdisciplinary Research in Biology, Collège de France, PSL Research University, CNRS UMR7241, INSERM U1050, 75005 Paris, France

Contact : mathieu.le-verge-serandour@college-de-france.fr

I - Introduction

The blastocoel is a **fluid-filled cavity**, characteristic of many embryos. Embryos are usually described as **foams**, where each cell corresponds to a bubble with given **pressure** and **surface tension**, adhering together.
In tightly compacted embryos, the mechanism underlying its emergence remains unclear : *how a large cavity would form at adhesive surfaces ?*
Based on experimental observations on the mouse embryo [1], we discuss a physical model by which a single cavity forms by **growth and coarsening** of micrometric cavities interconnected through the intercellular space [1, 2].

Scheme of the process of coarsening of micro-cavities. As time increases, the number of micro-cavities decreases but their average area increases.
TE : trophectoderm cell
ICM : Inner cell mass



II - Model

Micro-cavities are described with their **length** L_i and **number of solute** N_i

Mass Balance

$$\frac{dL_i}{dt} = 2\mu\nu\lambda_v\left[\mathcal{R}T\delta C_i - \delta P_i\right] - \frac{\mu}{2L_i}J_i^v$$

Solute Balance

$$\frac{dN_i}{dt} = 2\nu L_i\left[\lambda_s\mathcal{R}T\log\left(\frac{c_0}{C_j}\right) + j^a\right] - J_i^s$$

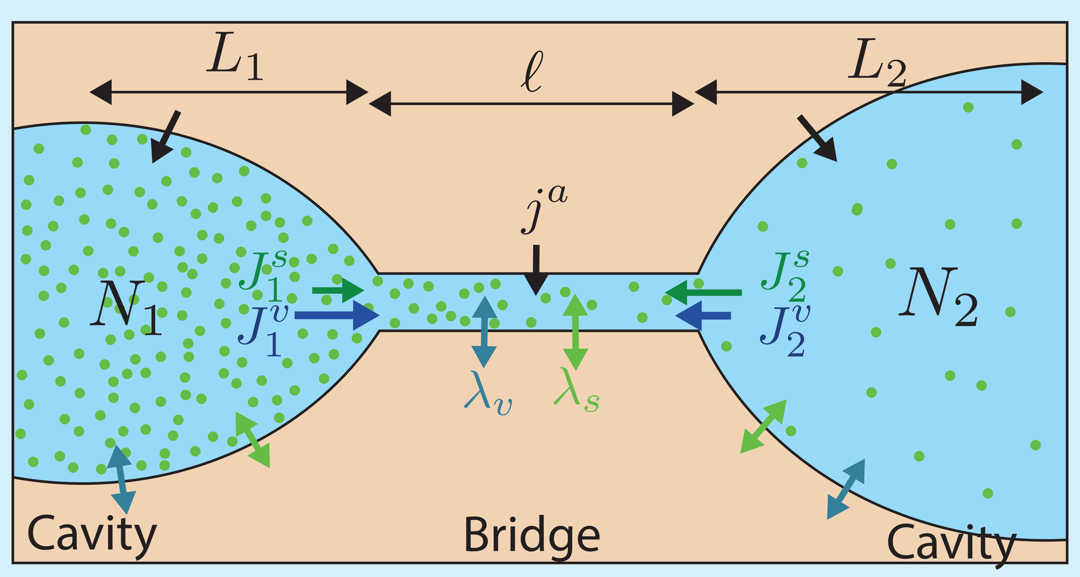
Permeation coefficients for solvent (λ_v) and solute (λ_s) control the passive exchanges of cavities with the cells.
Two **screening lengths** affect the pressure (ξ_v) and concentration (ξ_s) exchanges between cavities through the bridge.

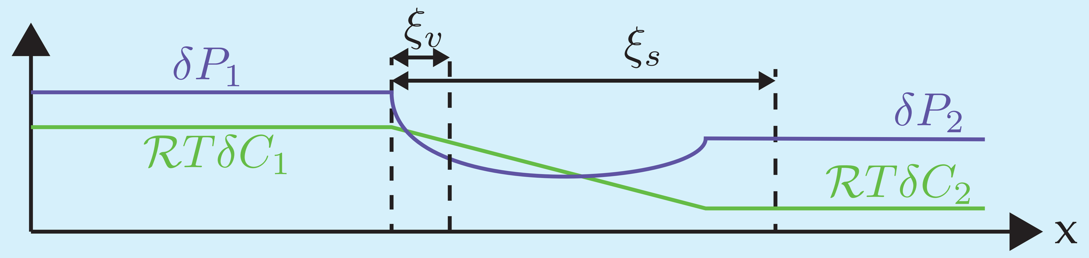
Pressure screening

$$\xi_v = \sqrt{\frac{\kappa_v}{2\lambda_v}}$$

Concentration screening

$$\xi_s = \sqrt{\frac{De_0c_0}{2\lambda_s\mathcal{R}T}}$$

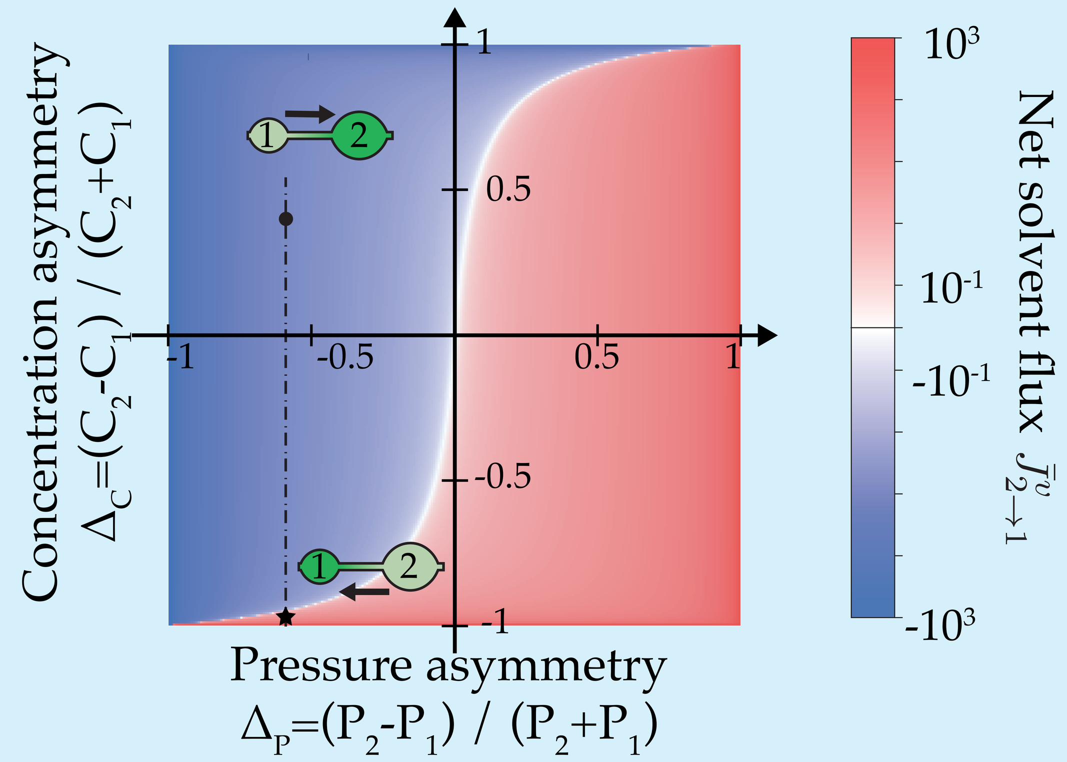




III - 2-cavity system

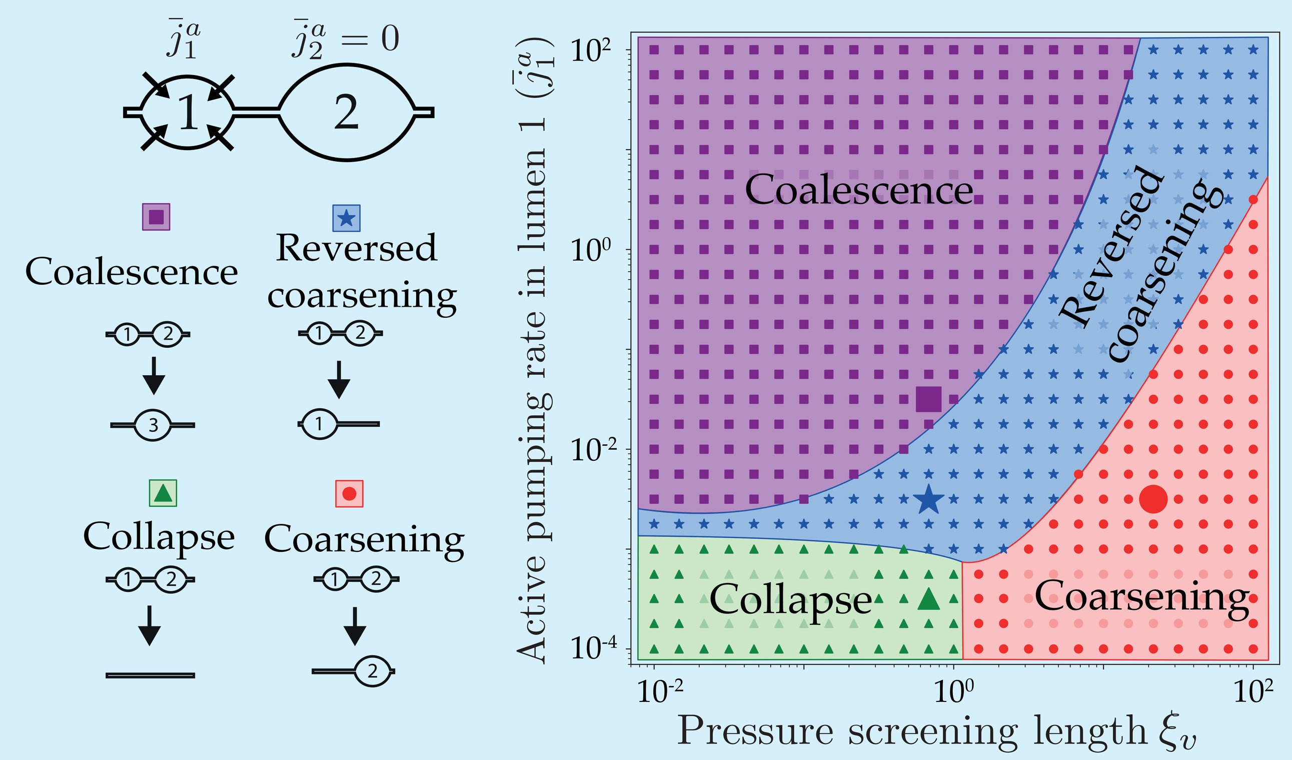
i - Osmotic vs Laplace pressures

The hydraulic flux is oriented from the smaller cavity to the larger one, but at large osmotic pressures (bottom case), the flux can be **reversed**.
The sharp profile shows that very large osmotic pressure differences are required, which is **unlikely in biological systems**.



ii - Effect of active pumping

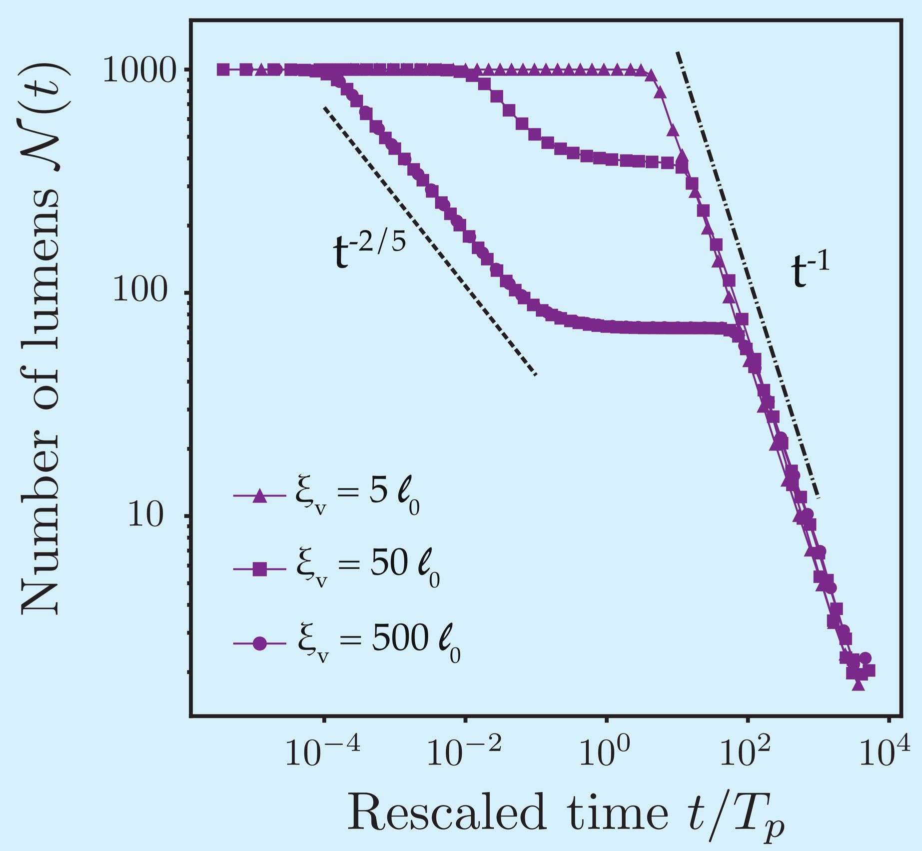
Cells typically pump solutes in or out via active pumps.
We observe four different fates 2 cavities :
i - **collapse** if the cavities cannot exchange
ii - **coarsening** if the cavities can exchange
iii - **reversed coarsening** if the pumping is strong
iv - **coalescence (fusion)** if the pumping overcomes the exchange



IV - Chain of cavities

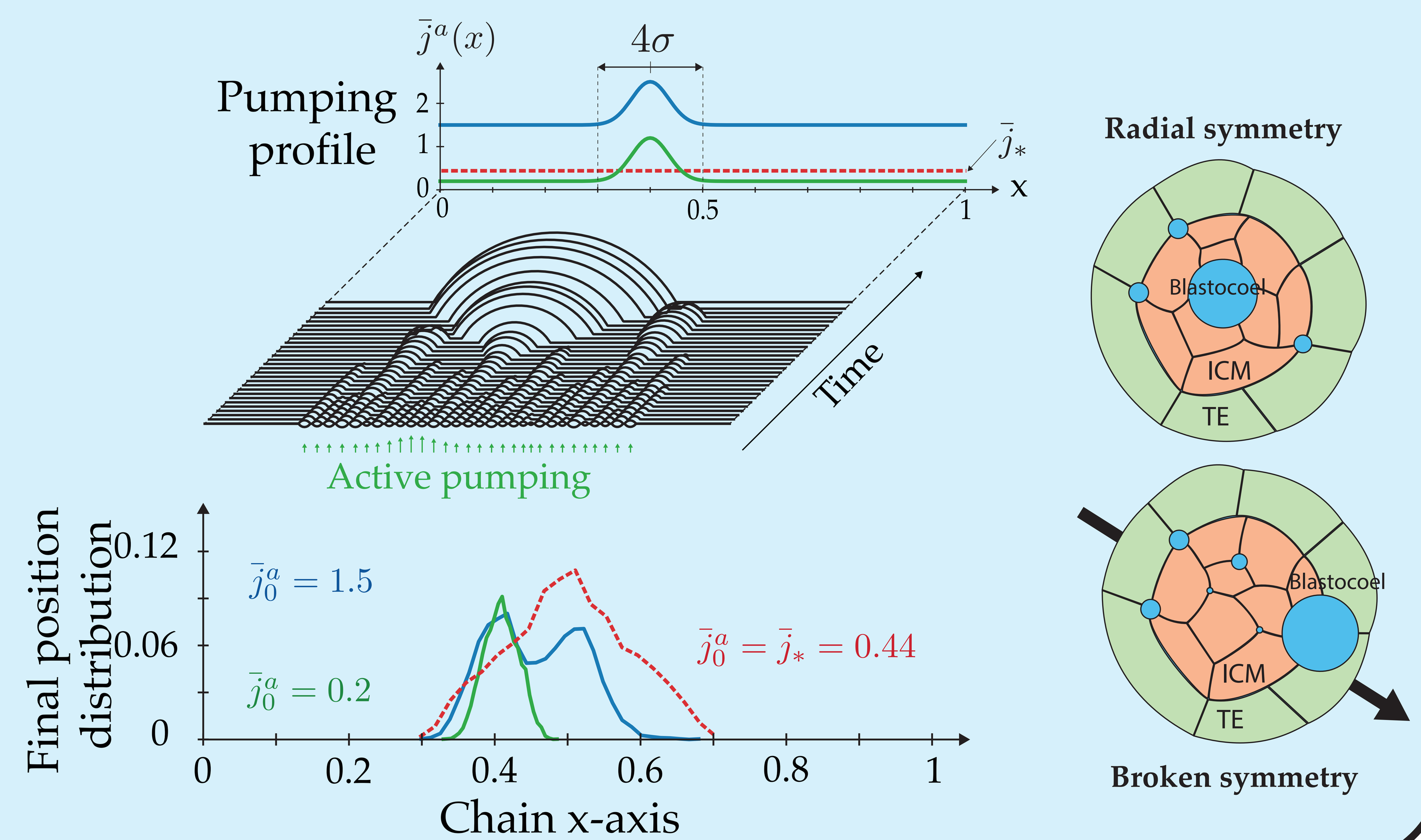
i - Coarsening dynamical scaling laws

A chain of hundreds of connected micro-cavities exhibits at small times a **hydraulic scaling law** due to mass exchange reminiscent of **dewetting films** [4], that switches to another scaling law due to **coalescence** at larger times in presence of active pumping.



ii - Symmetry breaking via active pumping

Mammalian cells are **polarized** with spatial heterogeneities of specialized active pumps for outer cells (trophectoderm cells) [5]. Such inhomogeneities are able to position the final micro-cavity under specific active pumping profiles.



Perspectives

Our work [6] presents a novel theory for the **coarsening of a network of connected cavities**, with robust predictions. We show that the hydraulic pressure dominates the osmotic contribution of osmolytes.

A scaling law have been calculated for a chain, but can be estimated for a 2-d network for hydraulic scaling law ($N(t) \sim t^{-3/4}$) and are not expected to change in the coalescence regime.

Active pumping induces a broad range of effects. First a **new dynamical scaling law** for coalescence regimes. Second, a **symmetry breaking** as a way to position the blastocoel in the embryo, in addition to the contractility asymmetry [1] of inner and outer cells.

Besides, **cell-cell contact fracking** [2] and micro-cavities formation, as well as the contribution of **electro-osmotic** effects still remain unclear and need to be characterized, opening the way for future research.

References

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[3] Dasgupta et al., *PNAS*, 2019
[4] Gratton, Witelski, *Physica D.*, 2009
[5] Barcroft et al., *Dev. Biol.*, 2003
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