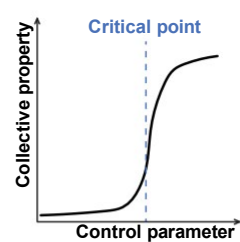
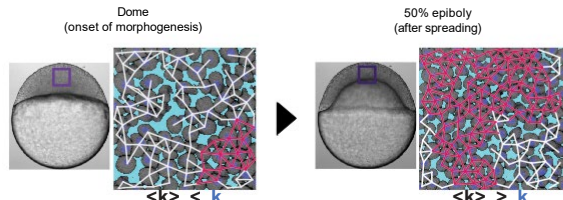


Background

- Tissue material phase transitions.**
 - Small changes in a **microscopic** control parameter lead to abrupt changes in a **macroscopic** collective property.
 - Biological tissues can undergo phase transitions between **material states**.



- The zebrafish embryo undergoes a phase transition.**
 - Zebrafish morphogenesis starts with a **tissue rigidity phase transition**.^{1,2}
 - Rigidity percolation theory predicts this phase transition at a critical point of cell connectivity ($\langle k \rangle$).³

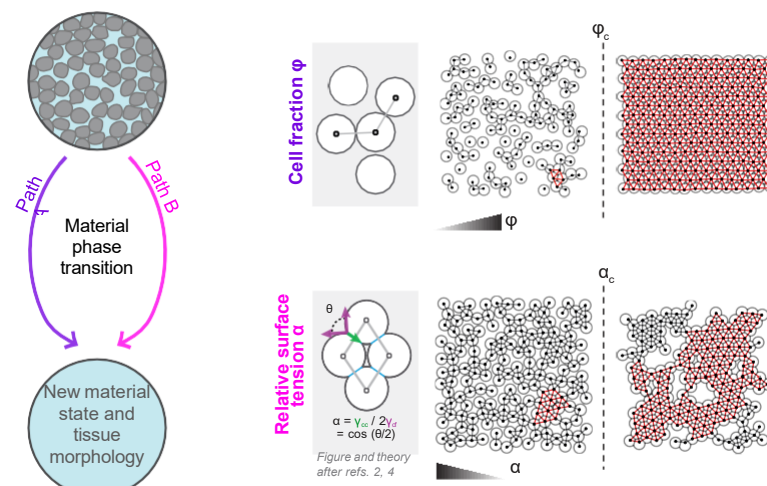


Collective property:
GRC size
Control parameter:
connectivity $\langle k \rangle$

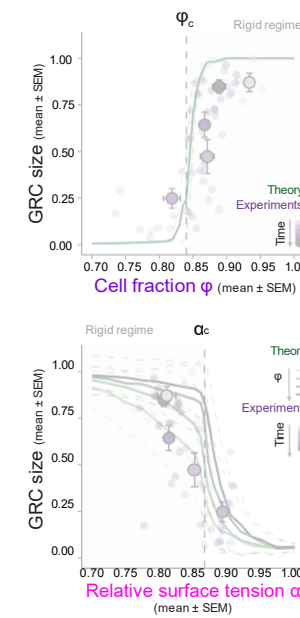
Connectivity map: GRC (Giant Rigid Cluster) Membrane Nuclei Interstitial fluid

Initial findings

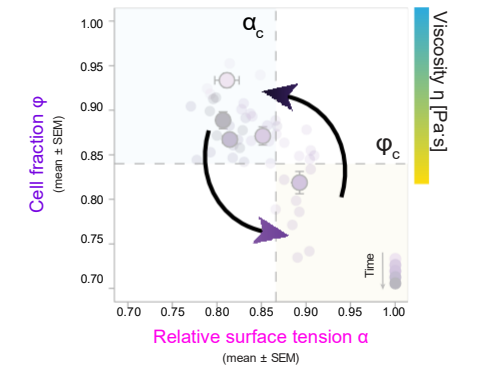
- Several cellular parameters trigger phase transitions *in vivo*.**



Tissue rigidity is determined by **cell fraction ϕ** and **relative surface tension α** .



- Adhesion- and density-dependent transitions are coupled in wildtype zebrafish embryos.**

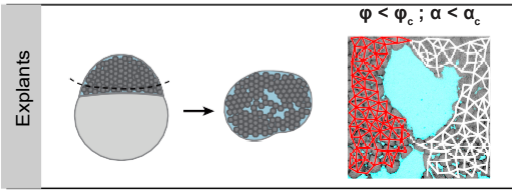
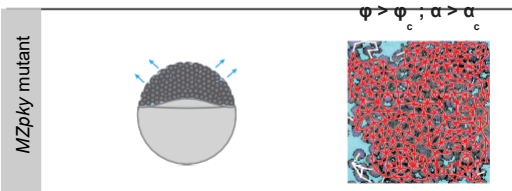
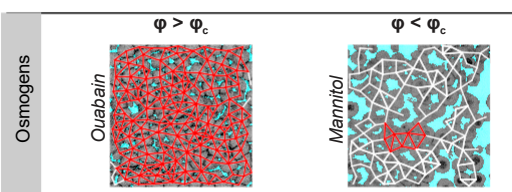
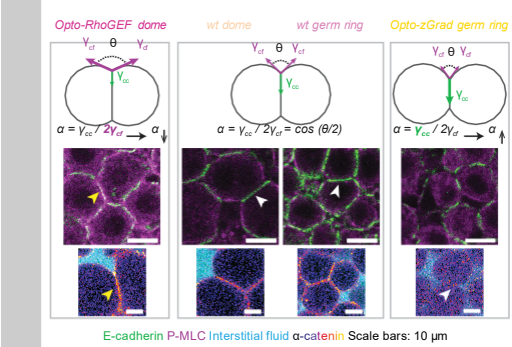
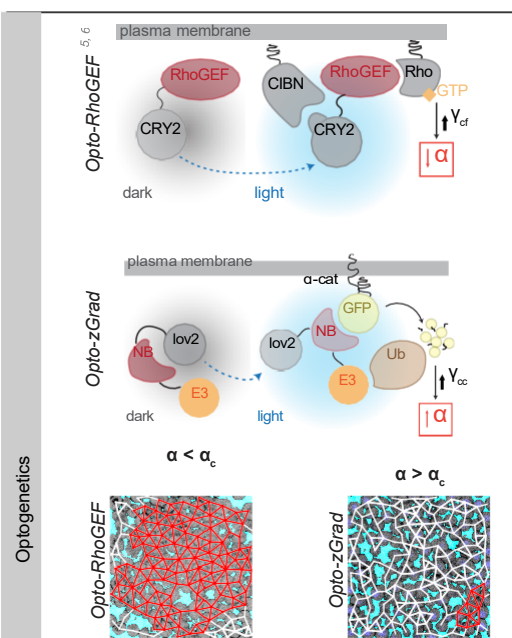


- Can the different types of material phase transitions be **uncoupled**?
- Do they have distinct **biological functions**?

Uncoupling adhesion- and density-driven rigidity transitions triggers epithelial organization in embryonic tissues

Toolkit

***In vivo* tuning of the tissue material phase transition control parameters $\langle k \rangle$, α , and ϕ .**



Nuclei Membrane Interstitial fluid Connectivity map (GRC)

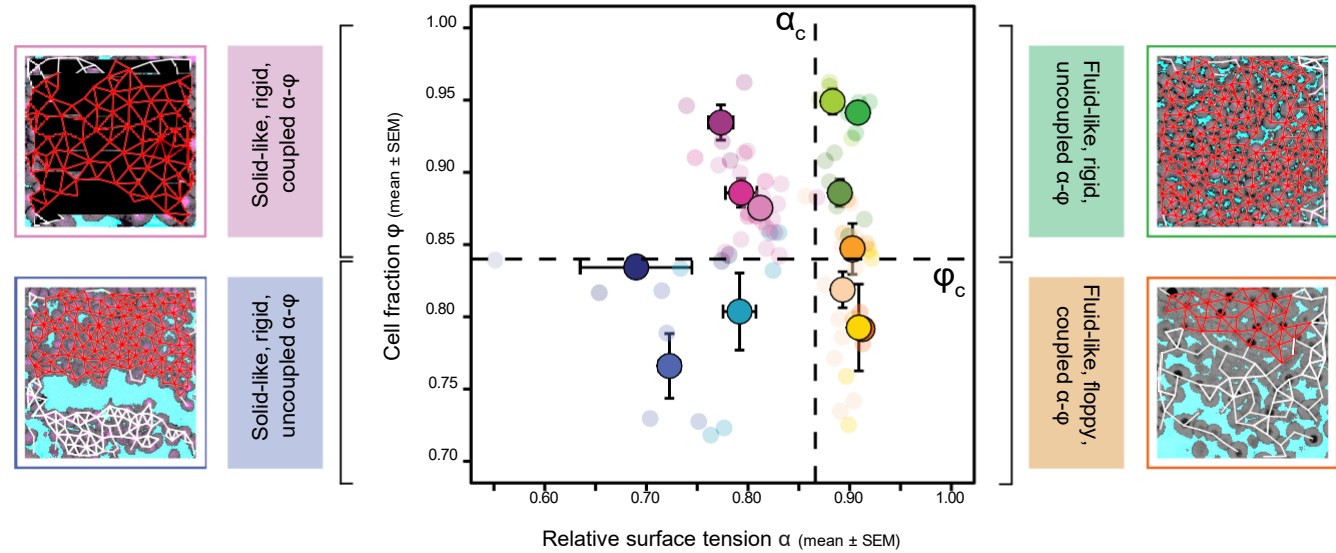
- References**
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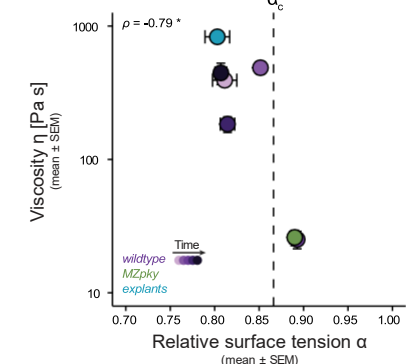


Results

- Precise engineering of tissue material states by uncoupling the multiple control parameters.**

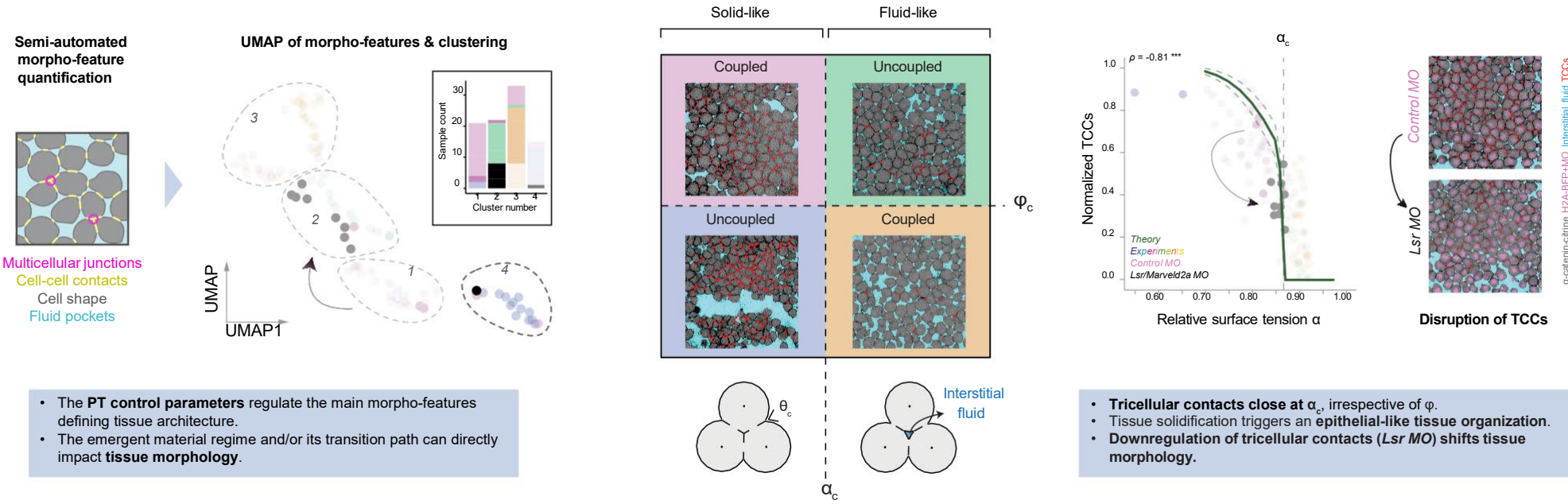


- The relative surface tension α determines the tissue material state *in vivo*.**



- ϕ is not predictive of tissue viscosity when uncoupled from α .
- Active cell adhesion dynamics**, captured by α , determine the material state.

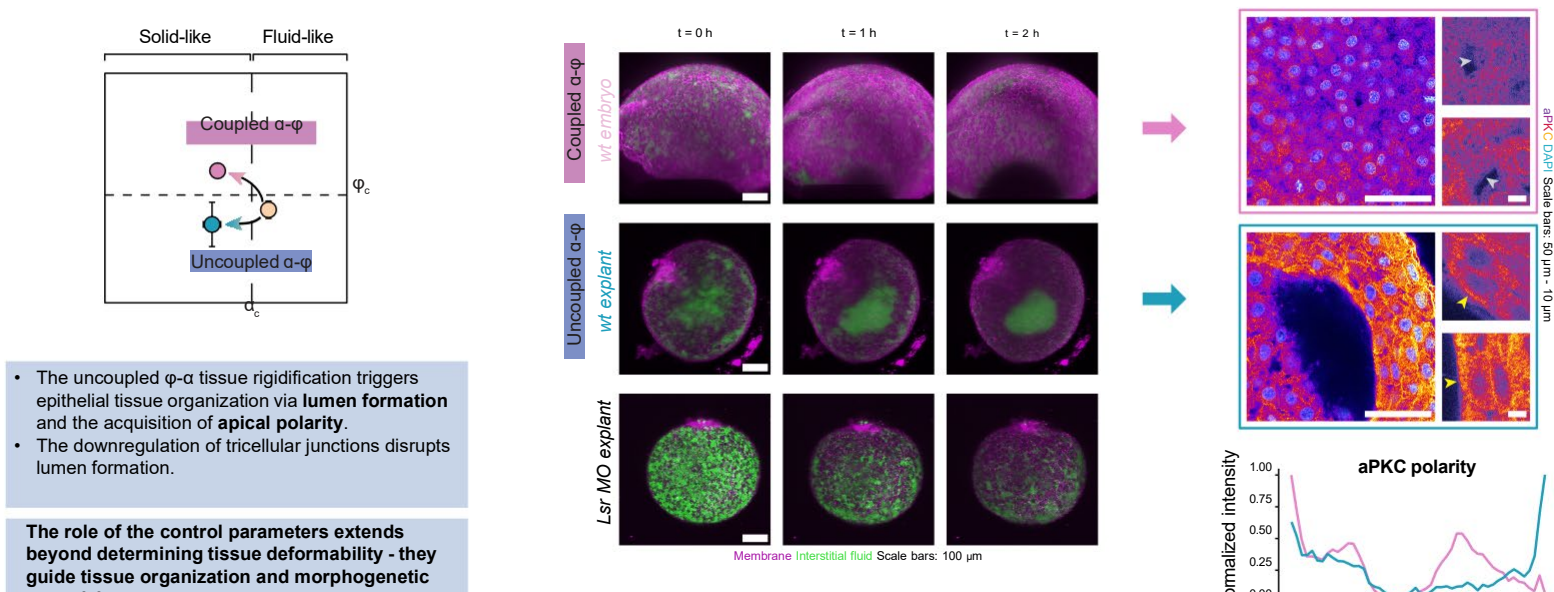
- The tissue material state discretizes tissue organization via the formation of tricellular contacts.**



- The PT control parameters regulate the main morpho-features defining tissue architecture.
- The emergent material regime and/or its transition path can directly impact tissue morphology.

- Tricellular contacts close at α_c , irrespective of ϕ .
- Tissue solidification triggers an epithelial-like tissue organization.
- Downregulation of tricellular contacts (*Lsr MO*) shifts tissue morphology.

- Adhesion-driven solidification triggers lumenogenesis and apical polarity in unjammed pluripotent tissues.**



- The uncoupled ϕ - α tissue rigidification triggers epithelial tissue organization via **lumen formation** and the acquisition of **apical polarity**.
- The downregulation of tricellular junctions disrupts lumen formation.

The role of the control parameters extends beyond determining tissue deformability - they guide tissue organization and morphogenetic potential.

- wt 50% epiboly to shield
- wt dome + Opto-RhoGEF
- wt 50% margin
- explants
- wt 50% + Opto-RhoGEF + Mannitol
- wt 50% margin + Mannitol
- MZpk 50%
- wt dome + Ouabain
- wt 50% + Opto-zGrad + Ouabain
- wt dome
- wt dome + Mannitol
- wt 50% + Opto-zGrad
- wt 50% margin + Opto-zGrad