MARANGONI-LIKE TISSUE FLOWS CONTRIBUTE TO SYMMETRY BREAKING OF EMBRYONIC ORGANOIDS

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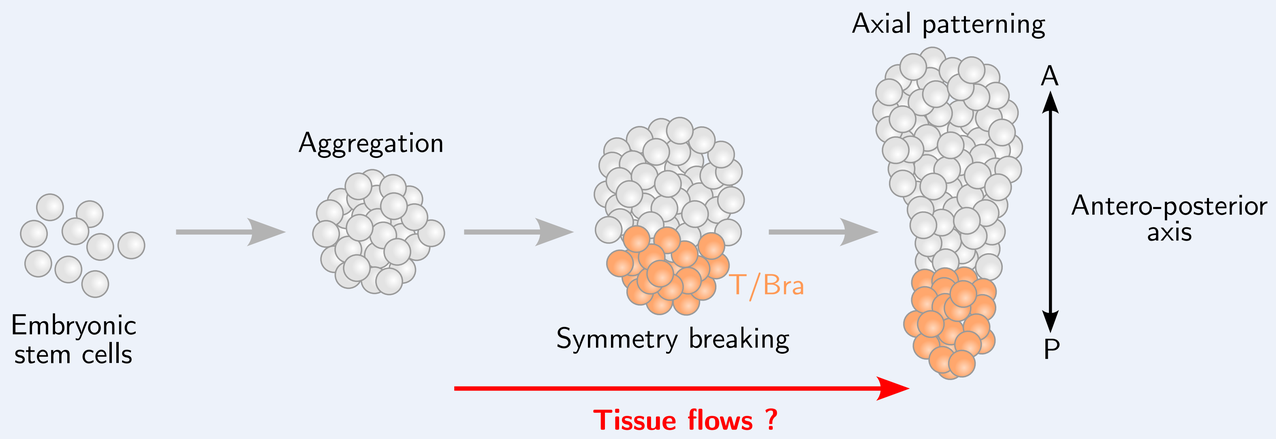
Introduction

- During embryonic development, cells need to exhibit coordinated motion to shape tissues and organs
- **The role of such tissue flows during axis formation of mammals is unknown**
- **Mouse embryonic stem cells** (**ESCs**) provide excellent experimental systems to address this question
- 3D spherical aggregates of mouse ESCs self-organize into **embryonic organoids** called **gastruloids** [1].
- They undergo **symmetry breaking of protein expression** (**T/Bra**) and exhibit axial organization analogous to in-vivo embryos

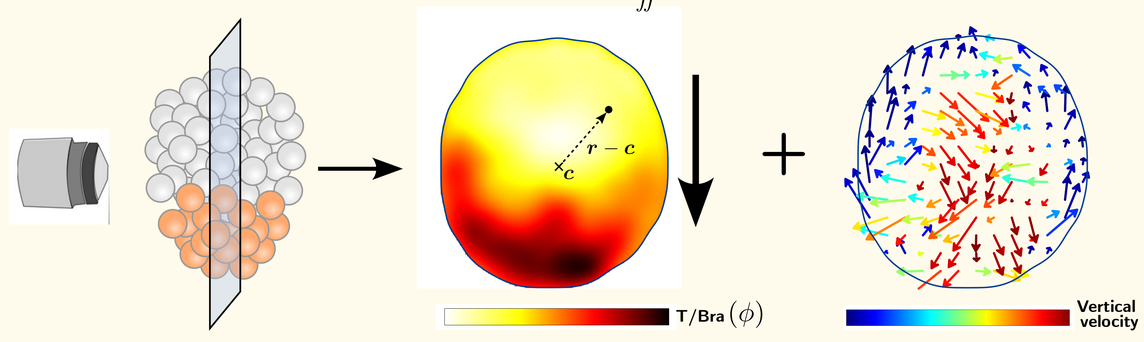


Glossary

- **Embryonic organoid**: 3D aggregate of differentiating stem cells self-organizing into an embryo-like body
- **Gastruloid**: embryonic organoid reproducing the process of body plan formation of embryos (gastrulation)
- **T/Bra**: early marker for the formation of conjunctive and muscular tissue, known to be involved in cell adhesion properties
- **Dipole moment**: vector quantifying the T/Bra symmetry breaking
- **Marangoni effect**: flow driven by differential tension at an interface

Experiments

Dipole moment $\boldsymbol{P} = \iint \phi(\boldsymbol{r})(\boldsymbol{r}-\boldsymbol{c})dS$

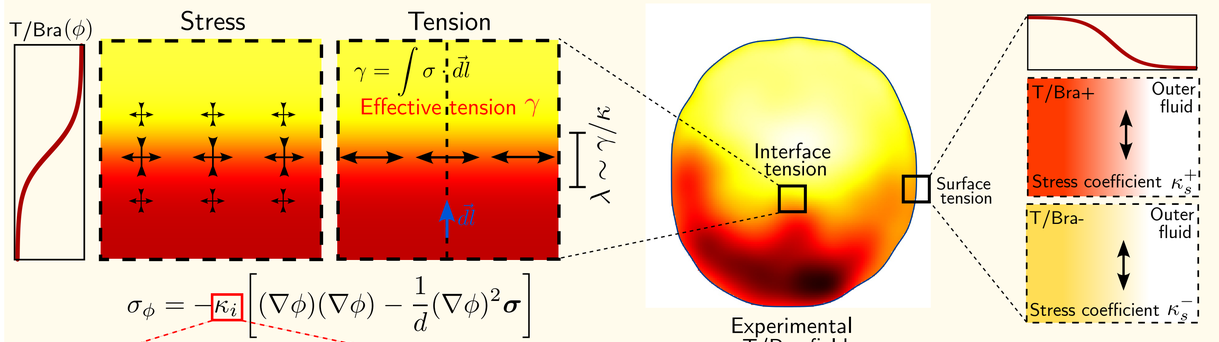


We image **gastruloids** using **two-photon microscopy** during the symmetry breaking process

We quantify the symmetry breaking based on **coarse-grained T/Bra expression patterns**

We use an optical flow technique to determine the **coarse-grained tissue velocity** during symmetry breaking

Modeling

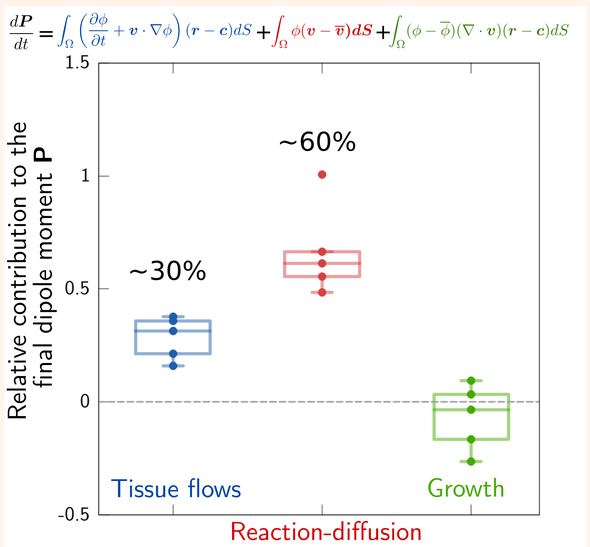


We assume **scalar-active stresses** [2] controlled by **T/Bra** gradients

We model **T/Bra** dependant **tension at the aggregate surface** [3]

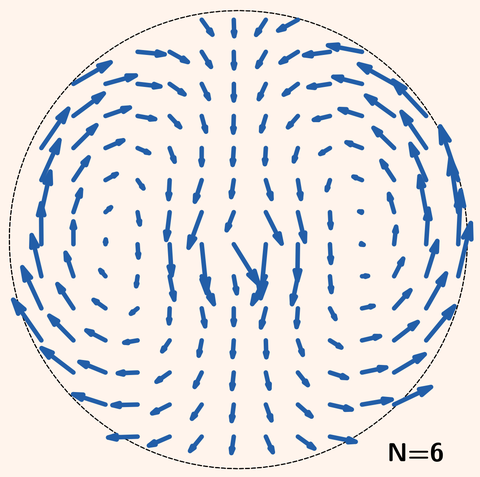
Results

1. Tissue flows substantially contribute to the symmetry breaking process



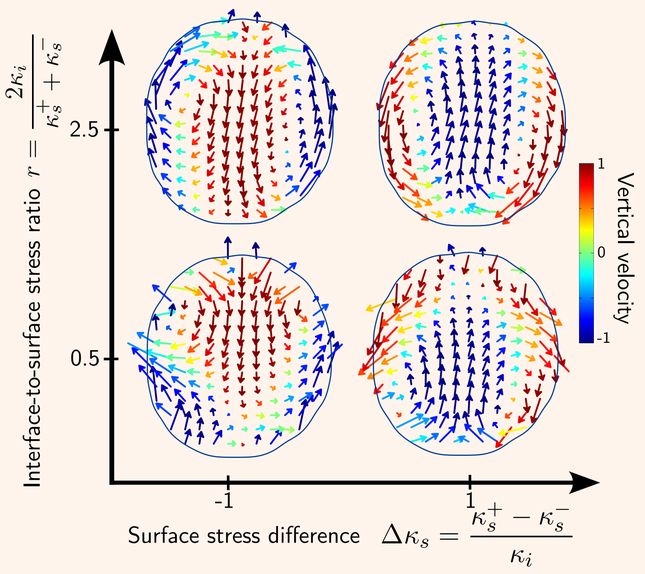
We combine **T/Bra** and tissue velocity fields to quantify the **contribution of different coarse-grained processes to symmetry breaking**

2. Tissue flows are dominated by a coherent recirculation flow



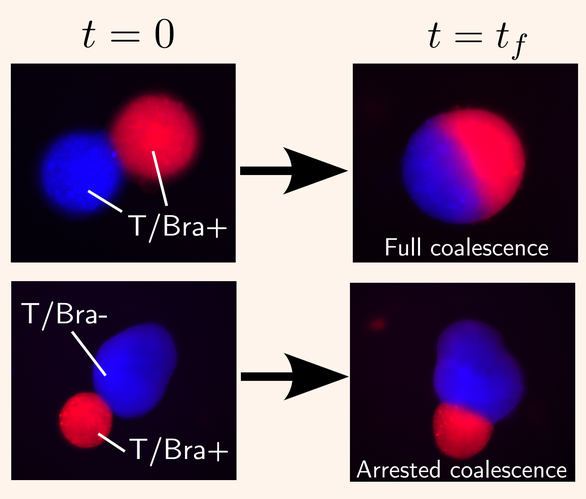
We project tissue flows on an ad-hoc basis of velocity fields to identify the **dominant velocity pattern accross samples**

3. Model simulations predict recirculation flows driven by Marangoni effect



We simulate tisse flows from experimental **T/Bra** fields over **ranges of the stress coefficient ratios**

4. Fusion experiments further confirm the existence of T/Bra-dependent tension



We analyze fusion angles to confirm the existence of **interface tension** between tissues as well as **differential tensions at the aggregate surface**

Conclusions

- Both reaction-diffusion and **recirculating tissue flows contribute to T/Bra symmetry breaking**
- **T/Bra gradients can drive recirculating tissue flows** through tissue interface tension and differential tension at the aggregate surface
- This suggests the existence of a **positive feedback loop reinforcing tissue flows during axis formation**

References

[1] Hashmi et al., *eLife*. 2022;11:e59371. doi:10.7554/eLife.59371
[2] Tiribocchi et al., *Phys. Rev. Lett*. 2015;115-188302. doi:10.1103/PhysRevLett.115.188302
[3] Gsell & Merkel, *Soft Matter*. 2022;18,2672-2683. doi:10.1039/D1SM01647D

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