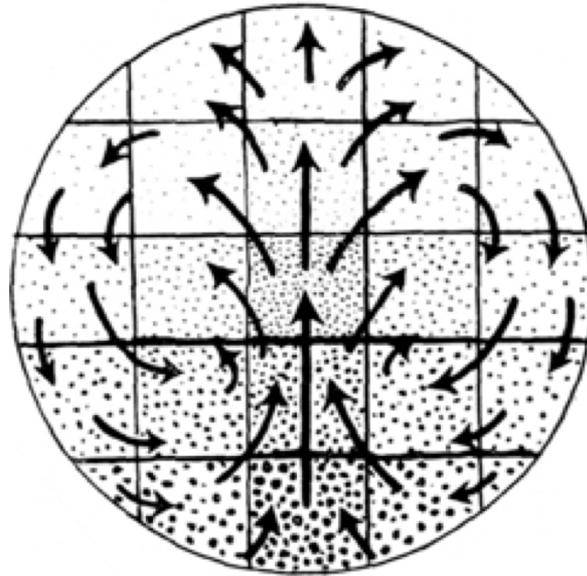


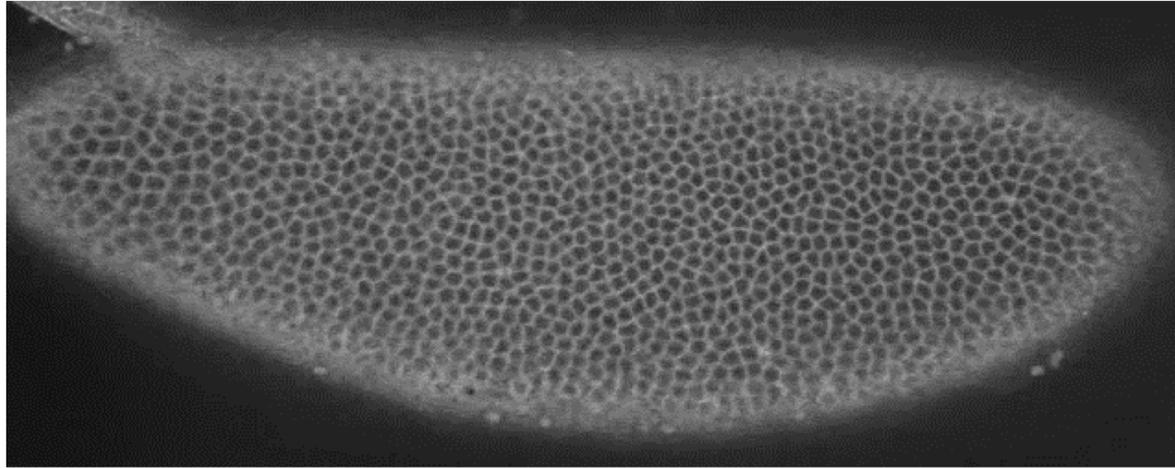
Mechanics of gastrulation

The forces that shape the early avian embryo



Francis Corson
Laboratoire de Physique de l'Ecole Normale Supérieure
with the group of Jérôme Gros, Institut Pasteur

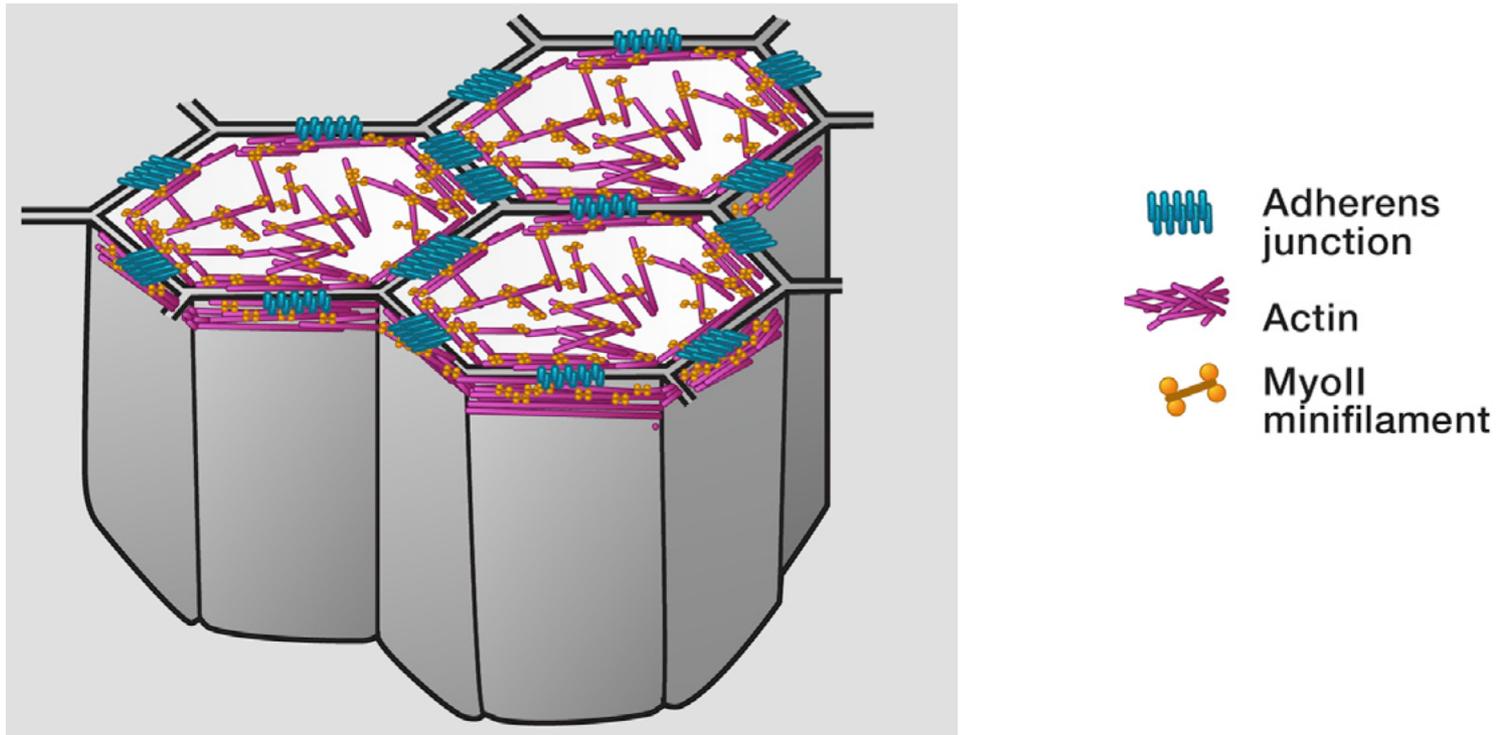
How do organisms acquire their shape?



Drosophila embryo

Morphogenesis involves coordinated cell shape changes, rearrangements, and motion

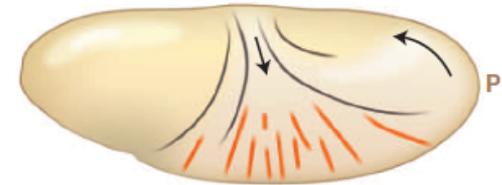
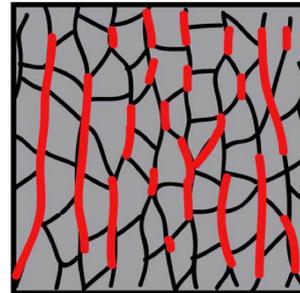
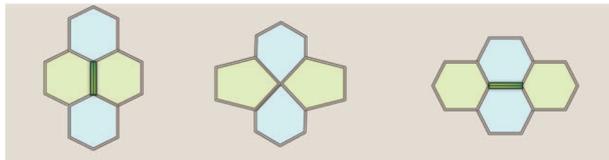
How do organisms acquire their shape?



Morphogenesis is driven by mechanical forces generated on the cellular scale

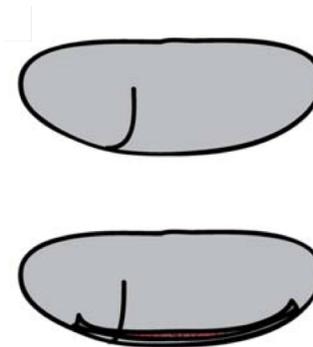
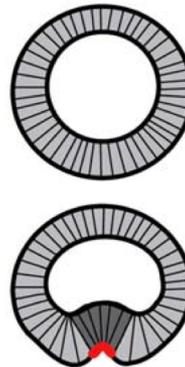
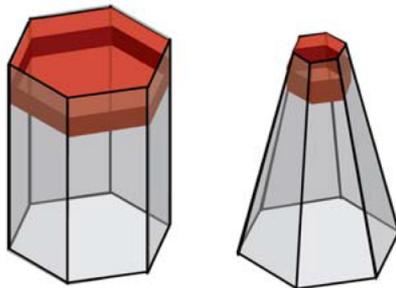
Simple morphogenetic processes

Convergent extension

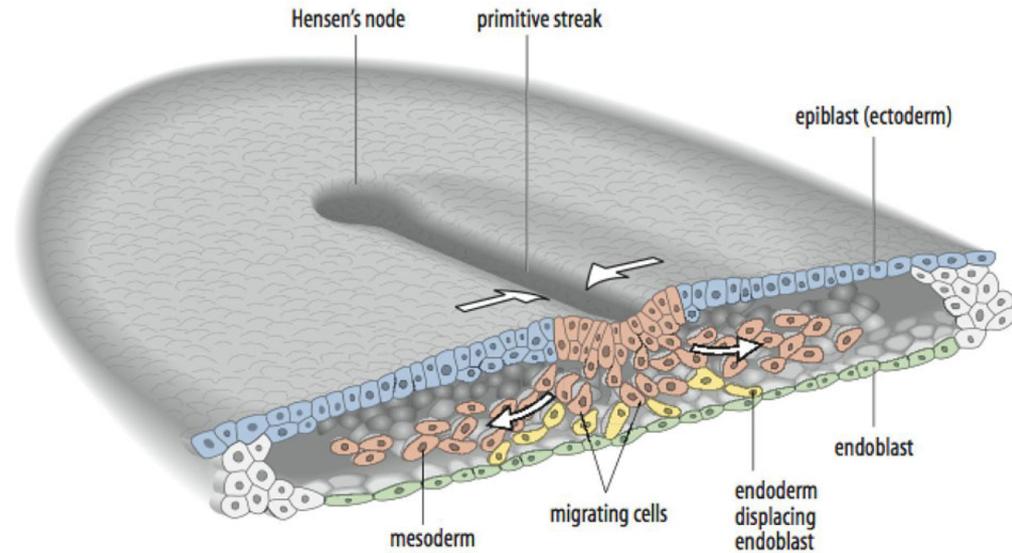
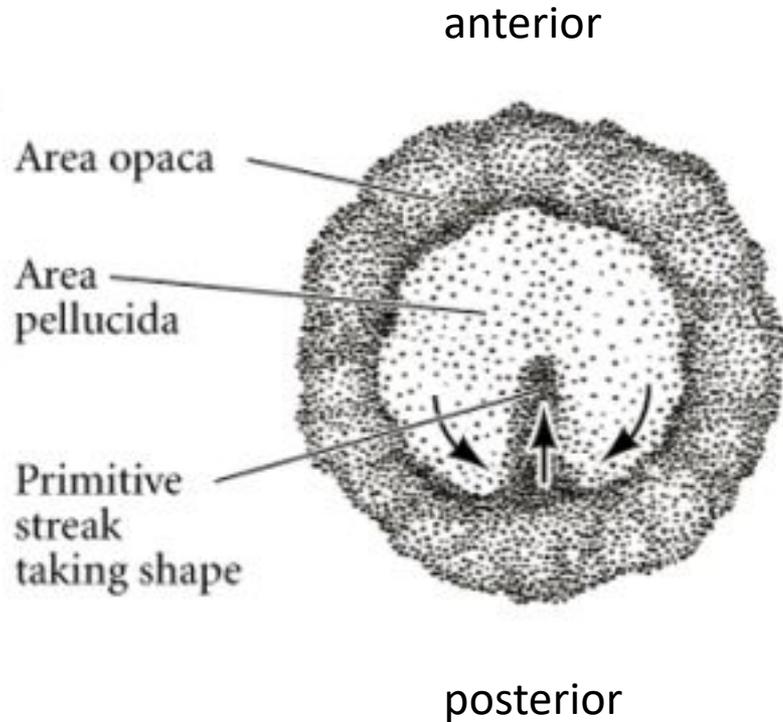


Germ band elongation
in *Drosophila* embryo

Invagination

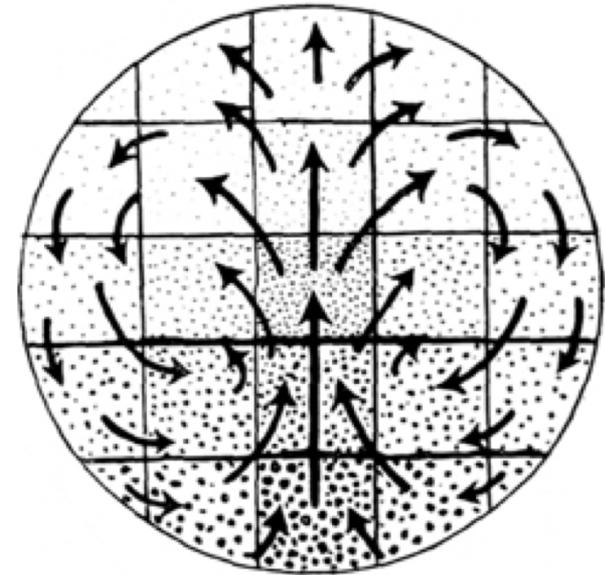
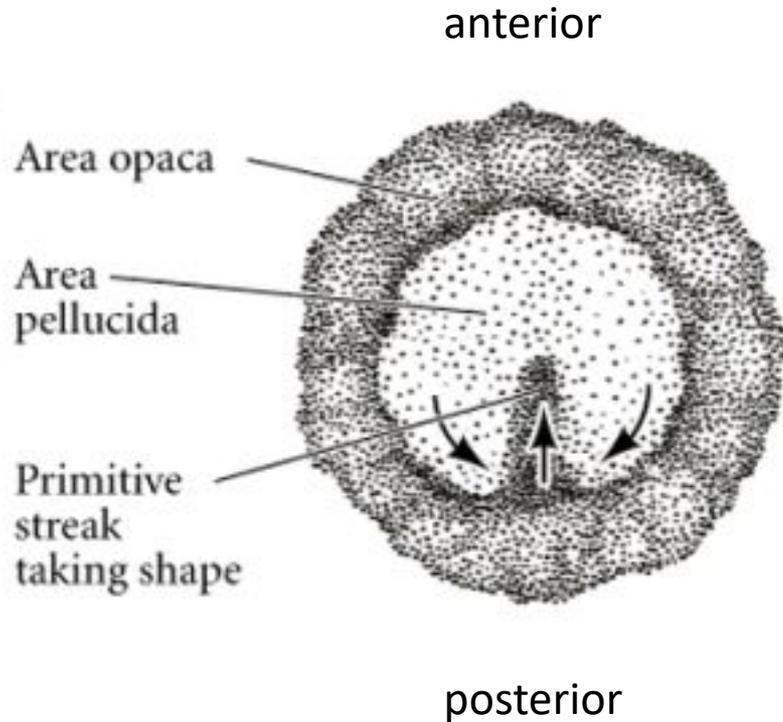


Gastrulation in the avian embryo



Epiblast cells converge towards the posterior to form the primitive streak

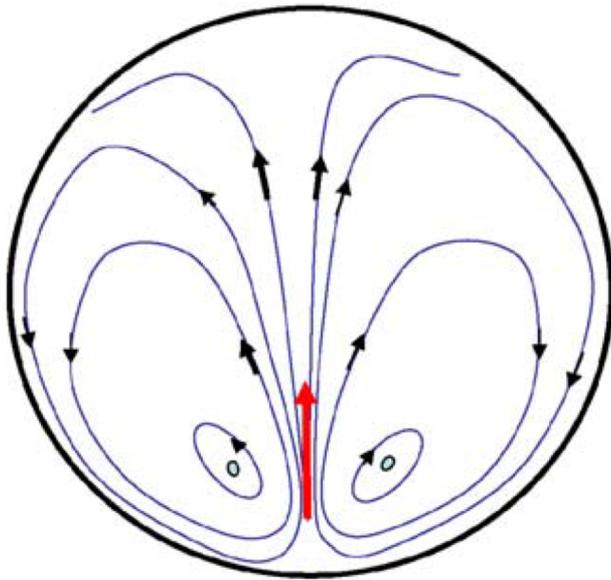
Gastrulation in the avian embryo



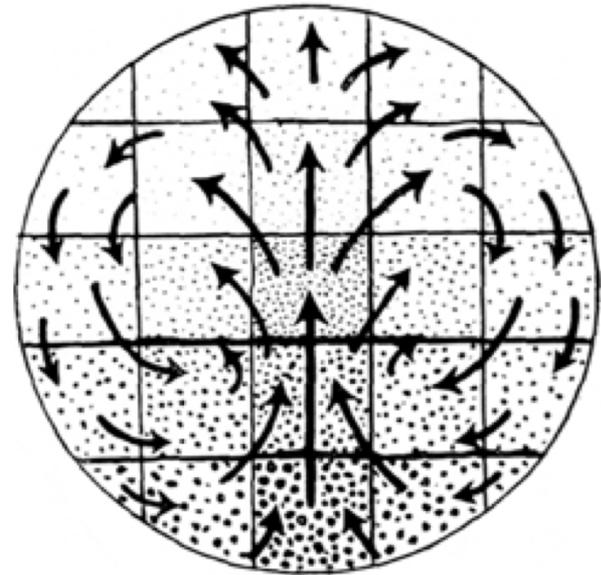
Gräper, Wetzel 1929

Primitive streak formation is accompanied by 'Polonaise' movements

Motions reminiscent of fluid flow

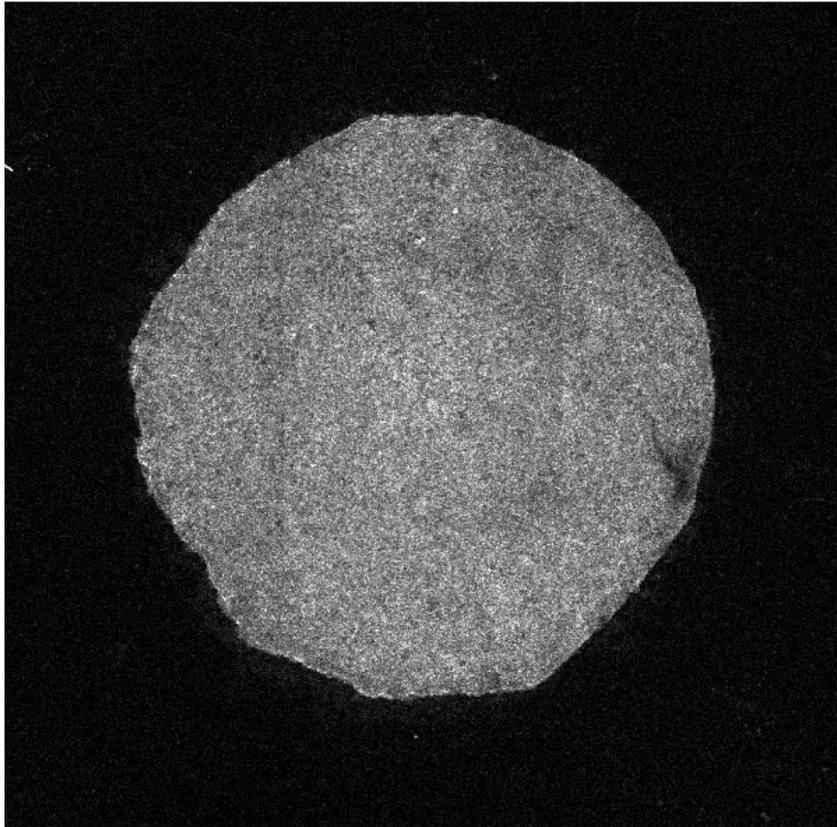


Chuai & Weijer 2008
Fleury 2005

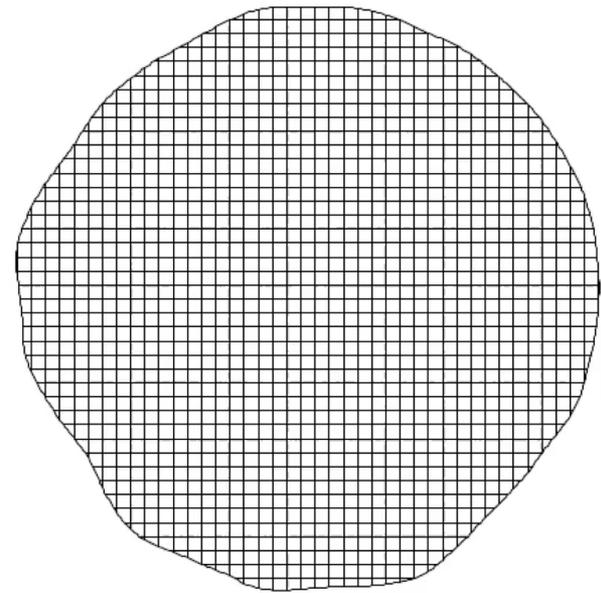


Gräper, Wetzel 1929

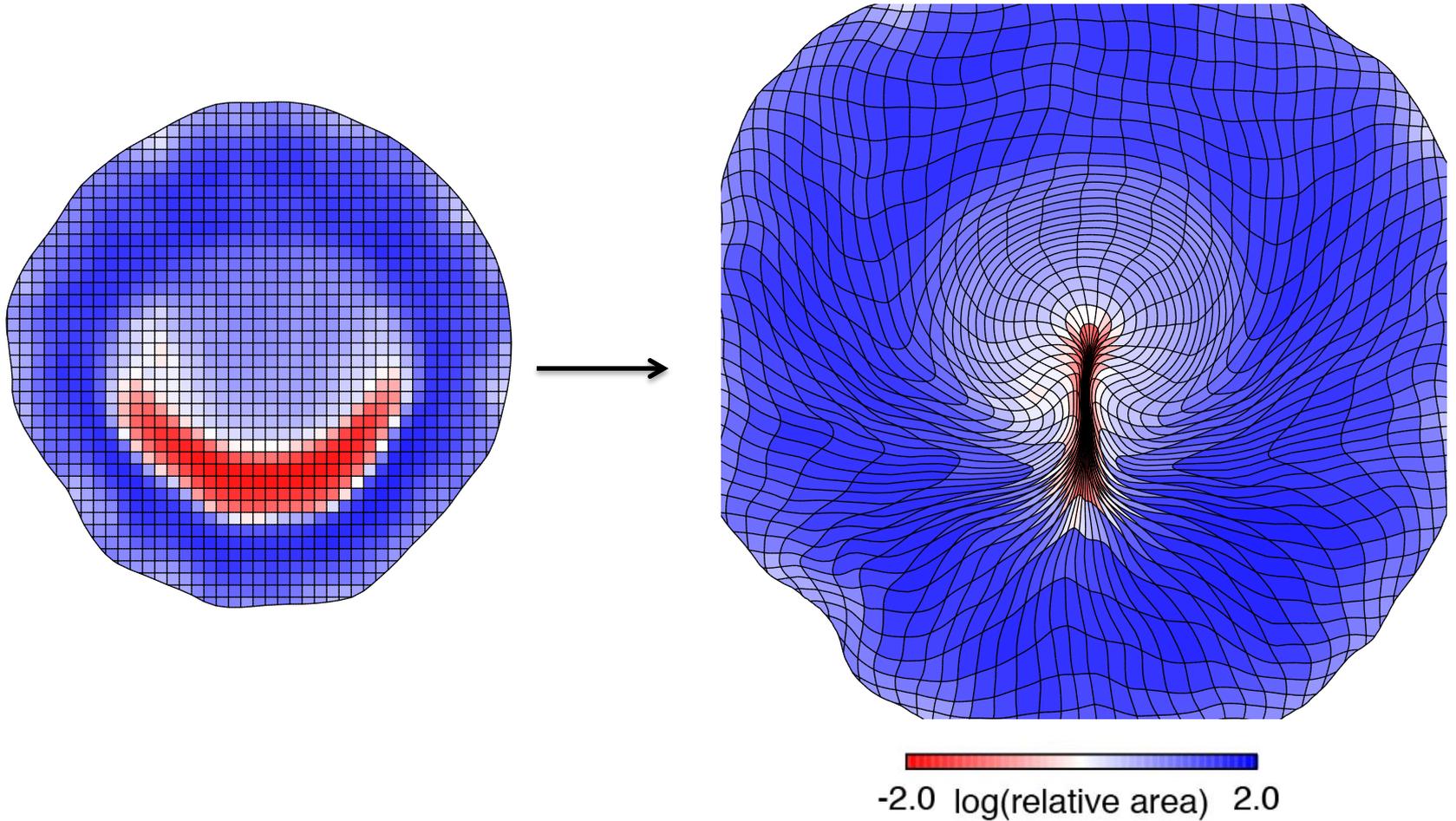
Tissue flows in the early embryo



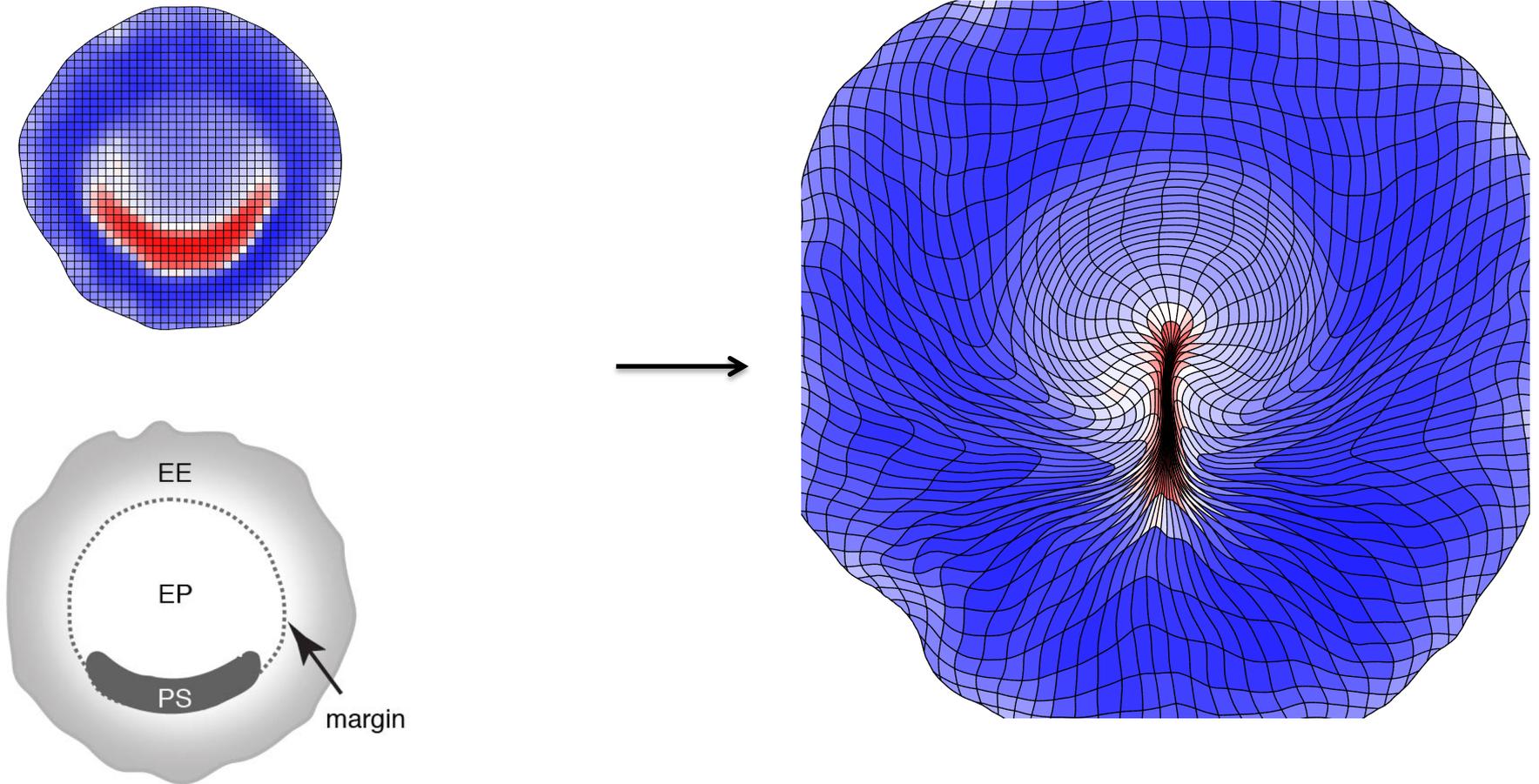
memGFP quail embryo



Tissue flows in the early embryo



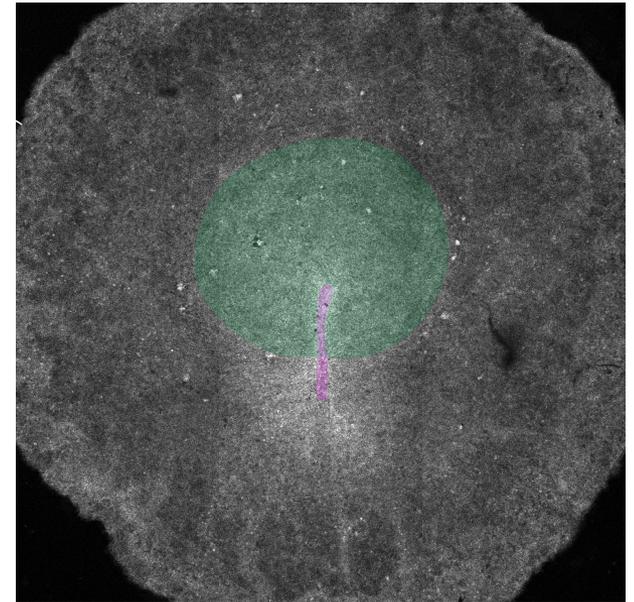
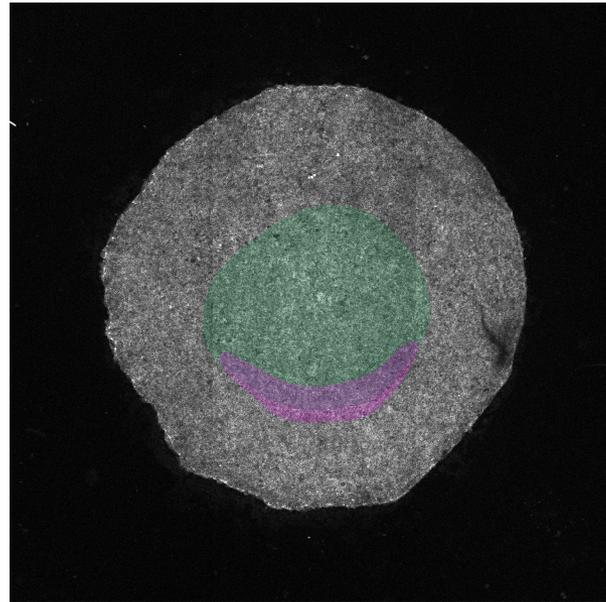
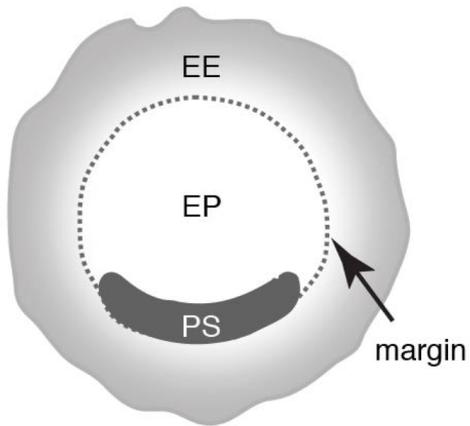
Automated fate mapping



Embryonic territories are readily identified in deformation maps

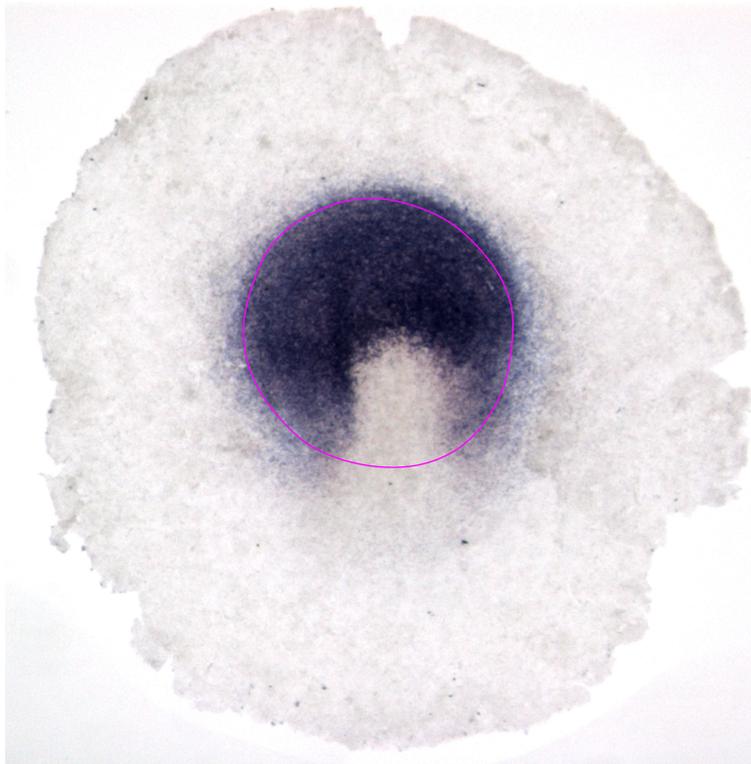
Automated fate mapping

embryo proper primitive streak

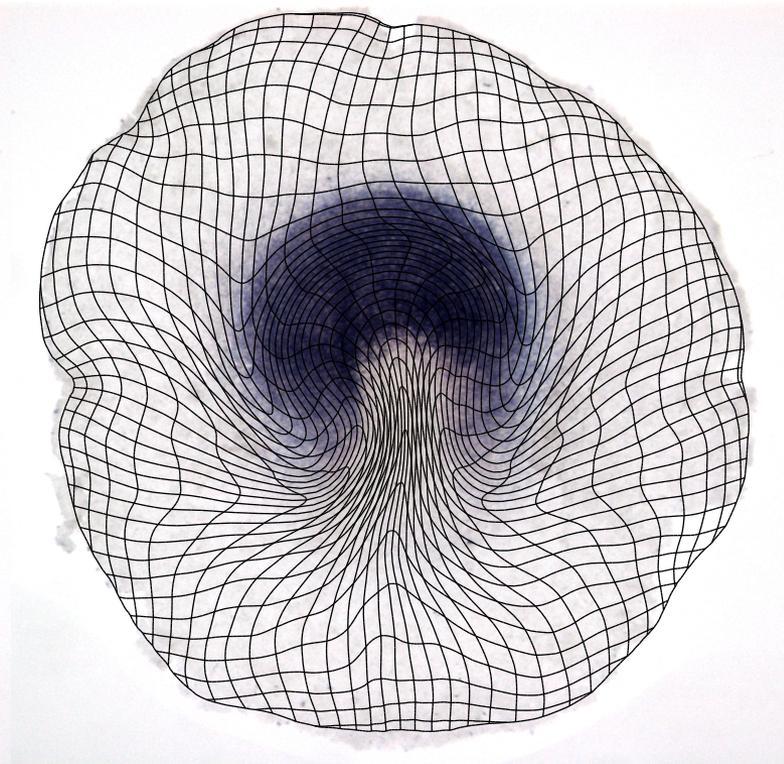


Embryonic territories can be identified from tissue motion

Automated fate mapping



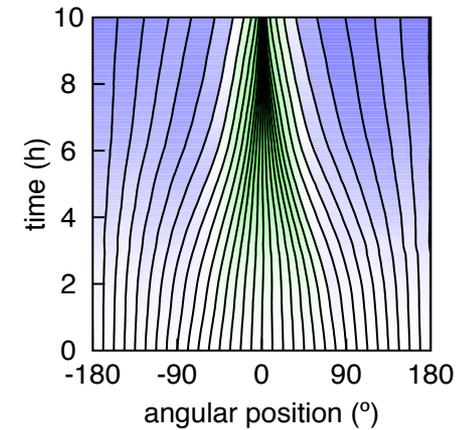
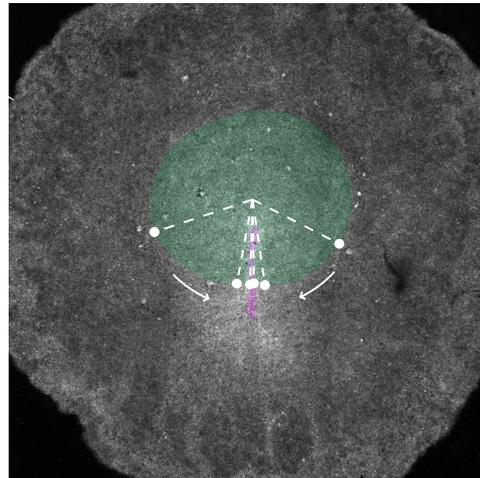
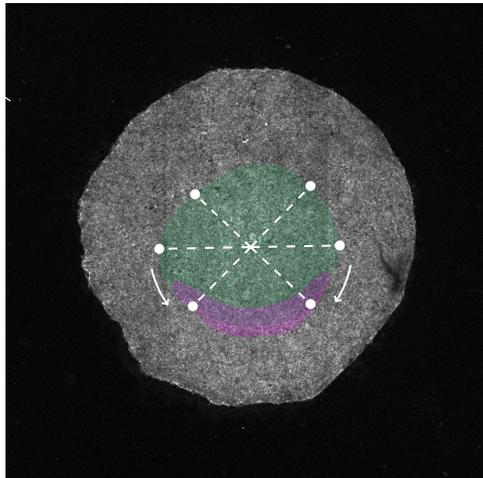
Sox3 + inferred margin



Sox3 + tissue deformation

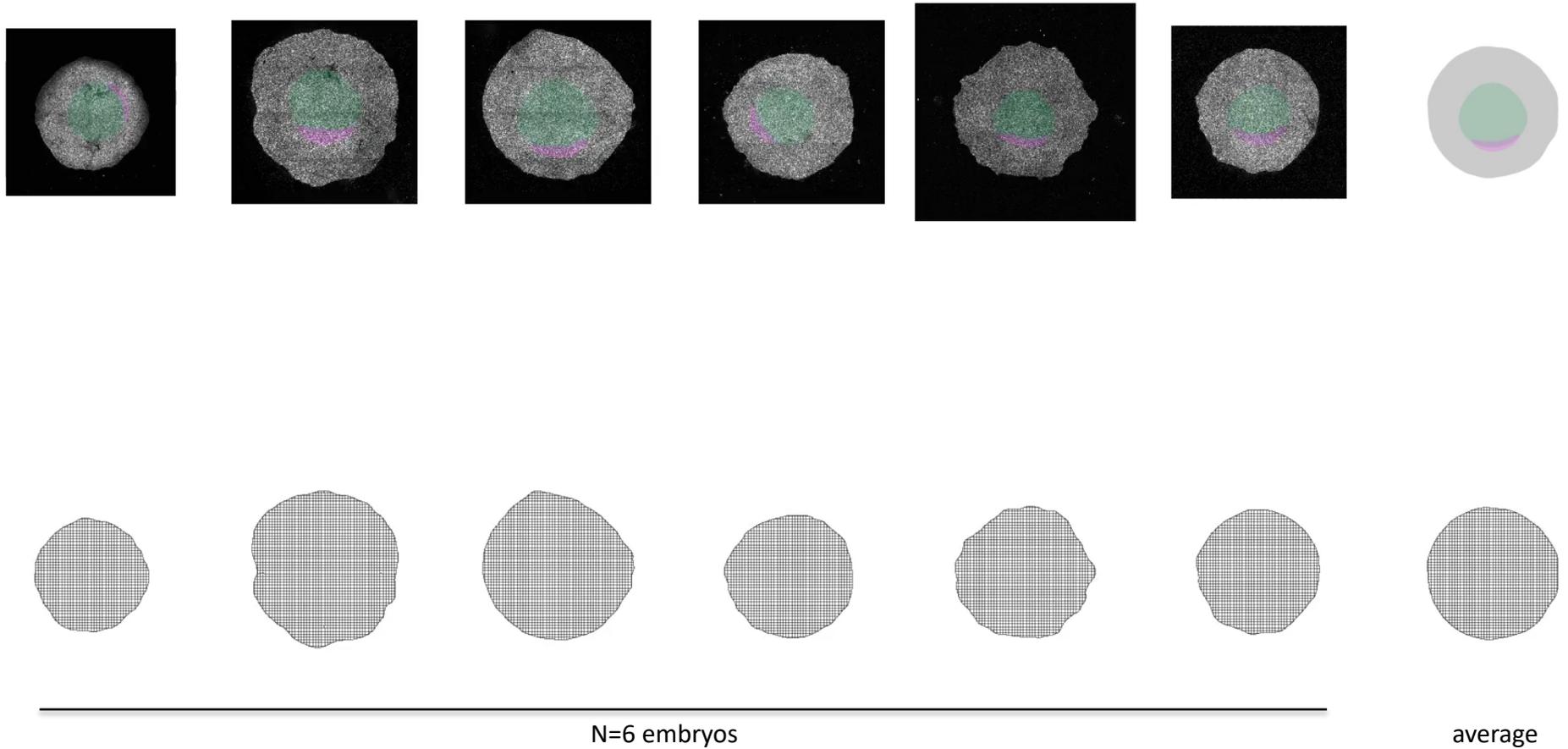
Measuring the progress of gastrulation

embryo proper primitive streak



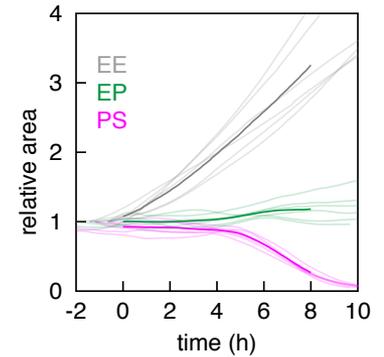
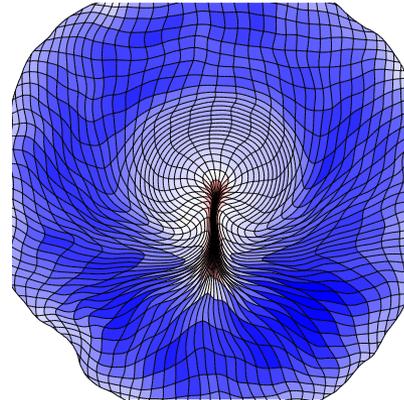
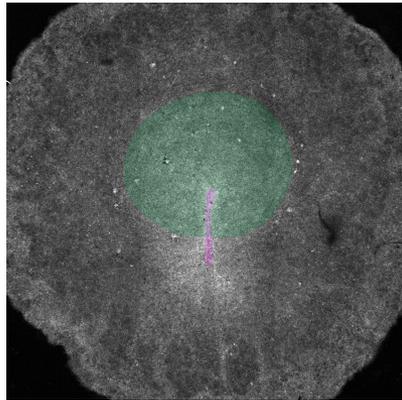
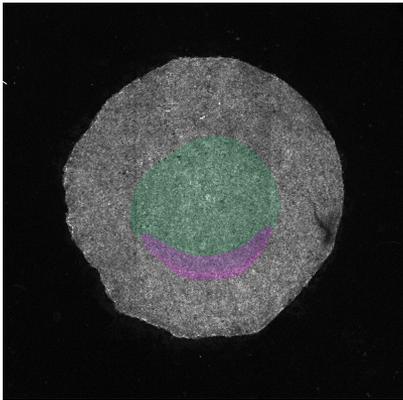
Points along the margin wind around the embryo proper

Building an average embryo



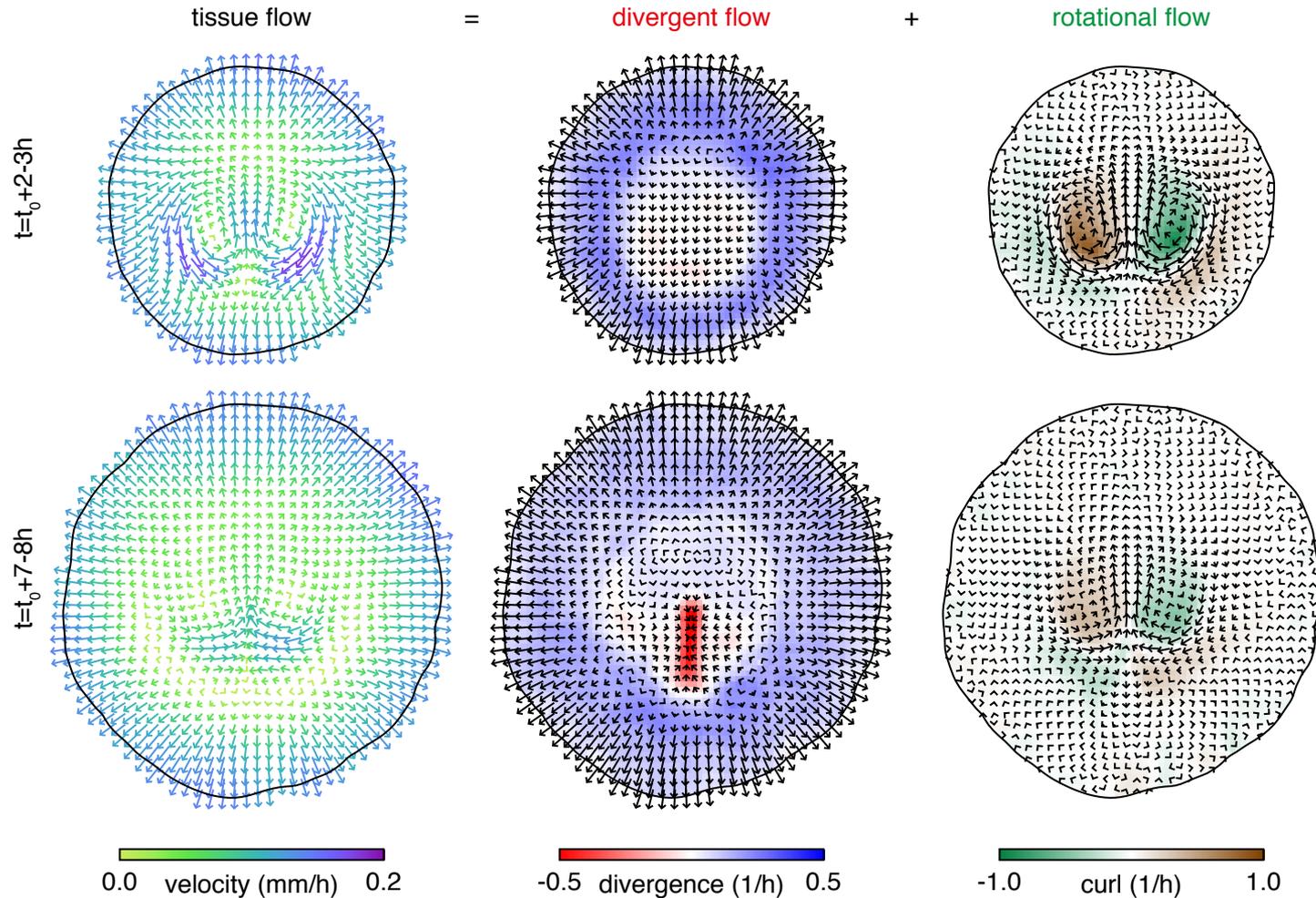
Differential tissue expansion

embryo proper primitive streak



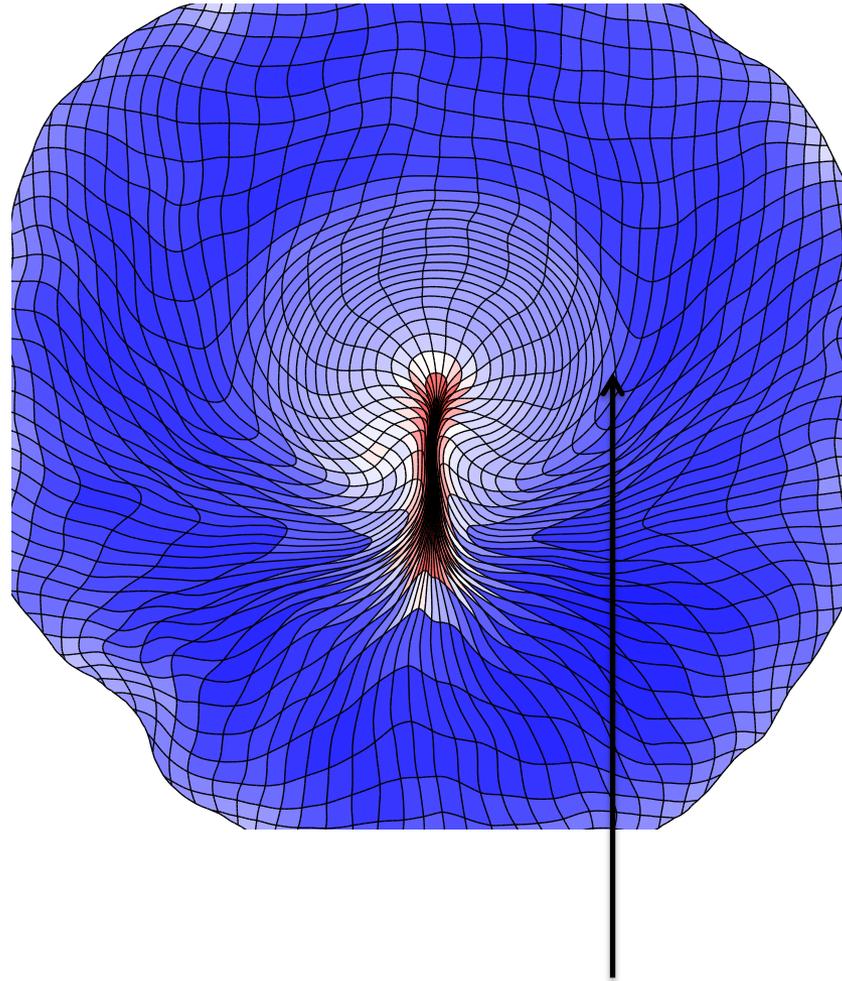
The embryo proper maintains a stable area, while extra-embryonic tissue expands

Tissue flows in the early embryo



Tissue motion can be seen as the sum of simpler flows

Driving forces



Discontinuous deformations suggest localized forces

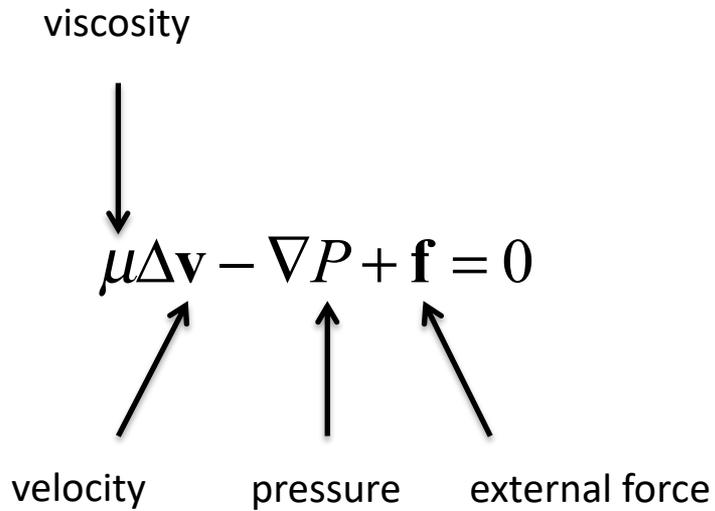
Driving forces

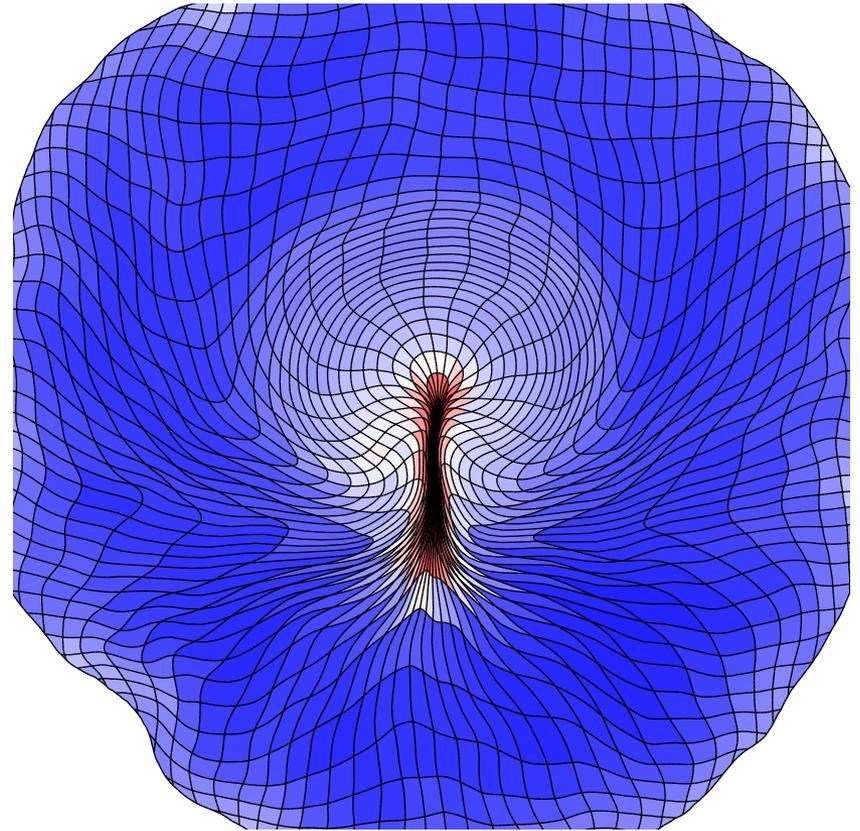
Stokes equation for viscous flow

viscosity

$$\mu \Delta \mathbf{v} - \nabla P + \mathbf{f} = 0$$

velocity pressure external force

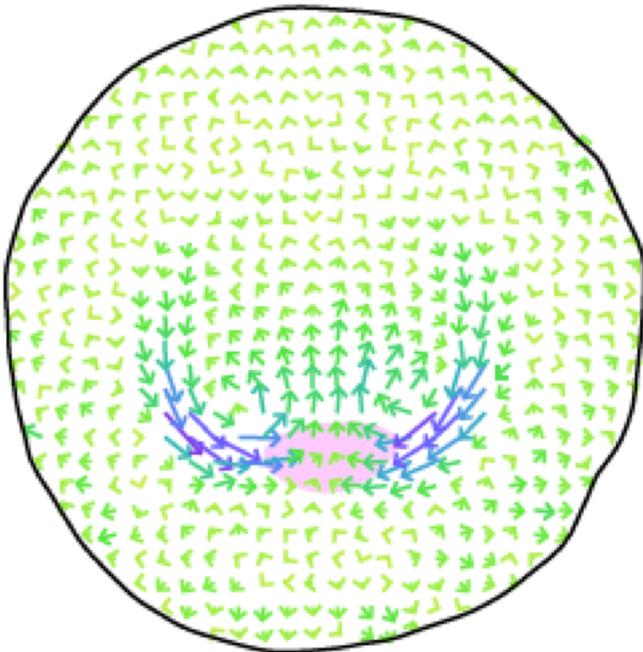
A diagram showing the Stokes equation $\mu \Delta \mathbf{v} - \nabla P + \mathbf{f} = 0$. The word "viscosity" is positioned above the equation with a downward-pointing arrow to the coefficient μ . Below the equation, three labels are placed: "velocity" with an upward-pointing arrow to \mathbf{v} , "pressure" with an upward-pointing arrow to P , and "external force" with an upward-pointing arrow to \mathbf{f} .



Driving forces

Stokes equation

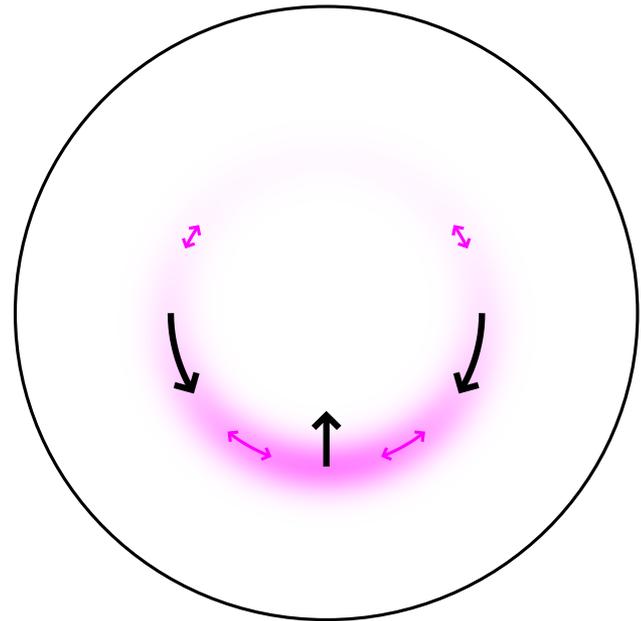
$$\mu\Delta\mathbf{v} - \nabla P + \mathbf{f} = 0$$



$$-\Delta\mathbf{v}$$

Flow driven by internal stresses

$$\mu\Delta\mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$



Graded tension along the embryo margin

A fluid mechanical model

For an incompressible fluid

$$\mu\Delta\mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$

$$\Delta \cdot \mathbf{v} = 0$$

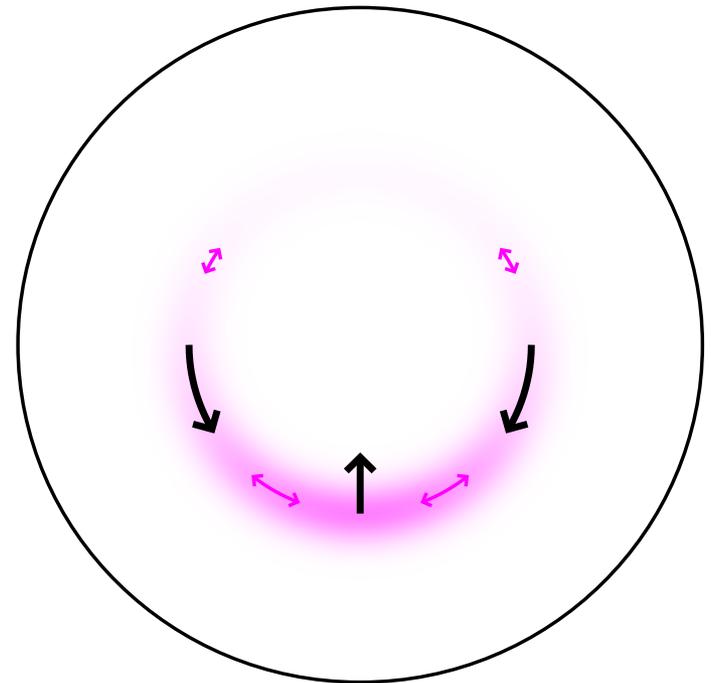
But here areas change

→ modified Stokes equation

$$\mu\Delta\mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$

$$\Delta \cdot \mathbf{v} = \gamma$$

Flow driven by active stresses



Area changes treated as intrinsic behaviors of embryonic territories

Active stresses

$$\mu \Delta \mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$

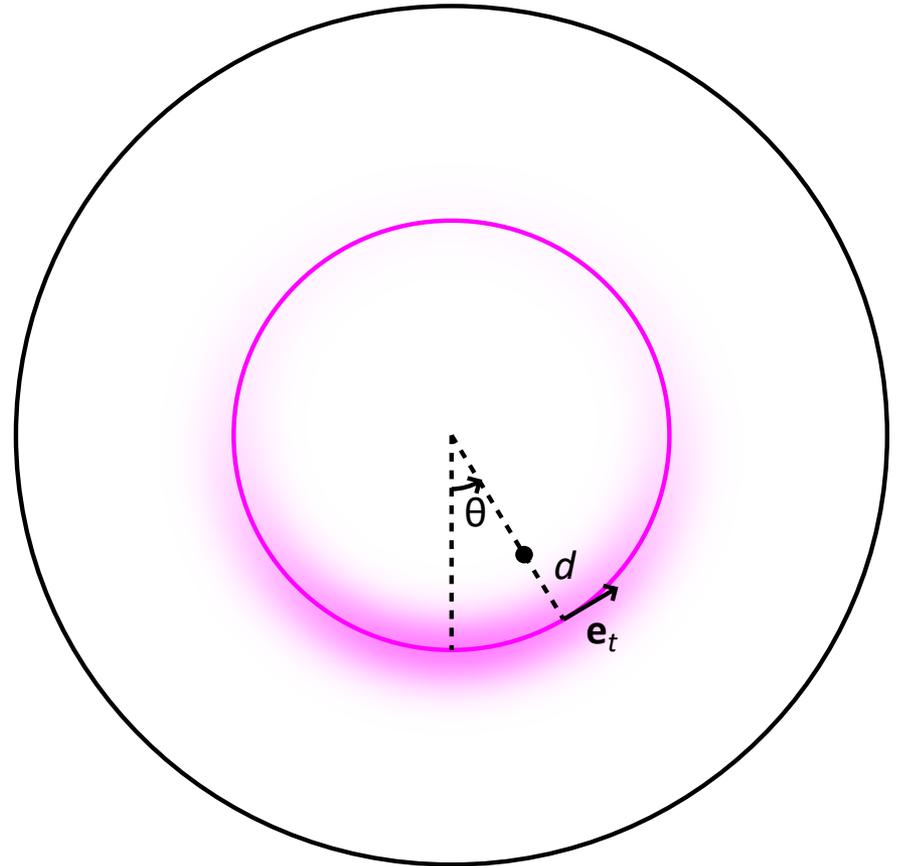
$$\Delta \cdot \mathbf{v} = \gamma$$

angular tension profile



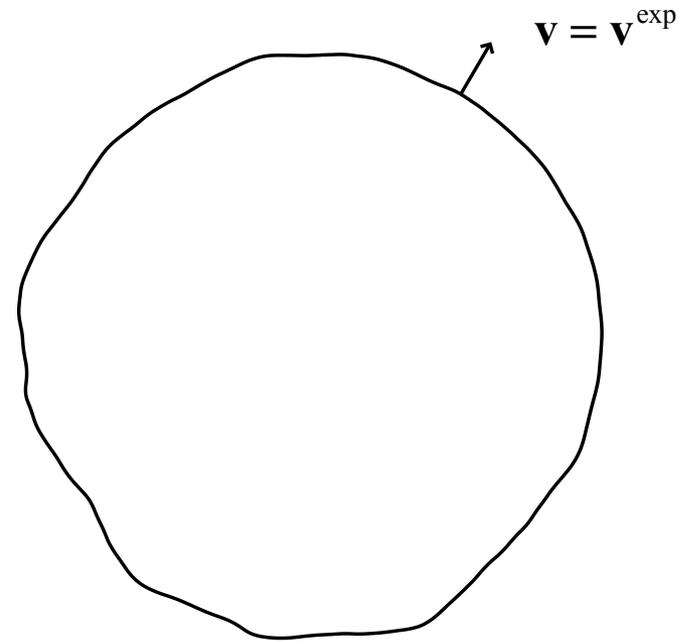
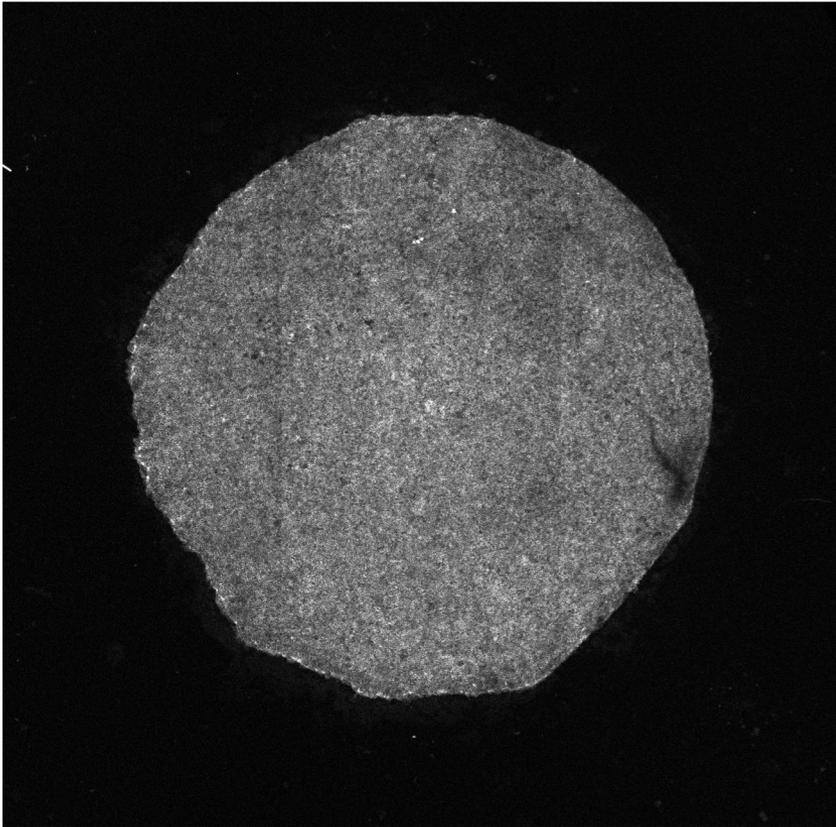
$$\boldsymbol{\sigma}_a(\mathbf{r}, t) = \frac{T(\theta, t)}{\sqrt{2\pi w^2}} e^{-\frac{d^2}{2w^2}} \mathbf{e}_t \otimes \mathbf{e}_t$$

constant, uniform width



Tensile ring that moves with the tissue

Boundary condition



The tissue border is attached to the vitelline membrane \rightarrow prescribed velocity

Tissue flows in the model

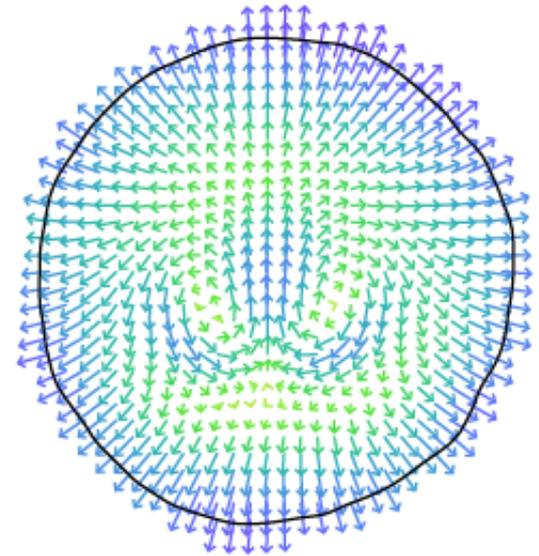
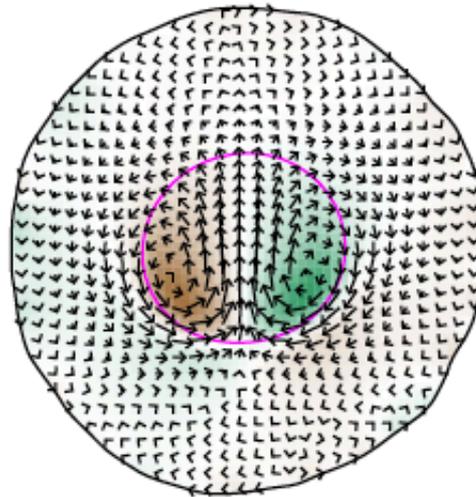
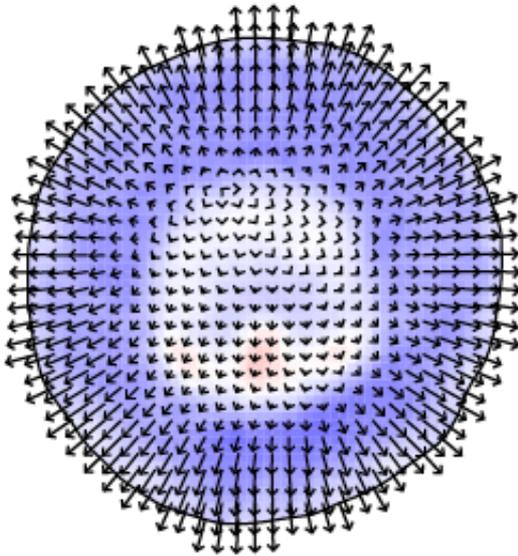
area changes

+

tension-driven flow

=

model flow

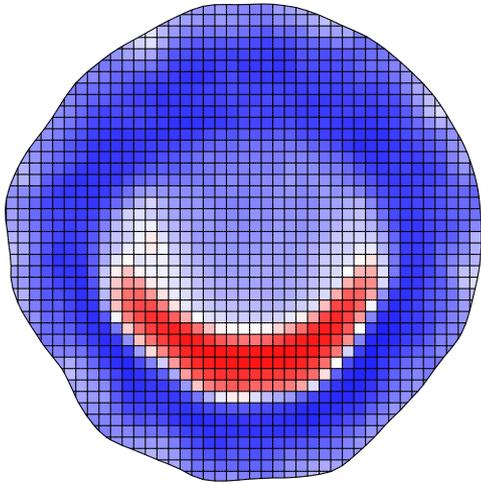


$$\mu \Delta \mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$

$$\Delta \cdot \mathbf{v} = \gamma$$

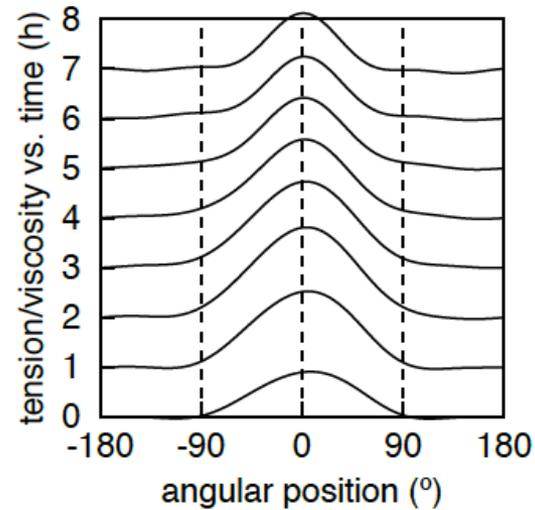
Fitting the model

area changes



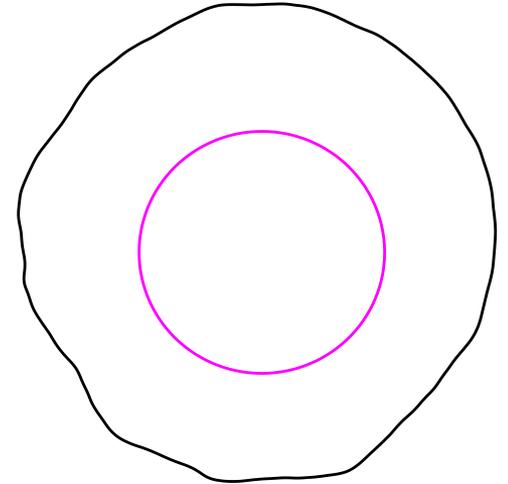
taken from experiment

time-dependent tension profile

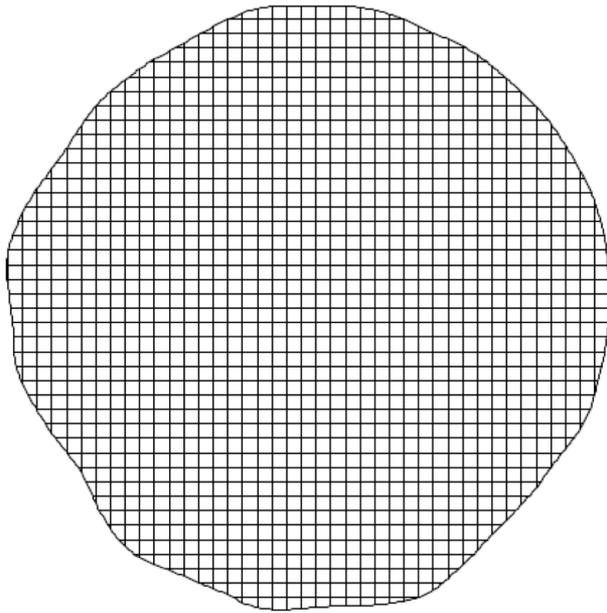


fit to observed motion

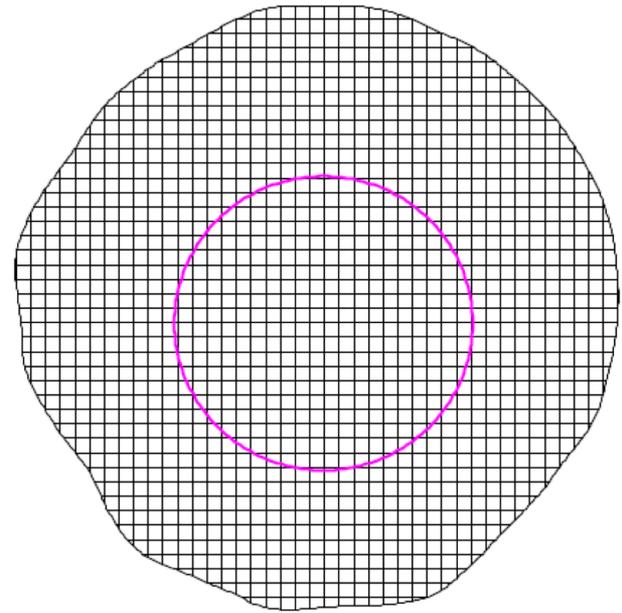
initial margin position



Model vs. experiment



experiment



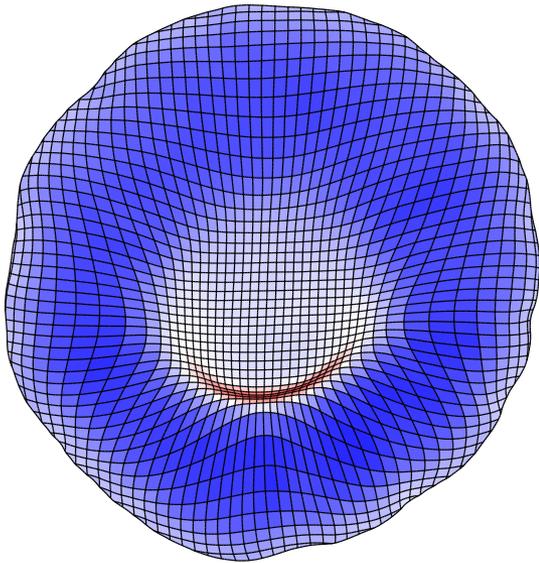
model

residual $\sim 10\%$

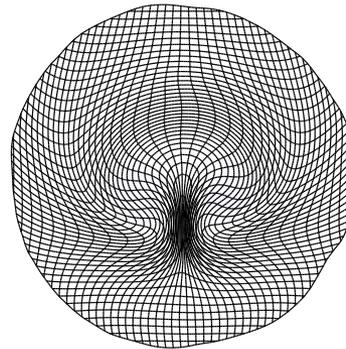
Relative contributions to morphogenesis

$$\mu\Delta\mathbf{v} - \nabla P + \Delta \cdot \boldsymbol{\sigma}_a = 0$$

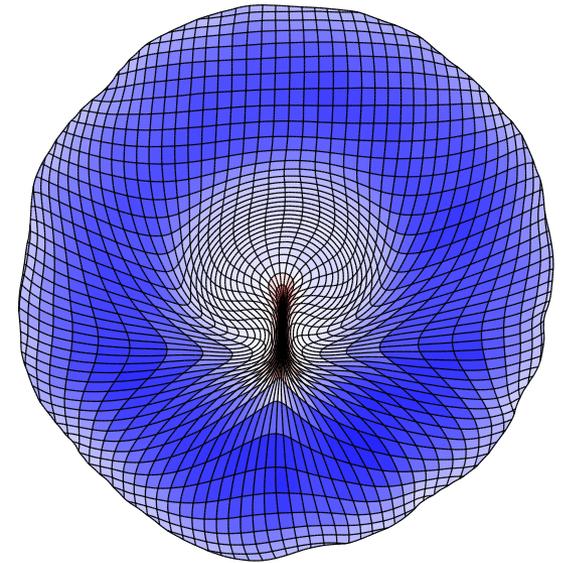
$$\Delta \cdot \mathbf{v} = \gamma$$



area changes alone



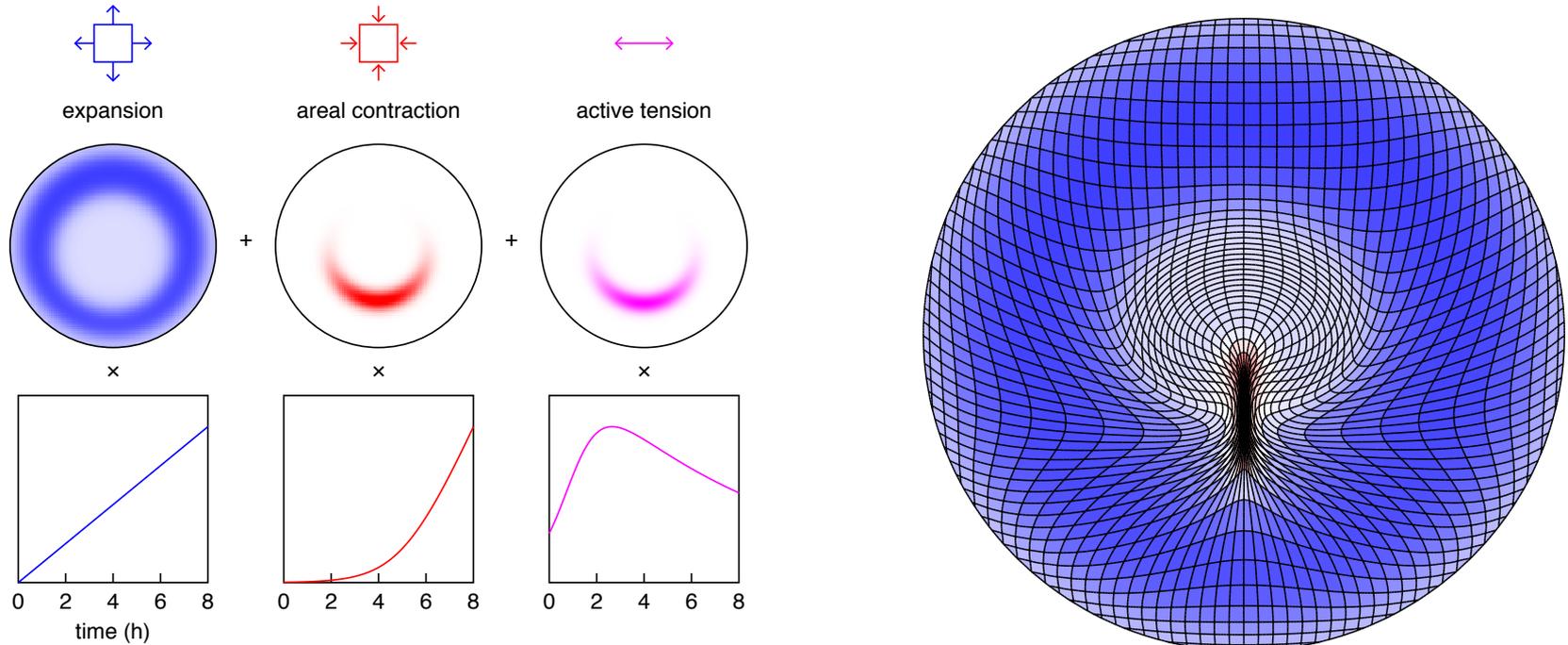
active stresses alone



both

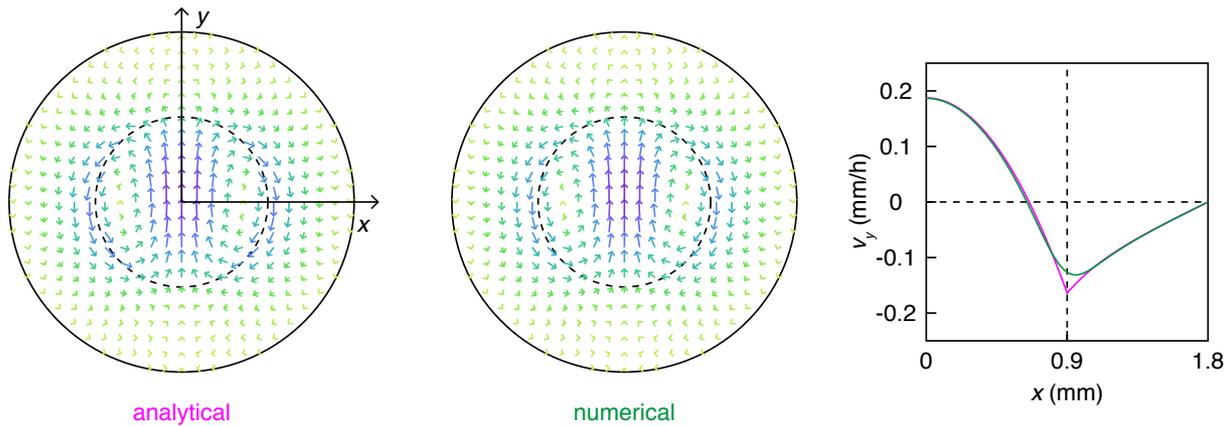
Active stresses largely account for the shaping of the embryo

A "synthetic" embryo



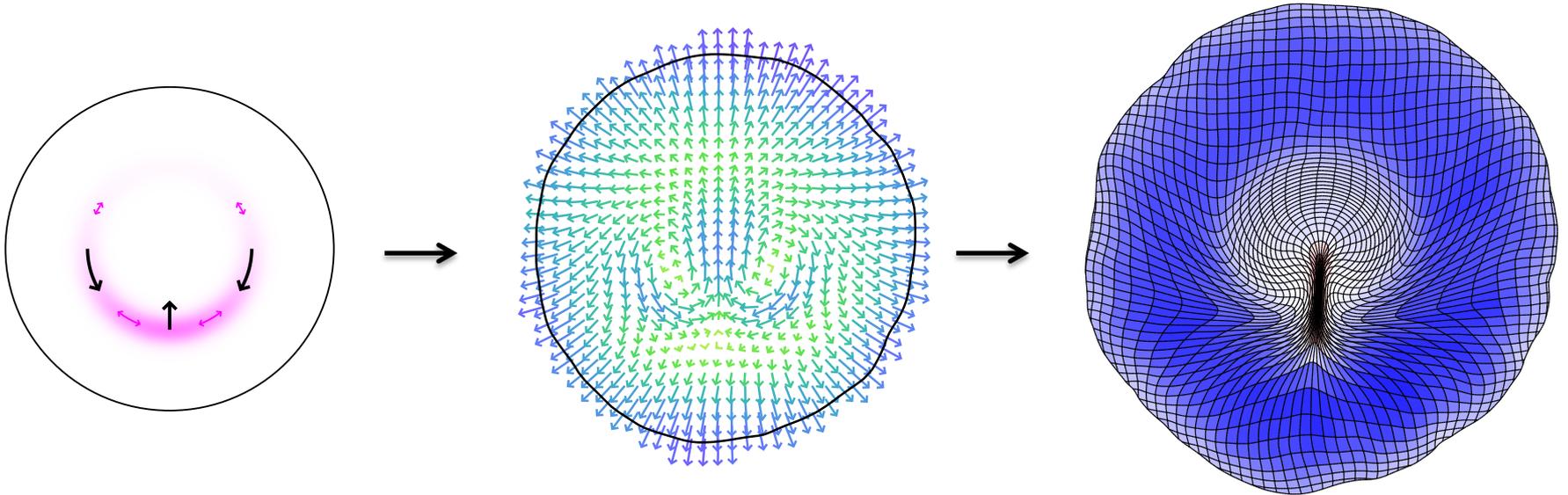
Source terms replaced by simple mathematical functions of space and time

Analytical model



The velocity field can be computed in the limit of a thin margin

Challenging the model



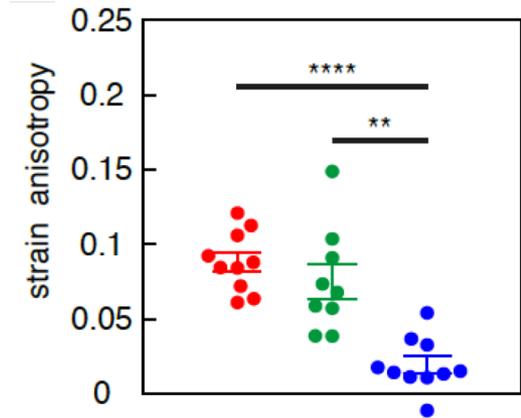
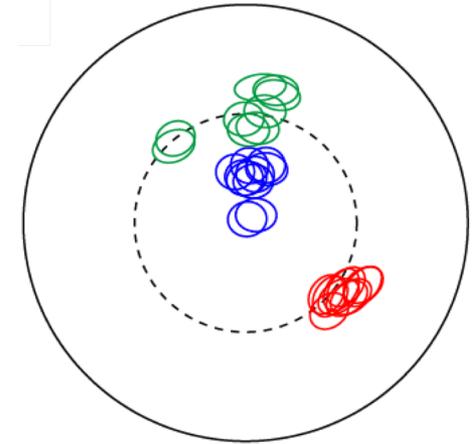
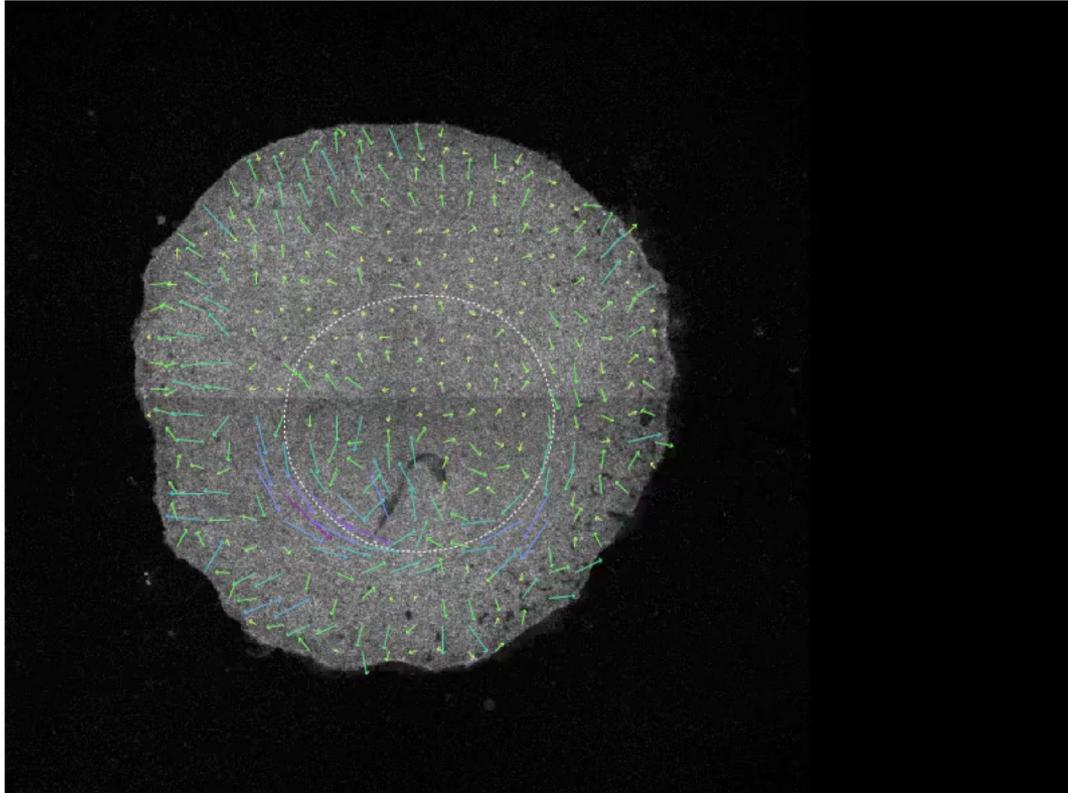
Can we directly evidence active stresses in the tissue?

How are active stresses generated?

What is the basis of tissue fluidity?

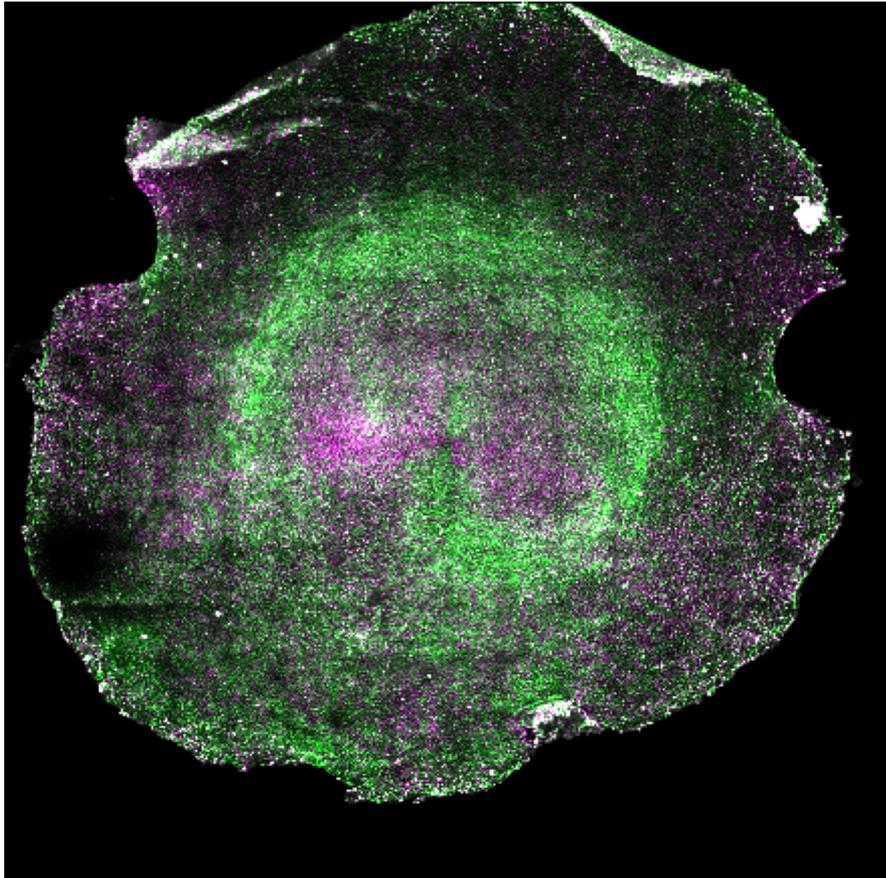
Can we manifest hydrodynamic effects in the epiblast?

A tensile margin revealed



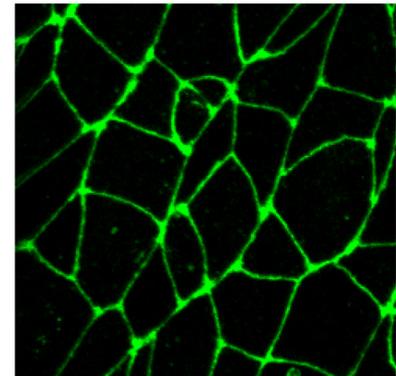
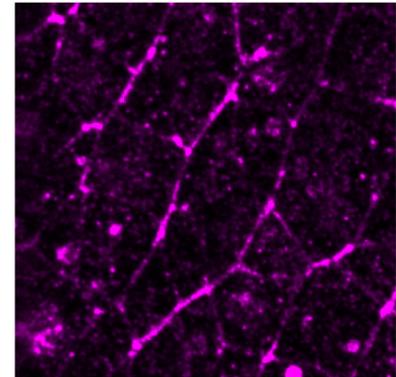
Laser ablations reveal anisotropic stresses

A tensile margin revealed



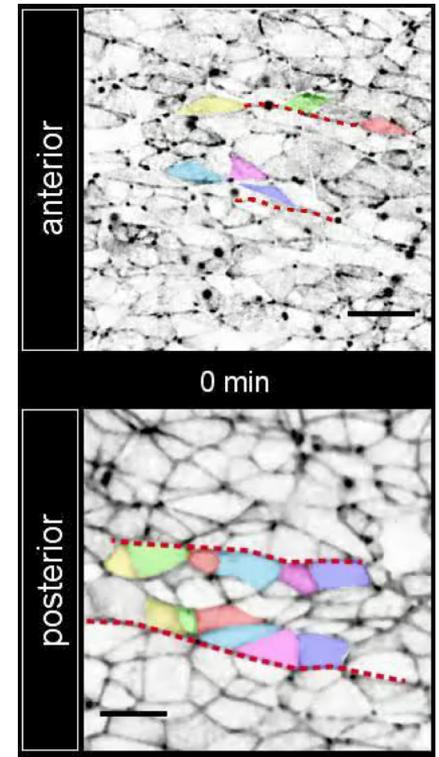
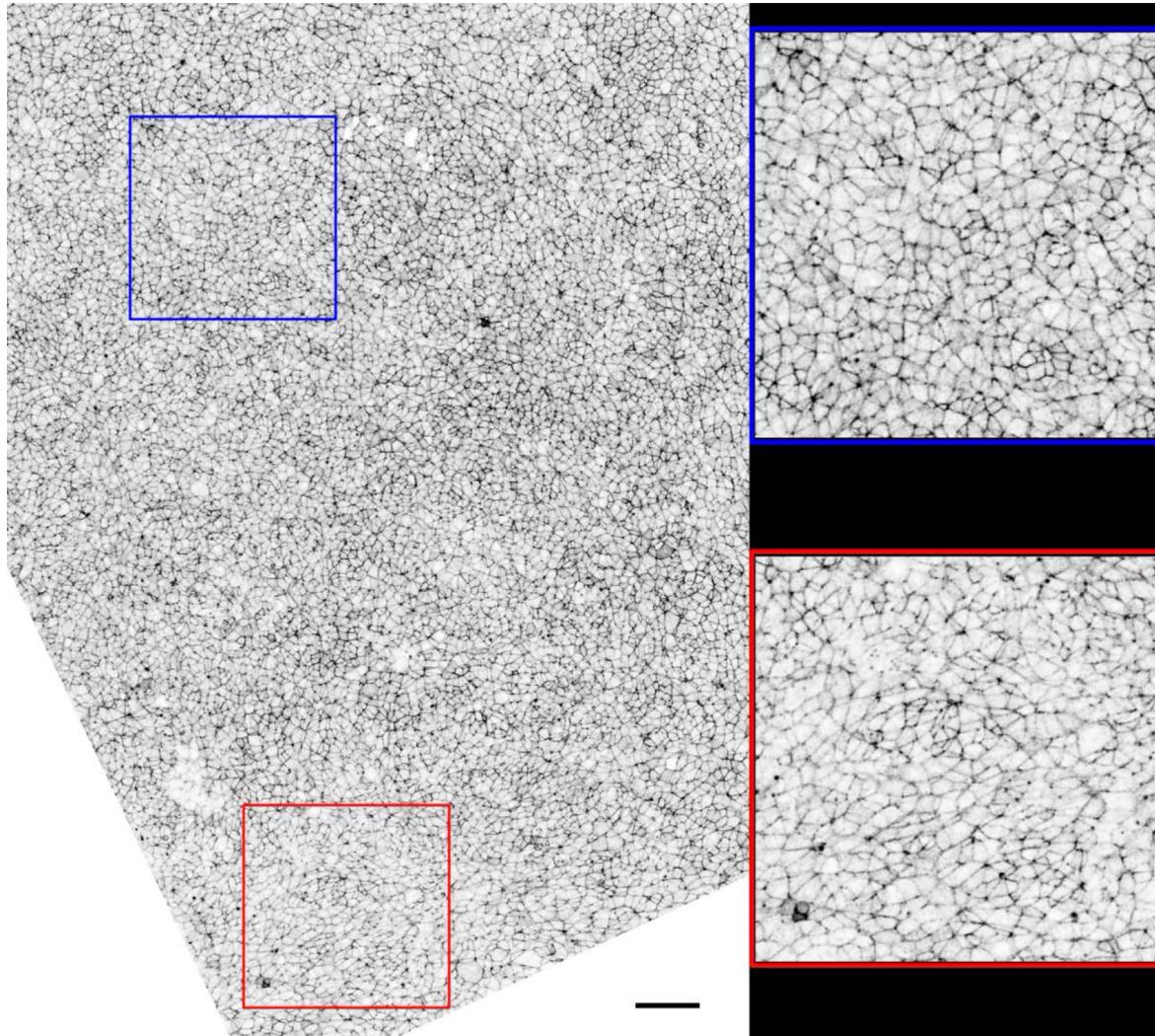
A supracellular actomyosin ring

p-Myosin ZO1



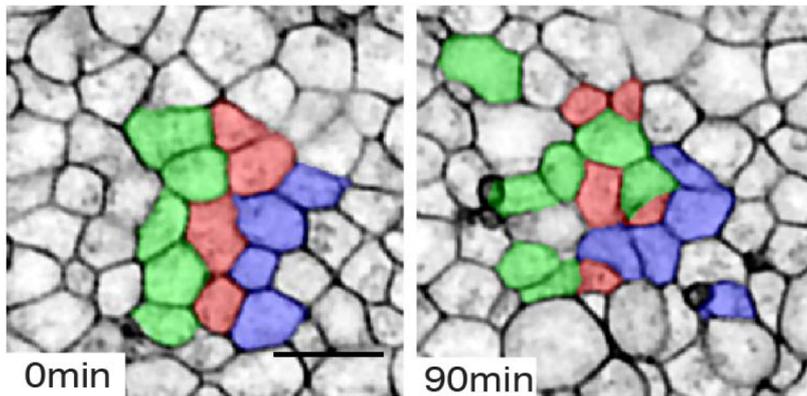
10µm

A tensile margin revealed

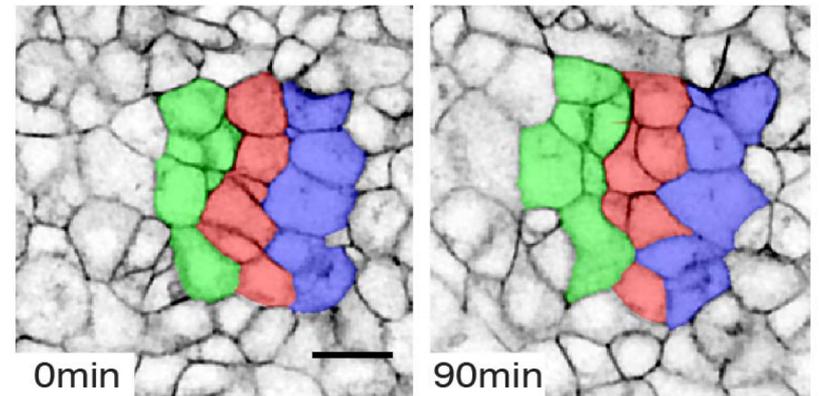


tdTomato myosin

Cell division and tissue fluidity



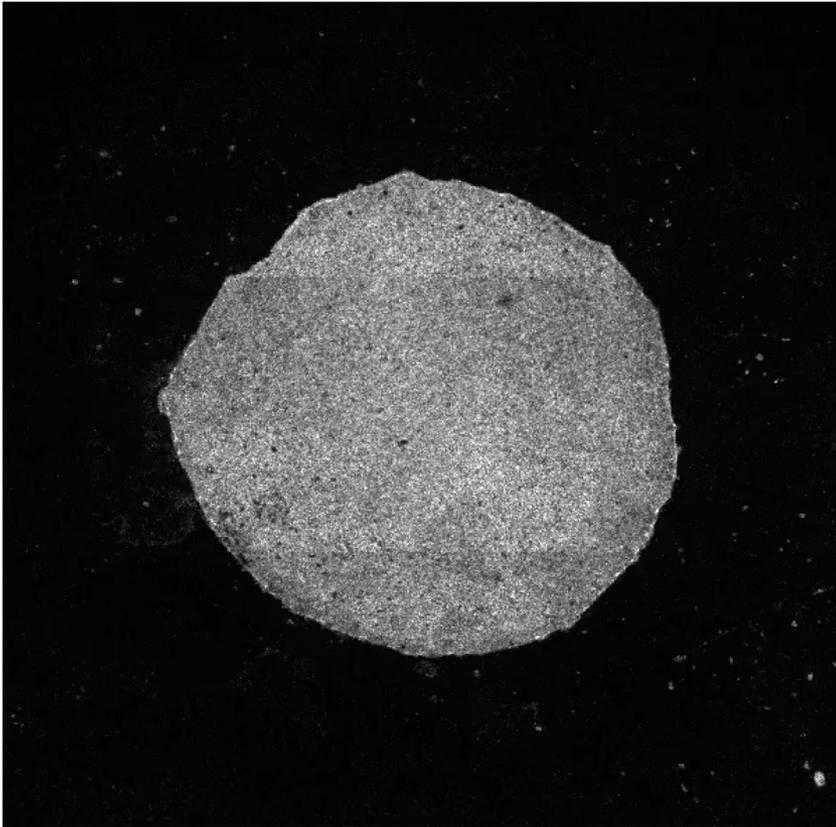
control



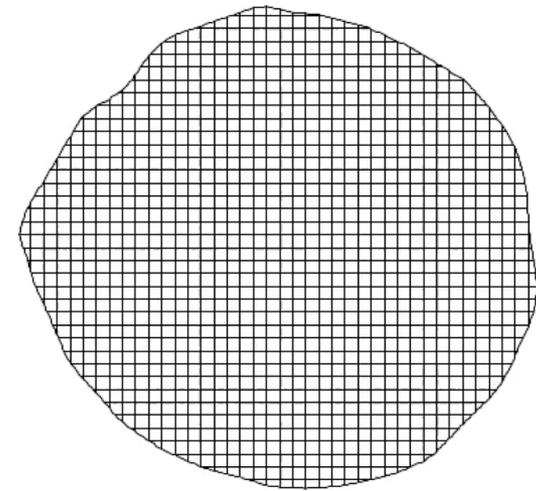
divisions inhibited
(HU+Q-VD-Oph)

Cell-division-mediated rearrangements

Cell division and tissue fluidity

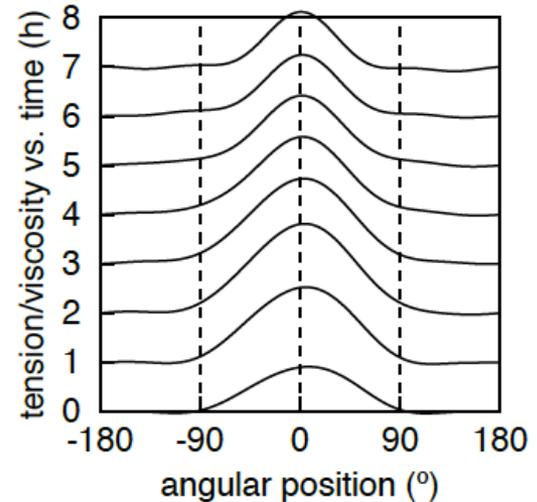
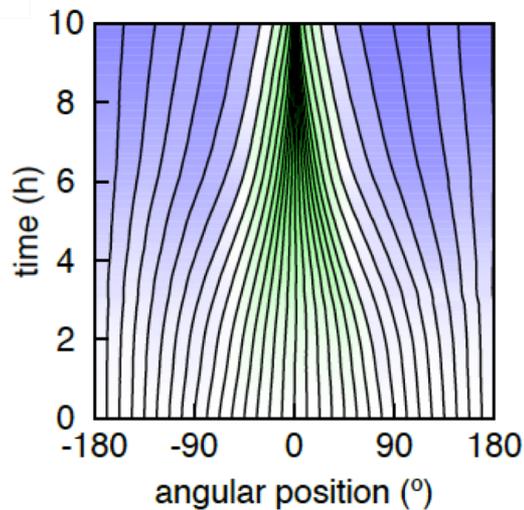


divisions inhibited
(HU+Q-VD-Oph)

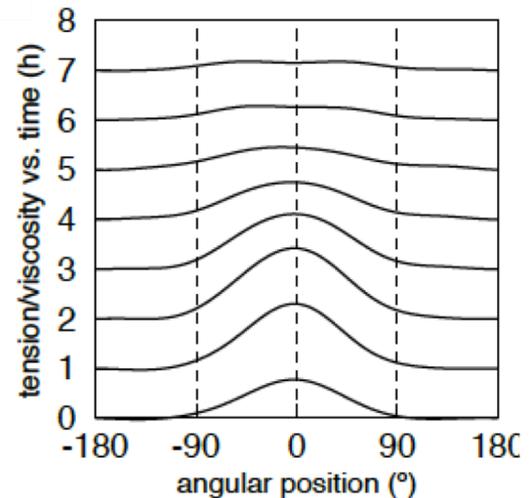
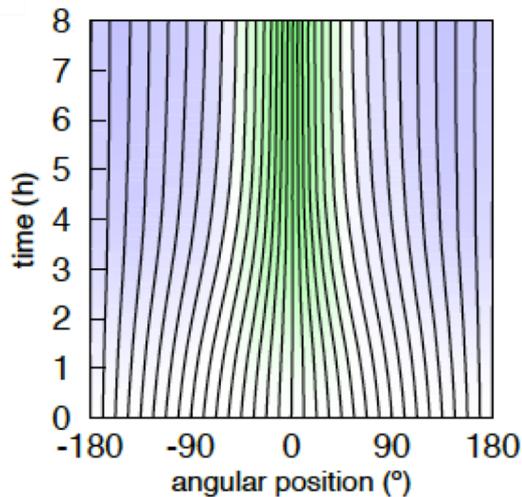


Cell division and tissue fluidity

control



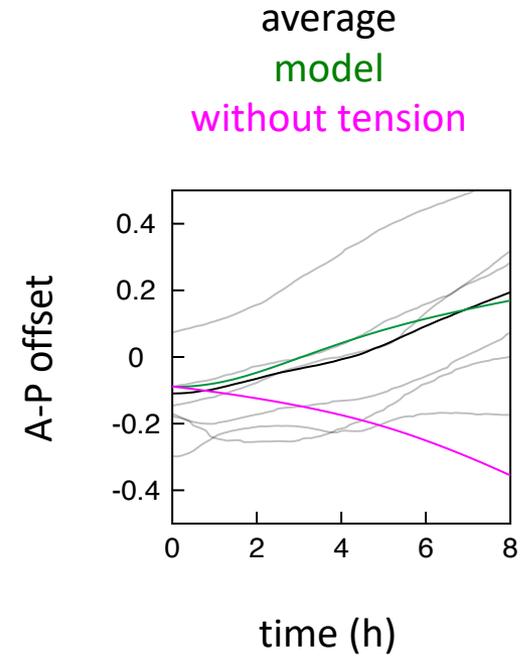
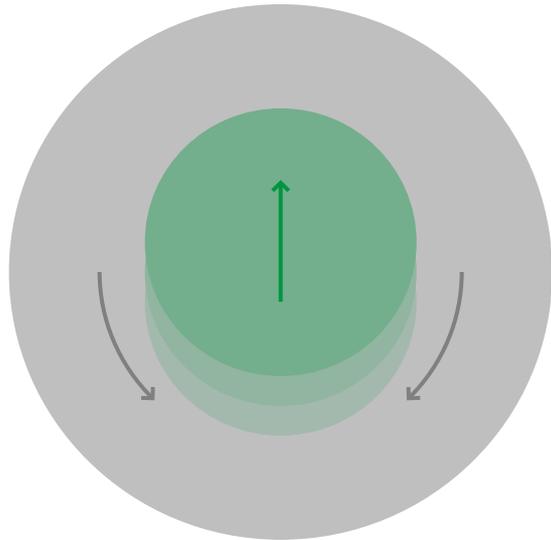
HU+Q-VD-Oph



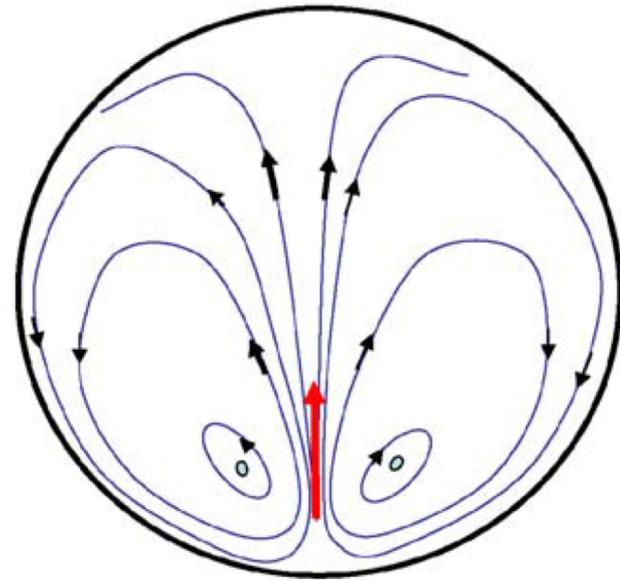
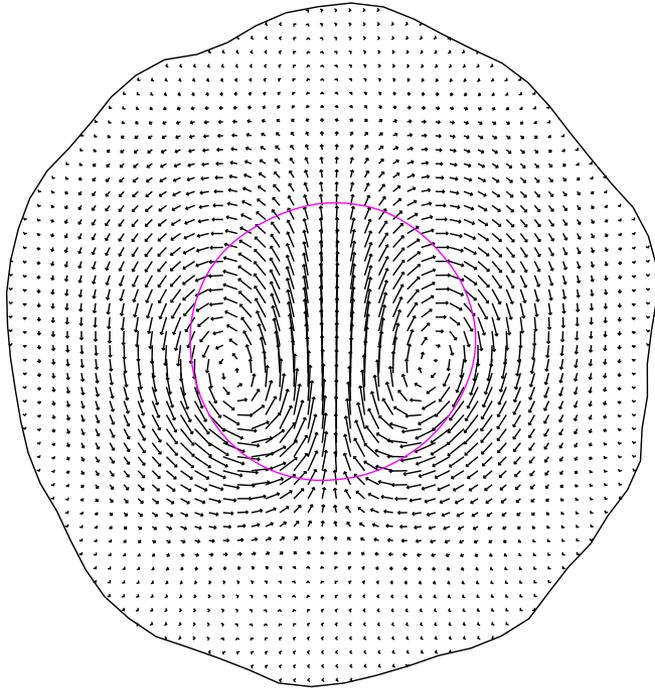
motion along the margin

tension/viscosity profiles

The embryo as a swimmer

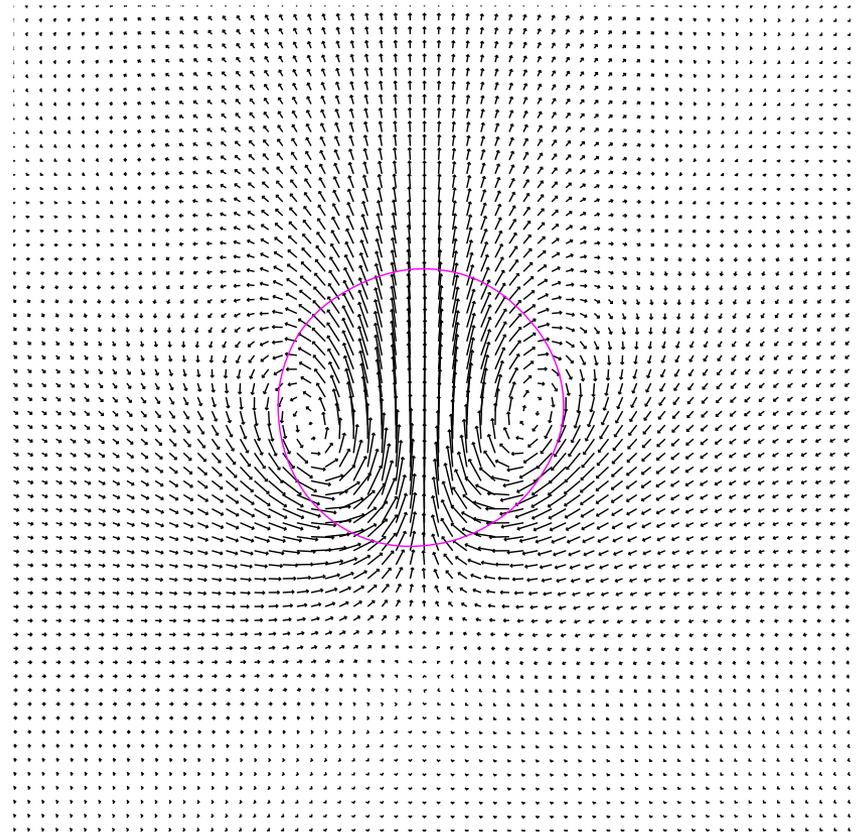
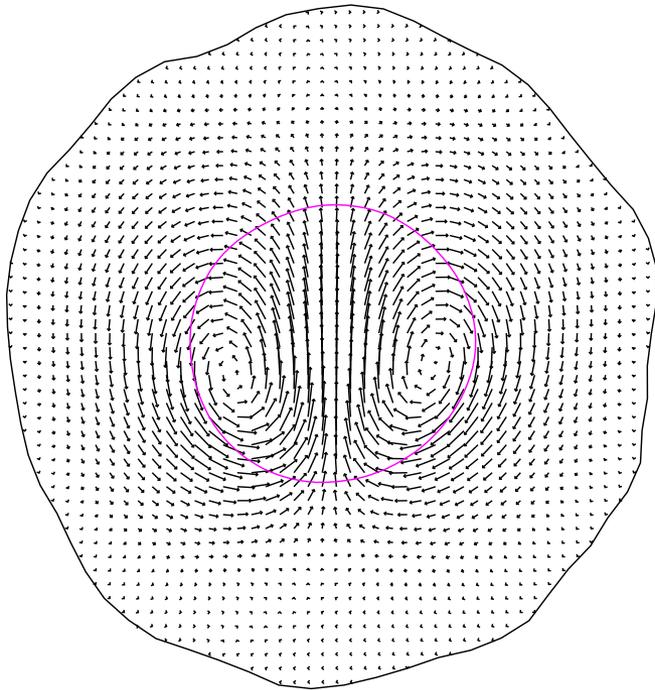


A limited role for boundary conditions



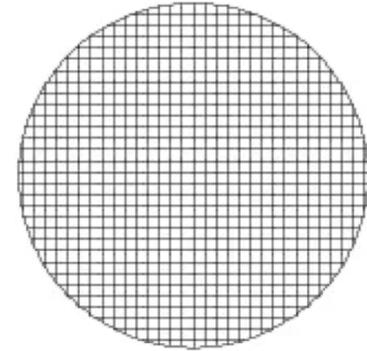
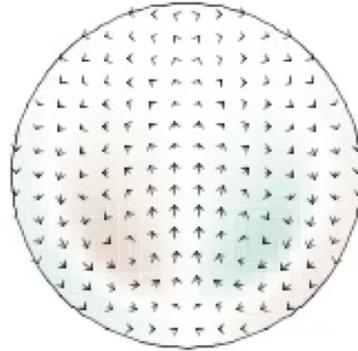
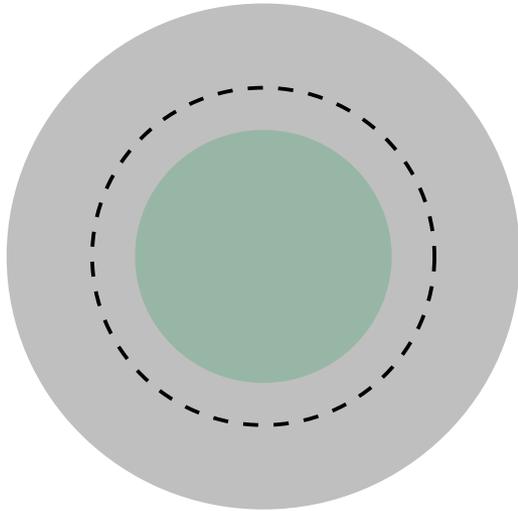
Chuai & Weijer 2008

A limited role for boundary conditions

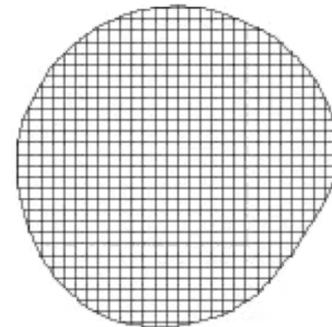
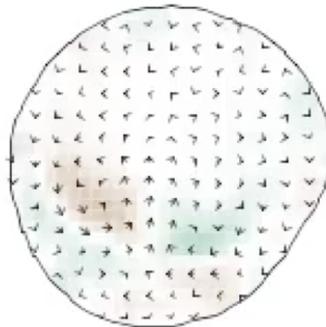
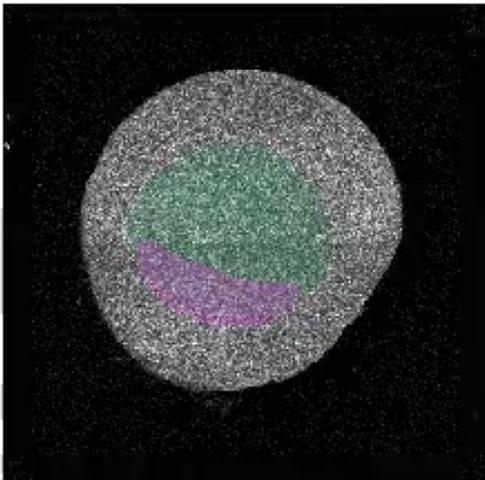


The force distribution shapes the flow

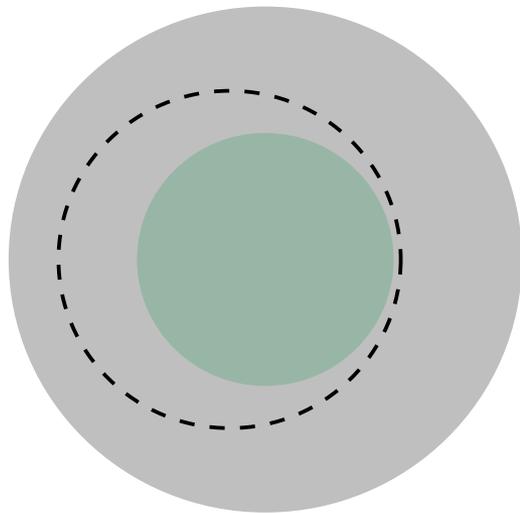
A limited role for boundary conditions



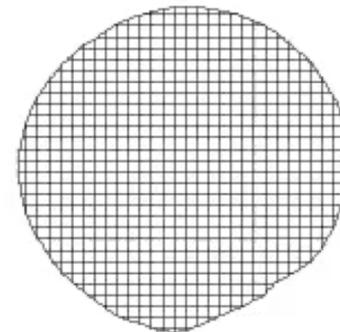
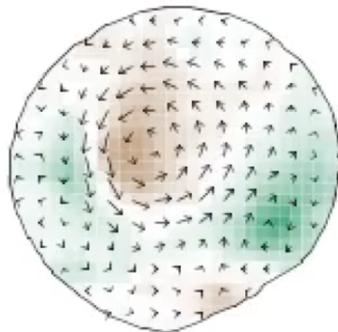
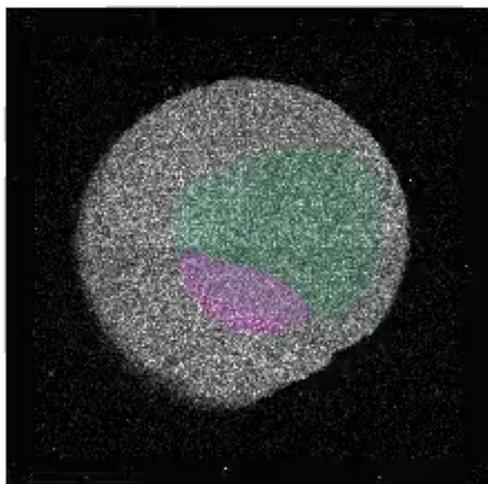
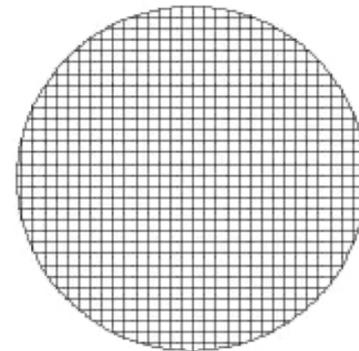
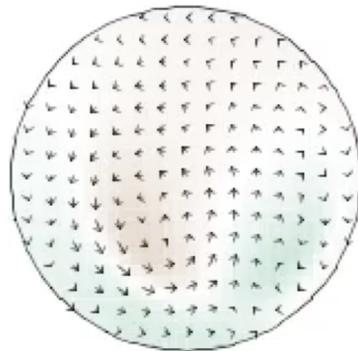
Ablation of extra-embryonic tissue



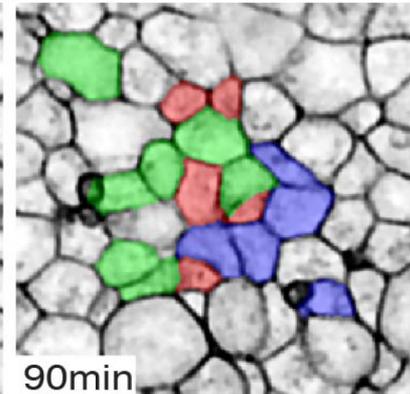
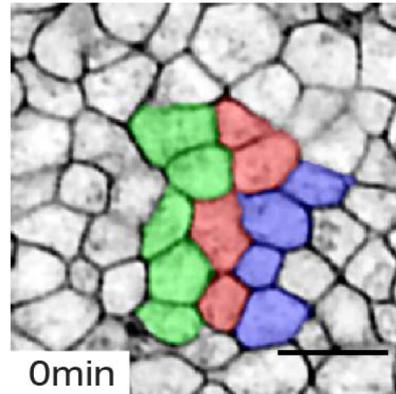
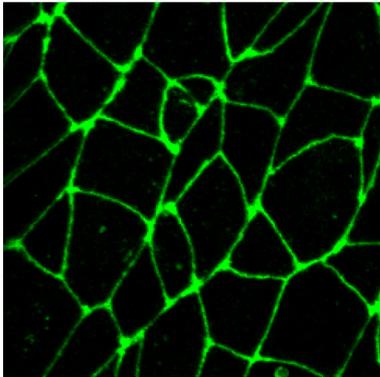
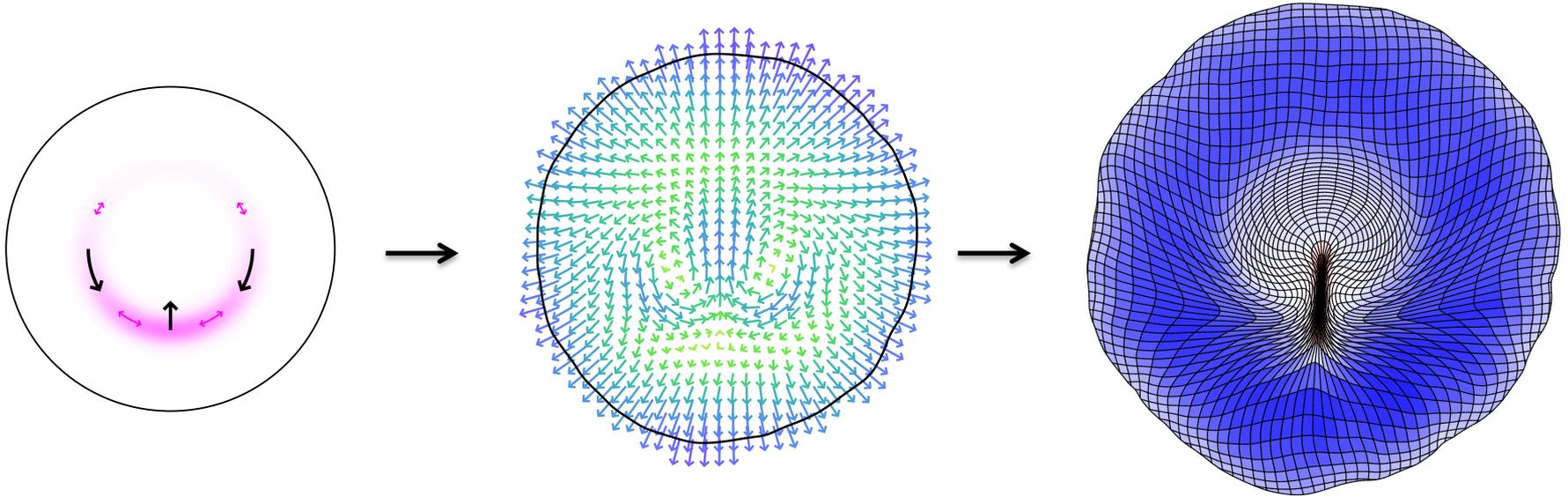
Interaction with the boundary



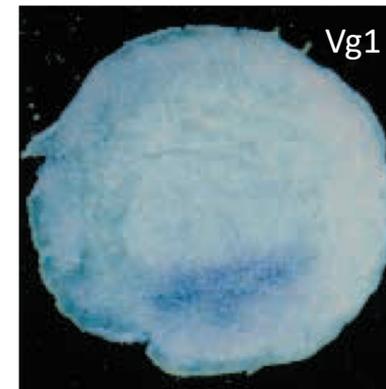
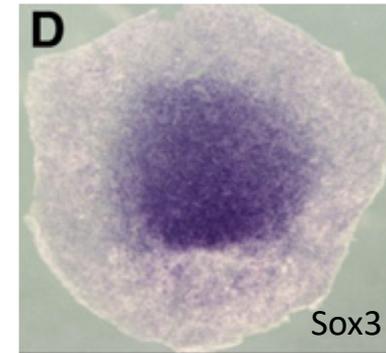
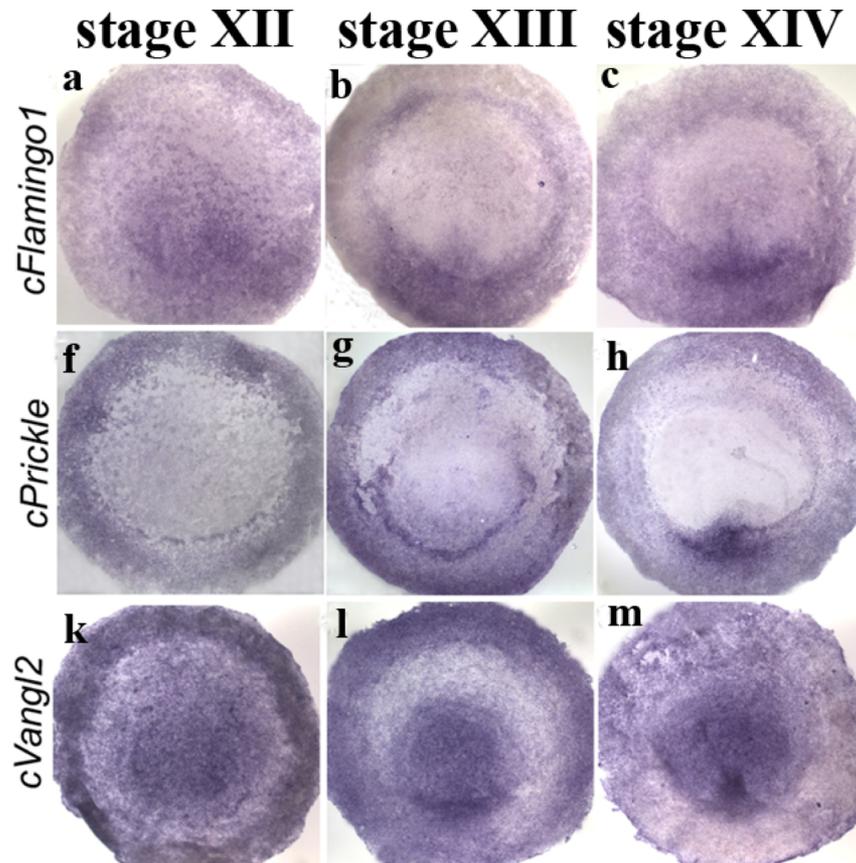
Off-centered cut



Conclusion



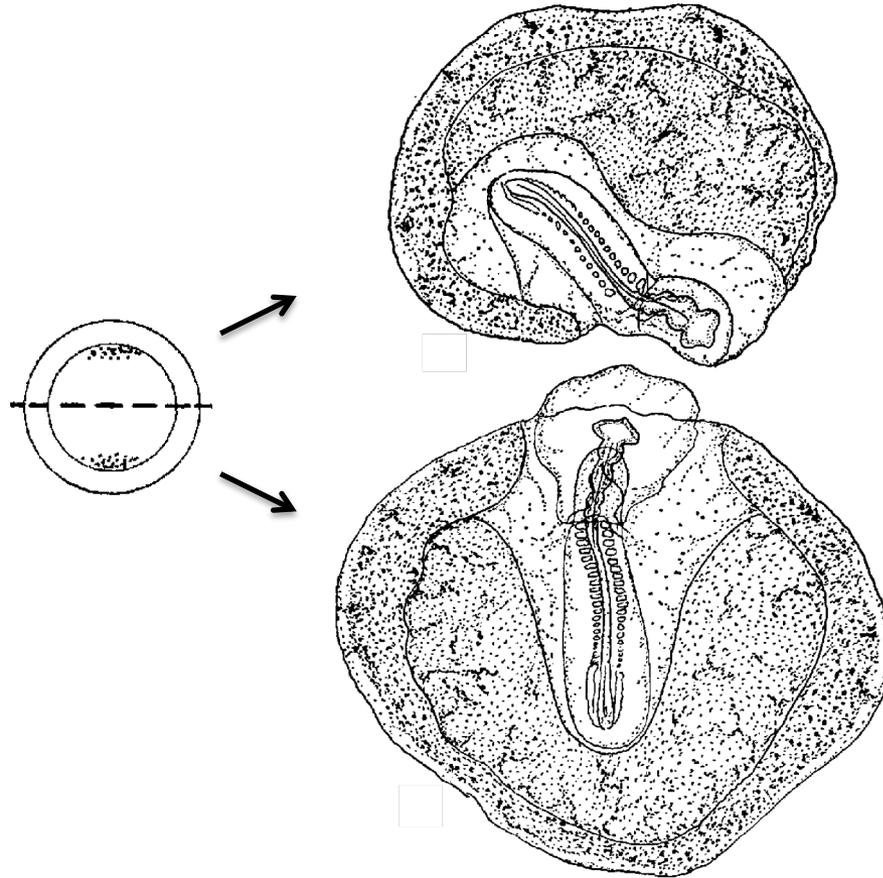
How is all this controlled?



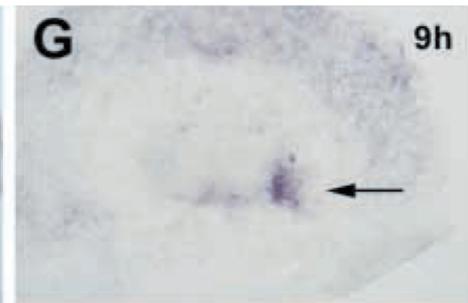
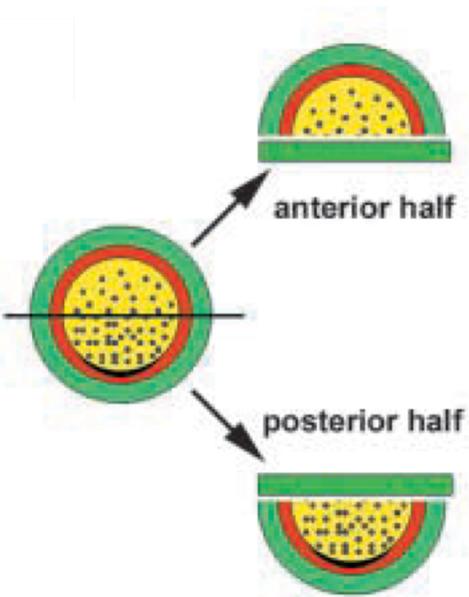
Downstream of gene expression patterning?

Voiculescu et al 2007
Acloque et al 2011
Shah et al 1997

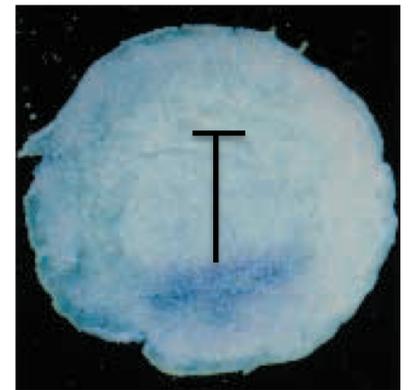
Embryonic regulation



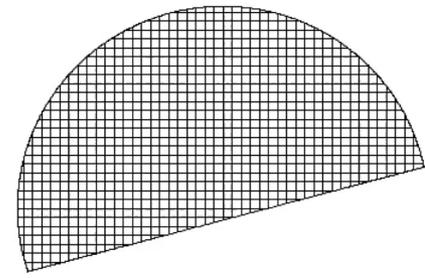
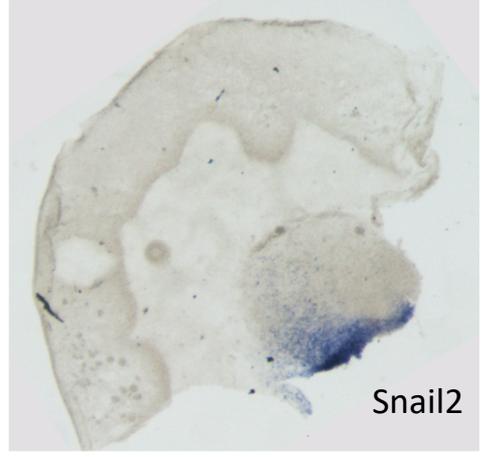
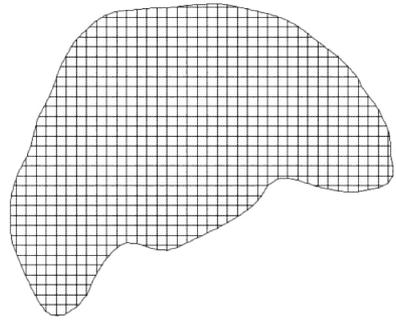
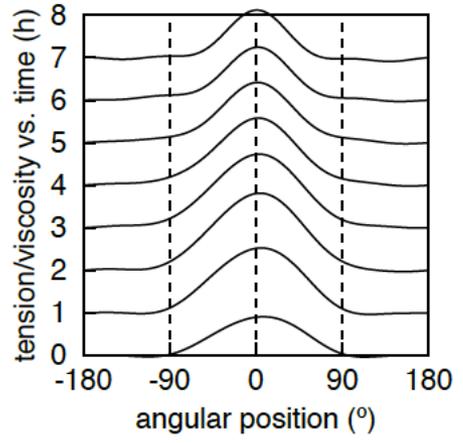
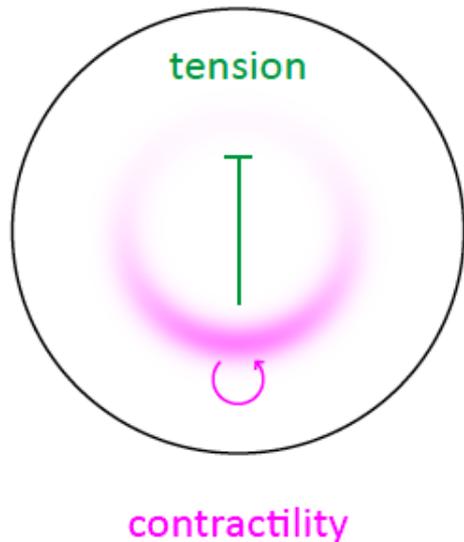
Molecular basis of regulation



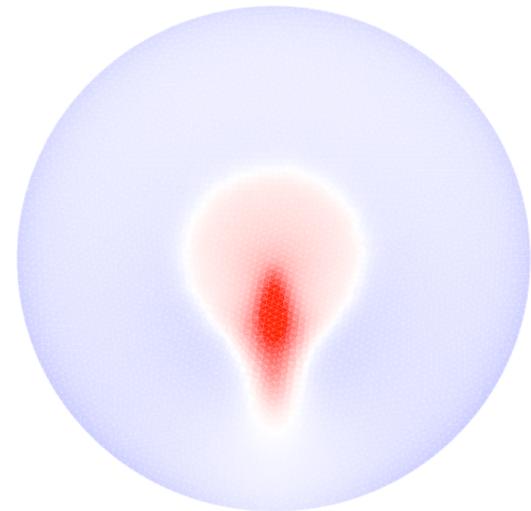
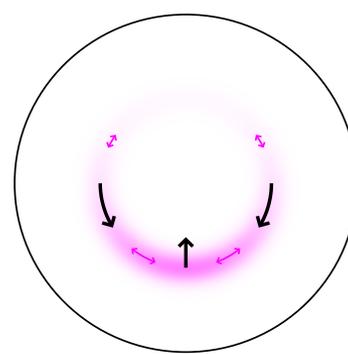
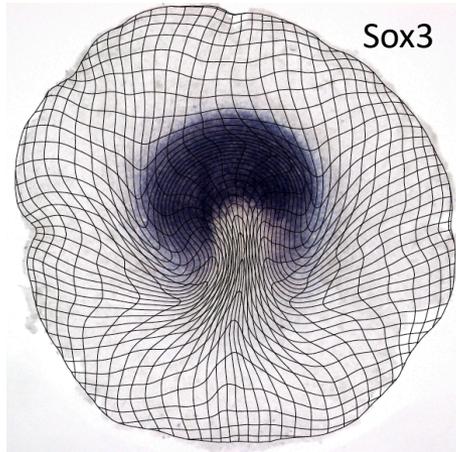
Diffusing inhibitor prevents ectopic embryo formation?



A mechanical basis for regulation?



Interplay between mechanics and fate specification?



stretching

compression

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