Mechanics of gastrulation
The forces that shape the early avian embryo

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How do organisms acquire their shape?

Morphogenesis involves coordinated cell shape changes, rearrangements, and motion.

*Drosophila* embryo
How do organisms acquire their shape?

Morphogenesis is driven by mechanical forces generated on the cellular scale.
Simple morphogenetic processes

Convergent extension

Invagination

Guillot & Lecuit Science 2013
Gastrulation in the avian embryo

Epiblast cells converge towards the posterior to form the primitive streak.
Gastrulation in the avian embryo

Primitive streak formation is accompanied by ‘Polonaise’ movements

Gräper, Wetzel 1929
Motions reminiscent of fluid flow

Chuai & Weijer 2008
Fleury 2005

Gräper, Wetzel 1929
Tissue flows in the early embryo

memGFP quail embryo

1mm

-2.0 log(relative area)  2.0
Tissue flows in the early embryo
Automated fate mapping

Embryonic territories are readily identified in deformation maps.
Automated fate mapping

Embryonic territories can be identified from tissue motion
Automated fate mapping

Sox3 + inferred margin

Sox3 + tissue deformation
Measuring the progress of gastrulation

Points along the margin wind around the embryo proper
Building an average embryo

N=6 embryos
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

\[ \text{tissue flow} = \text{divergent flow} + \text{rotational flow} \]
Driving forces

Discontinuous deformations suggest localized forces
Driving forces

Stokes equation for viscous flow

\[ \mu \Delta v - \nabla P + f = 0 \]
Driving forces

Stokes equation

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

Flow driven by internal stresses

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

Gradated tension along the embryo margin
A fluid mechanical model

For an incompressible fluid

\[ \mu \Delta v - \nabla P + \Delta \cdot \sigma_a = 0 \]
\[ \Delta \cdot v = 0 \]

But here areas change
\[ \rightarrow \text{modified Stokes equation} \]

\[ \mu \Delta v - \nabla P + \Delta \cdot \sigma_a = 0 \]
\[ \Delta \cdot v = \gamma \]

Area changes treated as intrinsic behaviors of embryonic territories
Active stresses

\[
\mu \Delta v - \nabla P + \Delta \cdot \sigma_a = 0
\]
\[
\Delta \cdot v = \gamma
\]

angular tension profile

\[
\sigma_a(r,t) = \frac{T(\theta,t)}{\sqrt{2\pi w^2}} e^{-\frac{d^2}{2w^2}} e_t \otimes e_t
\]

constant, uniform width

Tensile ring that moves with the tissue
Boundary condition

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

$\mathbf{v} = \mathbf{v}^{\text{exp}}$
Tissue flows in the model

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

\[ \Delta \cdot \mathbf{v} = \gamma \]
Fitting the model

- area changes taken from experiment
- time-dependent tension profile fit to observed motion
- initial margin position
Model vs. experiment

residual ~ 10%

experiment

model
Relative contributions to morphogenesis

\[ \mu \Delta v - \nabla P + \Delta \cdot \sigma_a = 0 \]

\[ \Delta \cdot v = \gamma \]

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

dtdTomato myosin
Cell division and tissue fluidity

Cell-division-mediated rearrangements

Control

Divisions inhibited (HU+Q-VD-Oph)

Firmino et al Dev Cell 2016
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
Cell division and tissue fluidity

Tensions are still present → viscosity increases
The embryo as a swimmer

![Diagram of an embryo swimming with arrows indicating movement.]

![Graph depicting A-P offset over time (h) with different models and tensions.]

- **Average model without tension**

The graph shows the A-P offset over time, with various models and tensions plotted. The average model without tension is highlighted.
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

Saadaoui et al bioRxiv 2018
How is all this controlled?

Downstream of gene expression patterning?

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

Spratt & Haas J Exp Zool 1960
Molecular basis of regulation

Diffusing inhibitor prevents ectopic embryo formation?
A mechanical basis for regulation?
Interplay between mechanics and fate specification?

Sox3

stretching

compression

Snail2
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