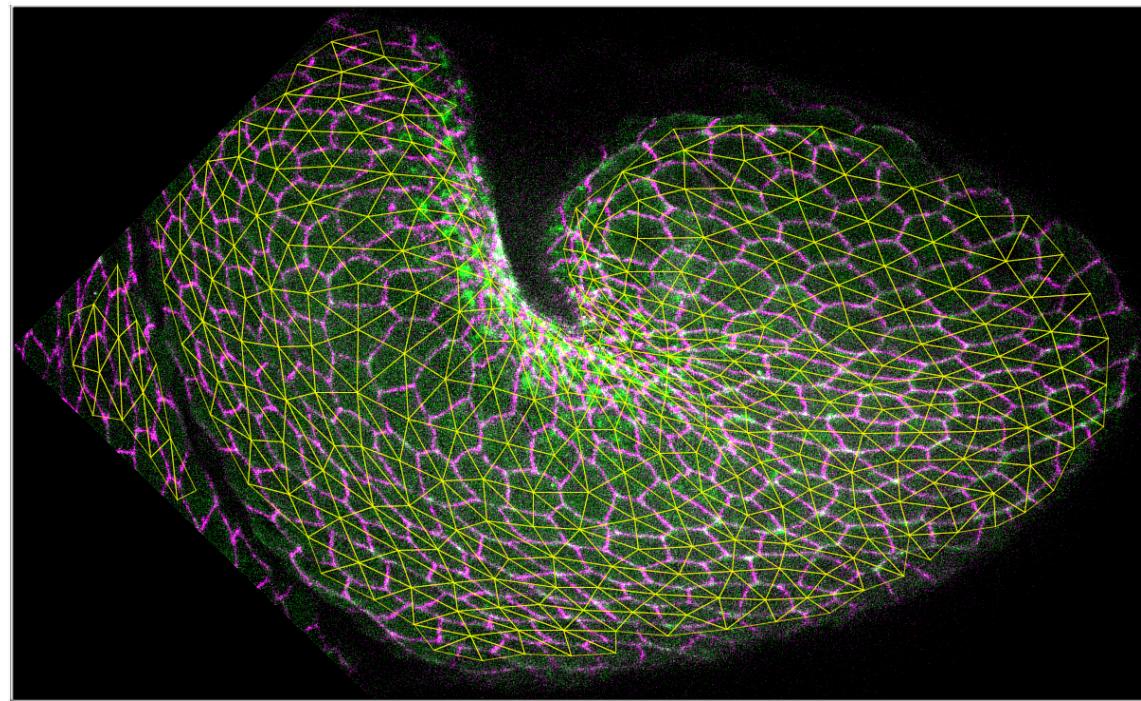
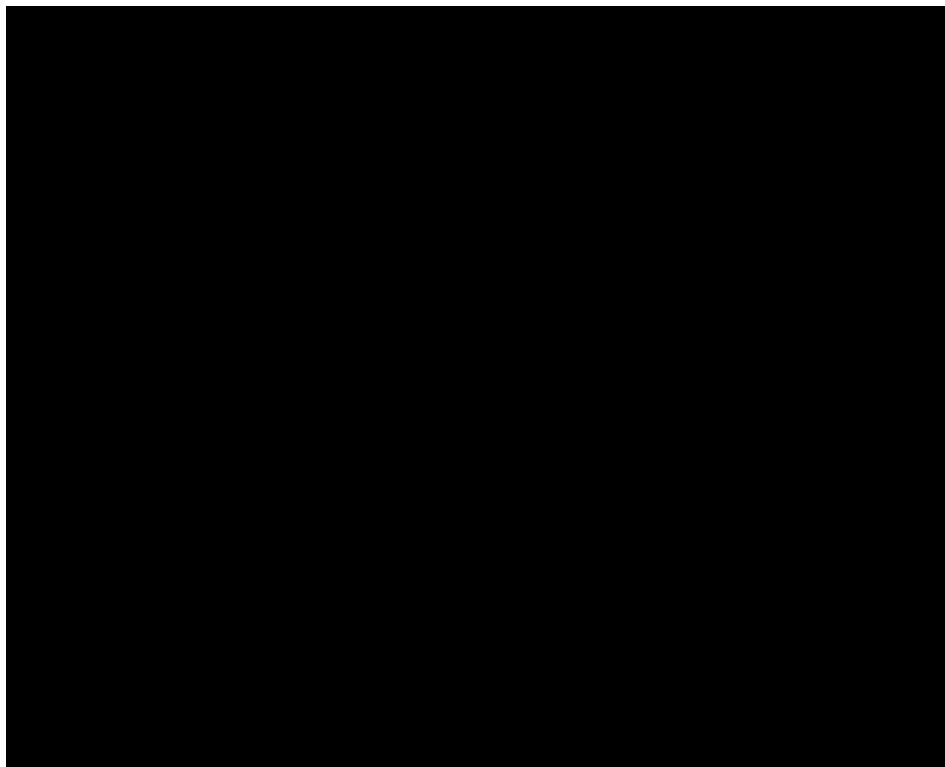


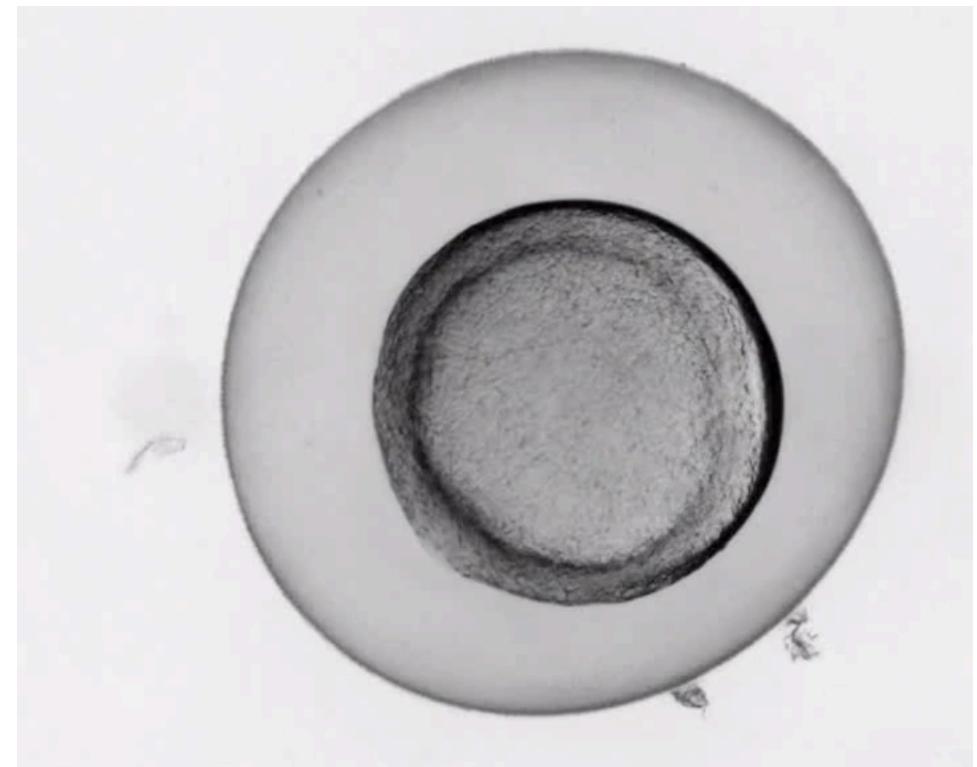
# Control and self-organisation during tissue morphogenesis



# Morphogenesis: Space, Time, Information

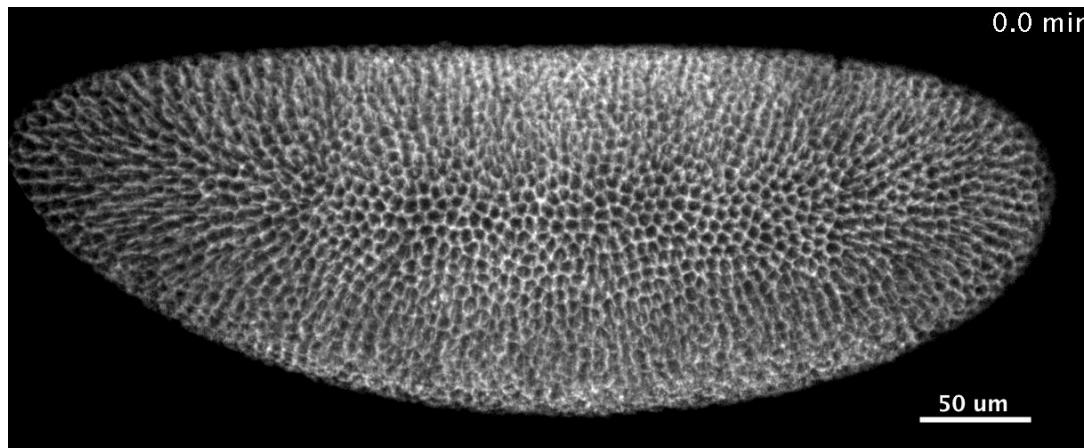


Sea Urchin



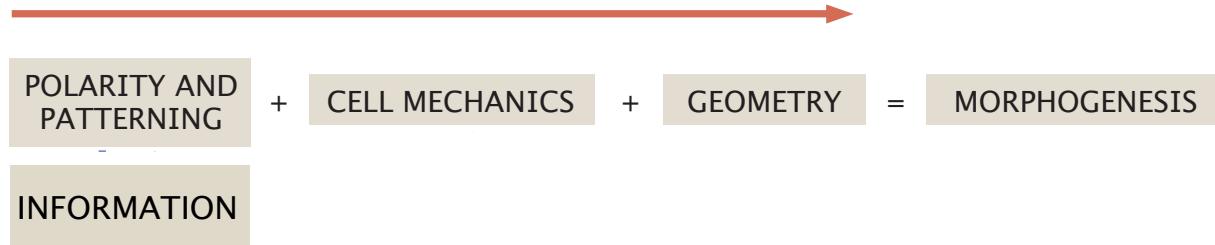
Zebrafish

# Mechanochemistry of development



- **Information:**  
Where, When, Vector?
- **Mechanics:**  
Forces, material response?
  - define Length and Time scales

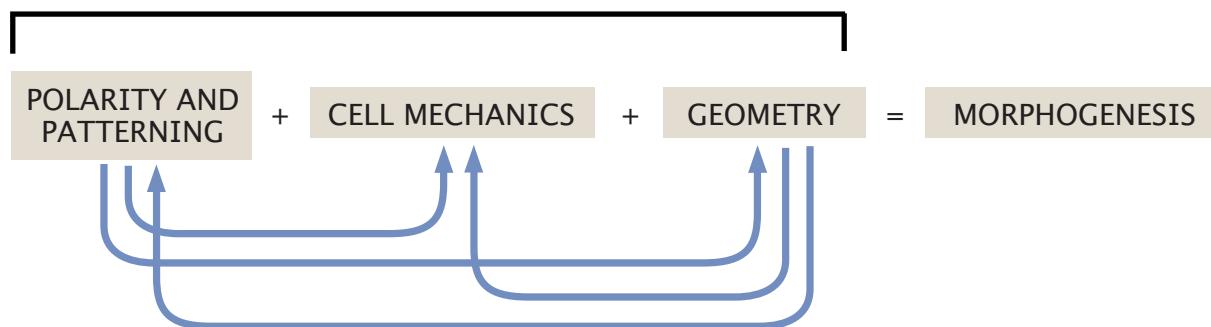
# PROGRAM



- hierarchy
- modularity
- long and short range interactions
- deterministic rules

# SELF-ORGANIZATION

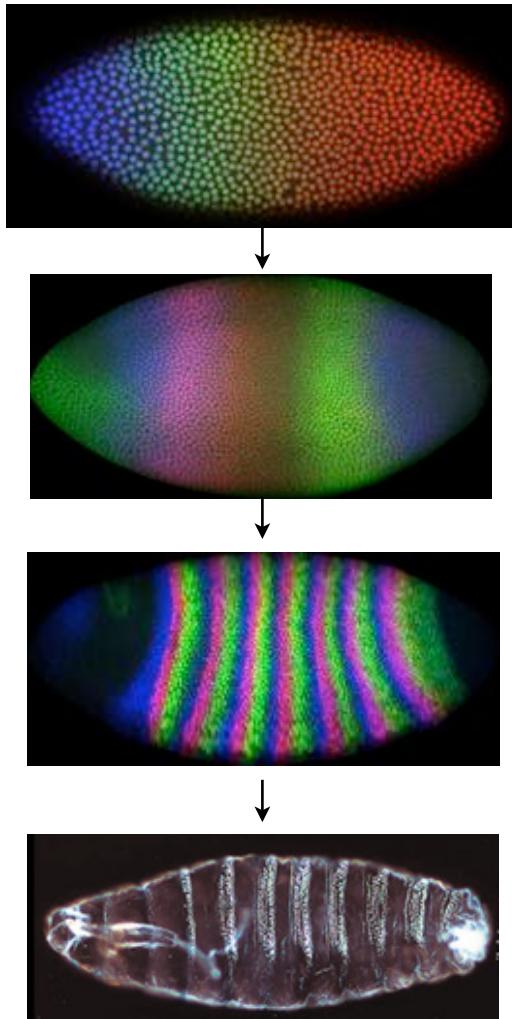
## Information



- **no** hierarchy
- local interactions
- many feedbacks
- statistical rules

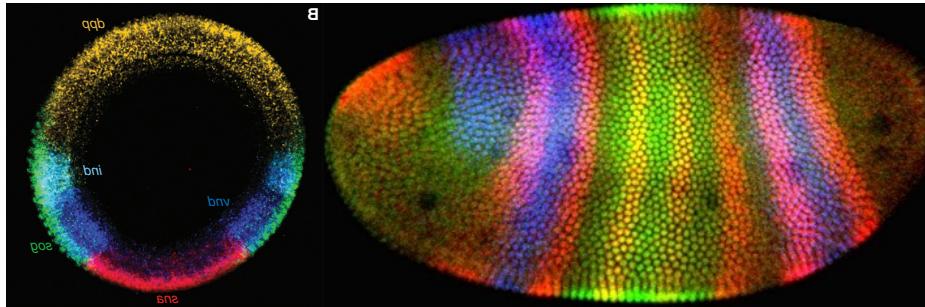
# Morphogenesis as a Program:

- positional information



# Morphogenesis as a Program

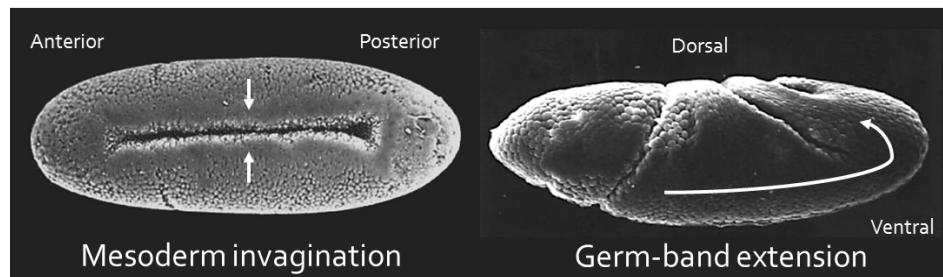
Genetically programmed positional information



Cortical mechanics

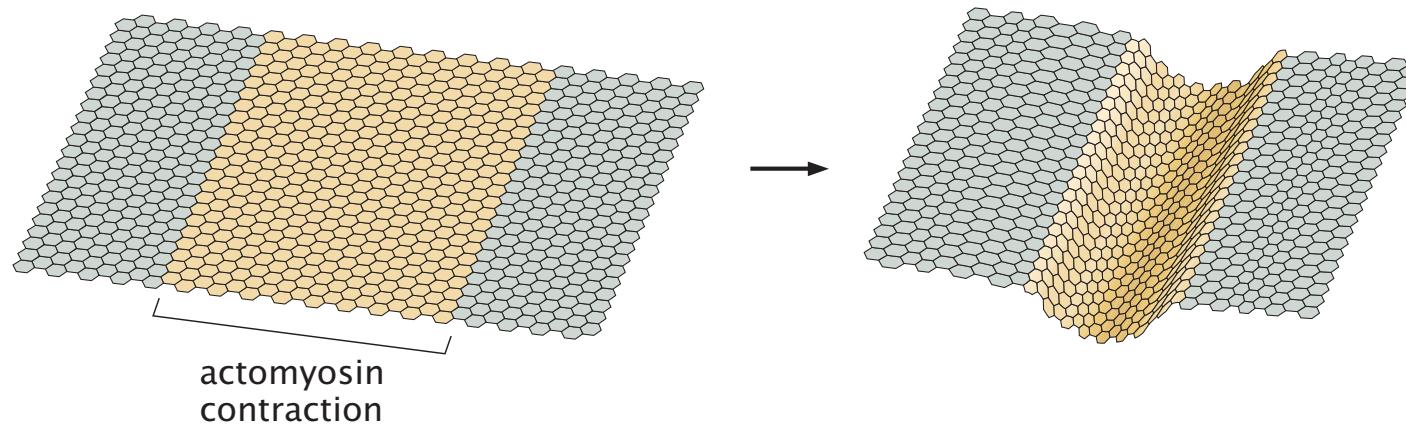
Cell behaviour

Tissue morphogenesis

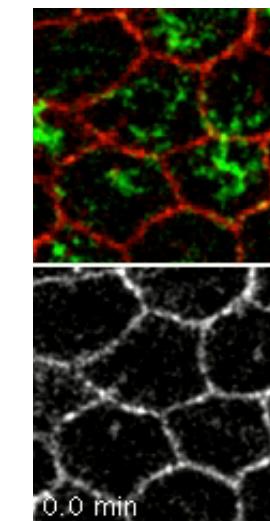
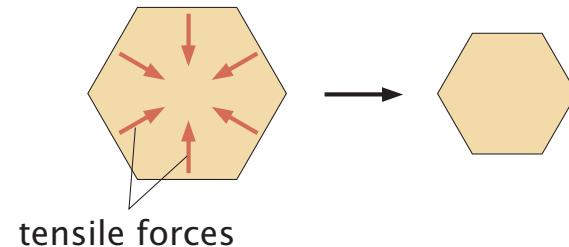


# Tissue invagination requires cell apical constriction

(A) tissue invagination



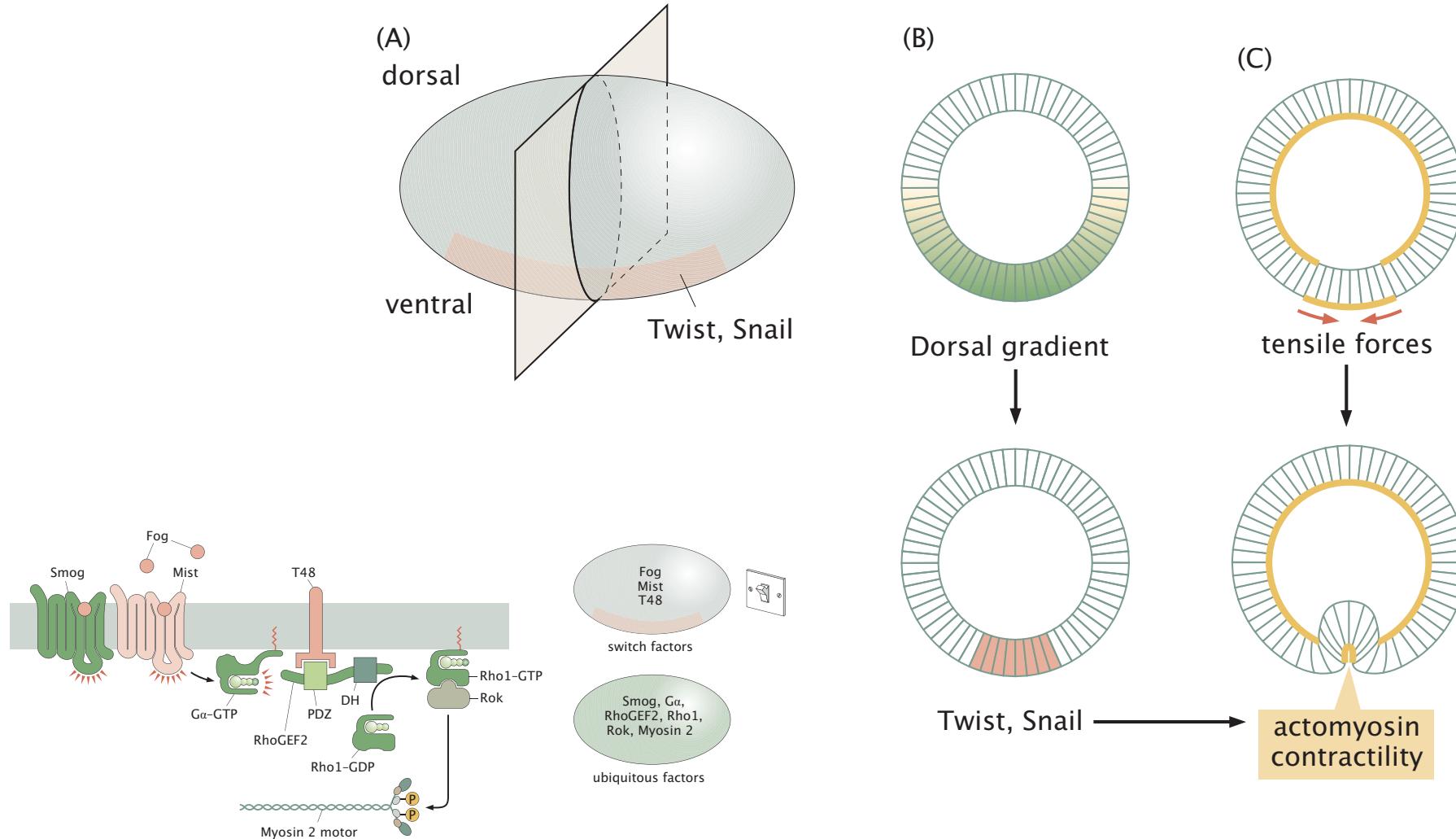
(B) apical constriction



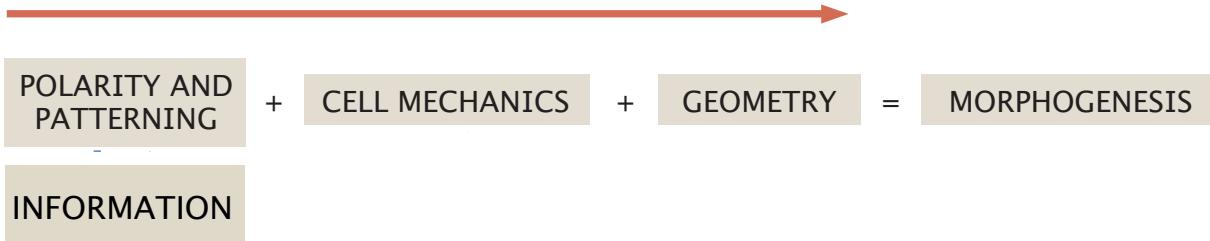
Myosin-II:RLC::GFP

Goldstein, Leptin, Lecuit,  
Martin, Munro, de Renzis,  
Rodgers, Wieschaus labs  
etc

# The genetic program of tissue invagination



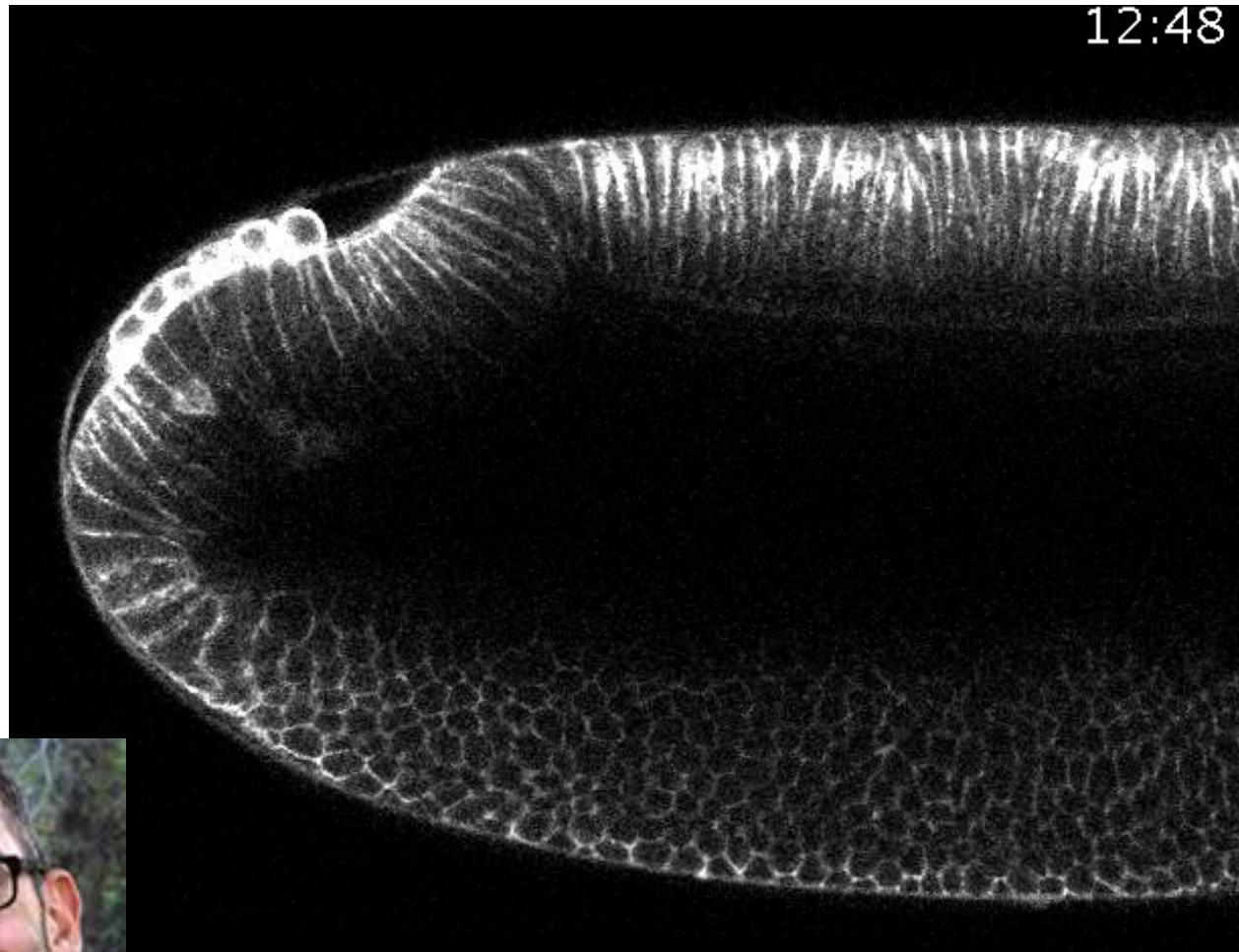
# PROGRAM



- hierarchy
- modularity
- long and short range interactions
- deterministic rules

# Endoderm morphogenesis comprises Rotation - Invagination - Progression

12:48

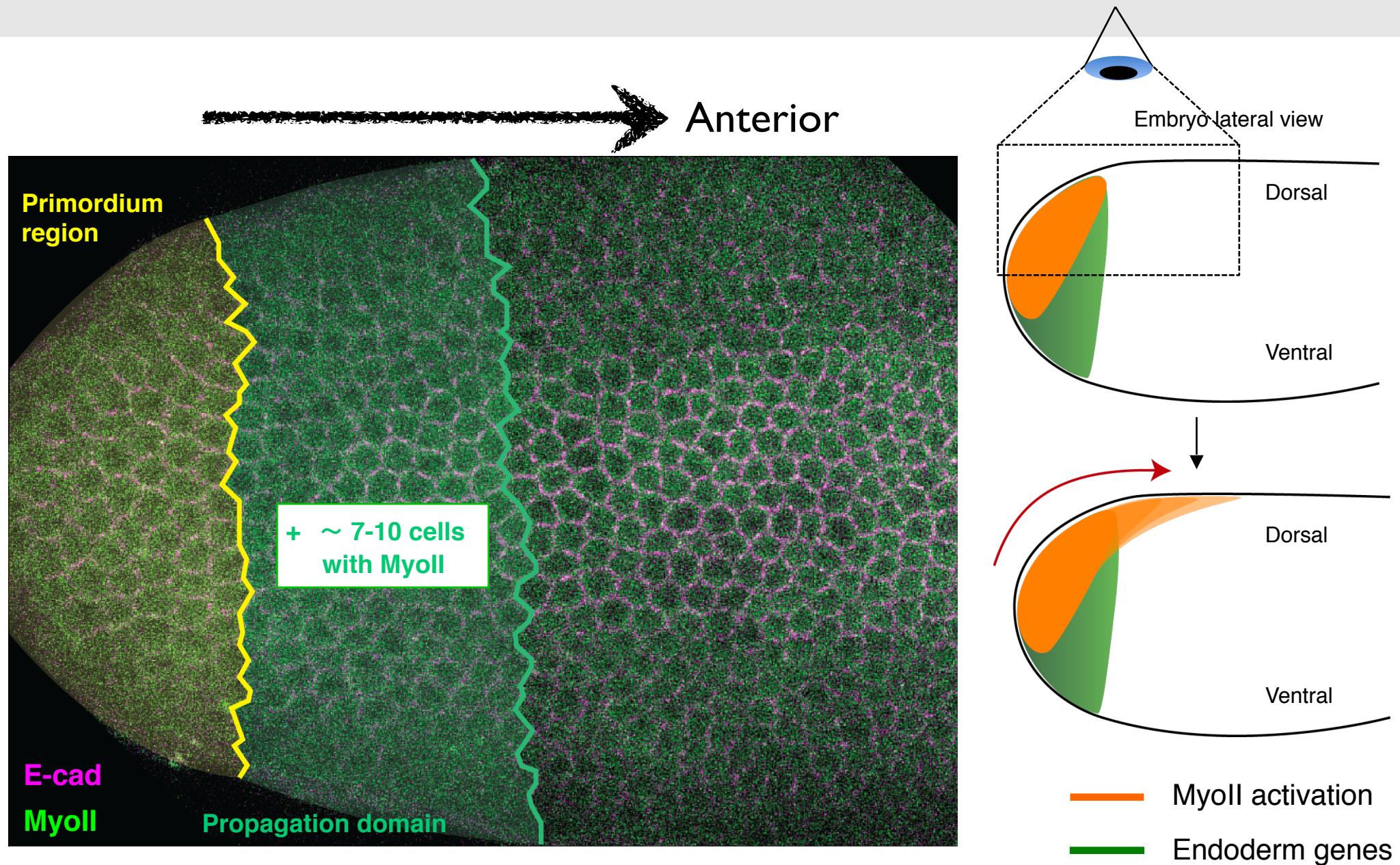


Anais Bailles

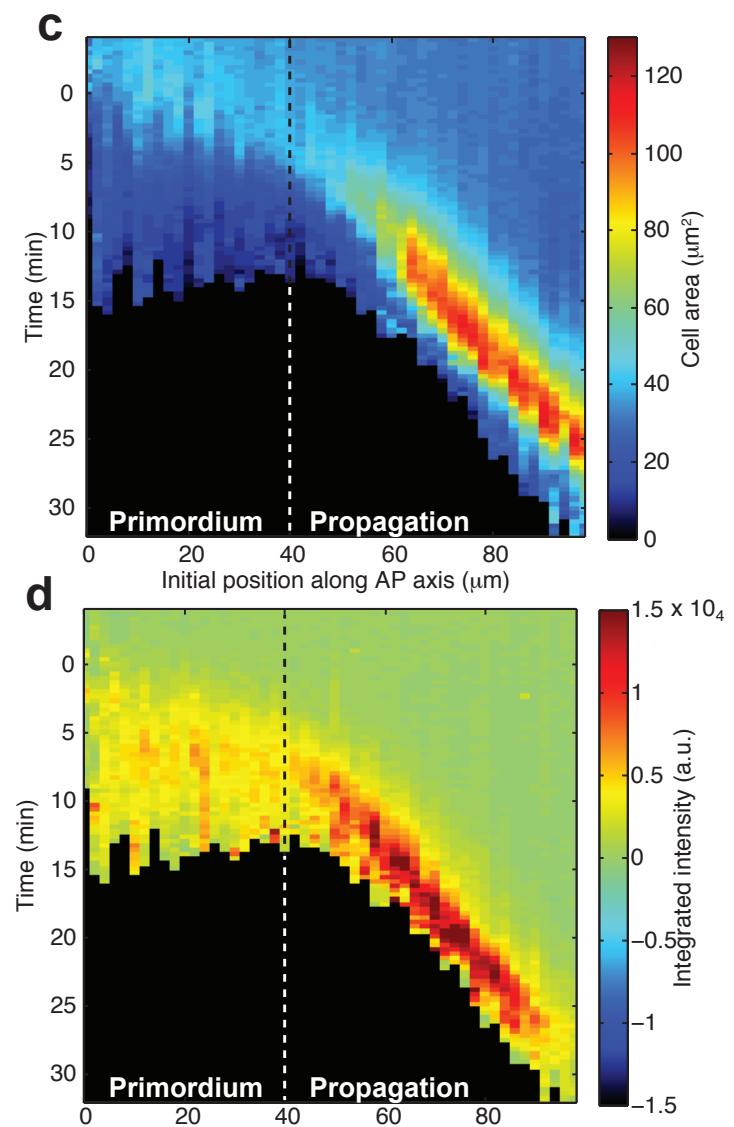
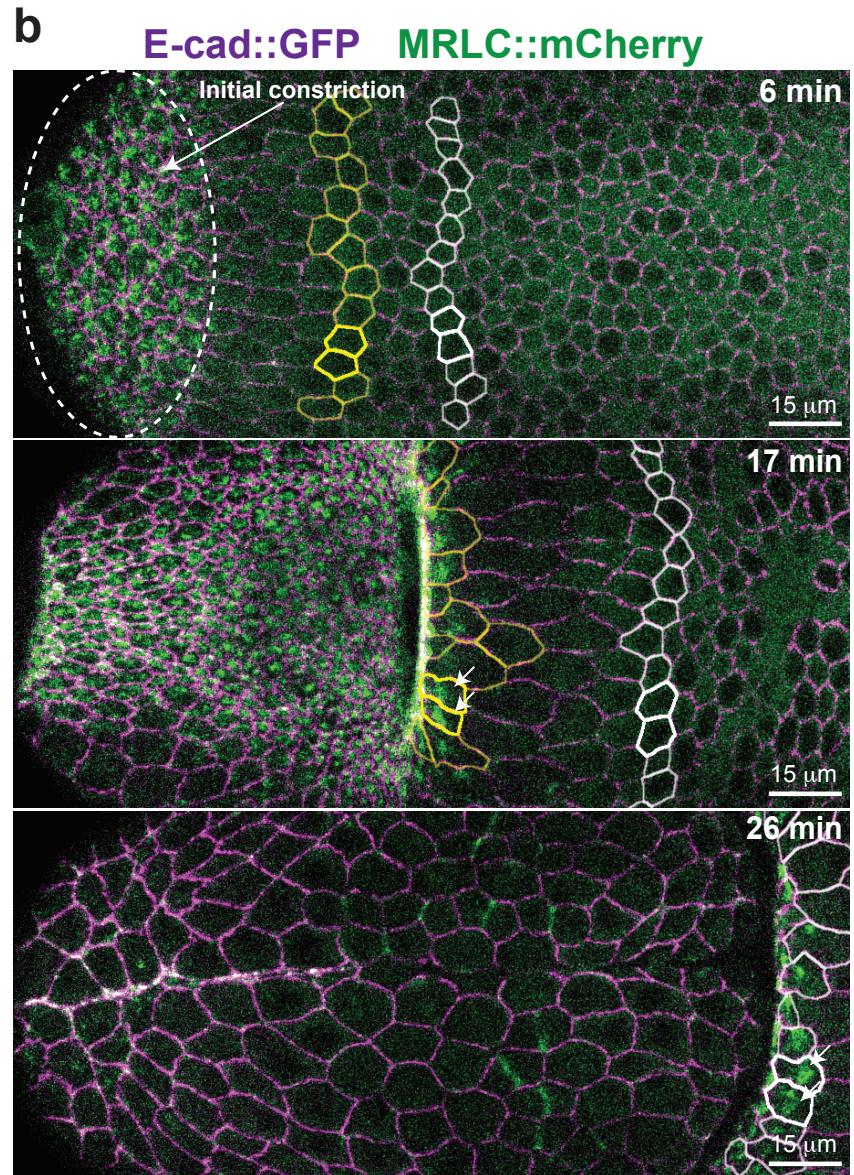


Claudio Collinet

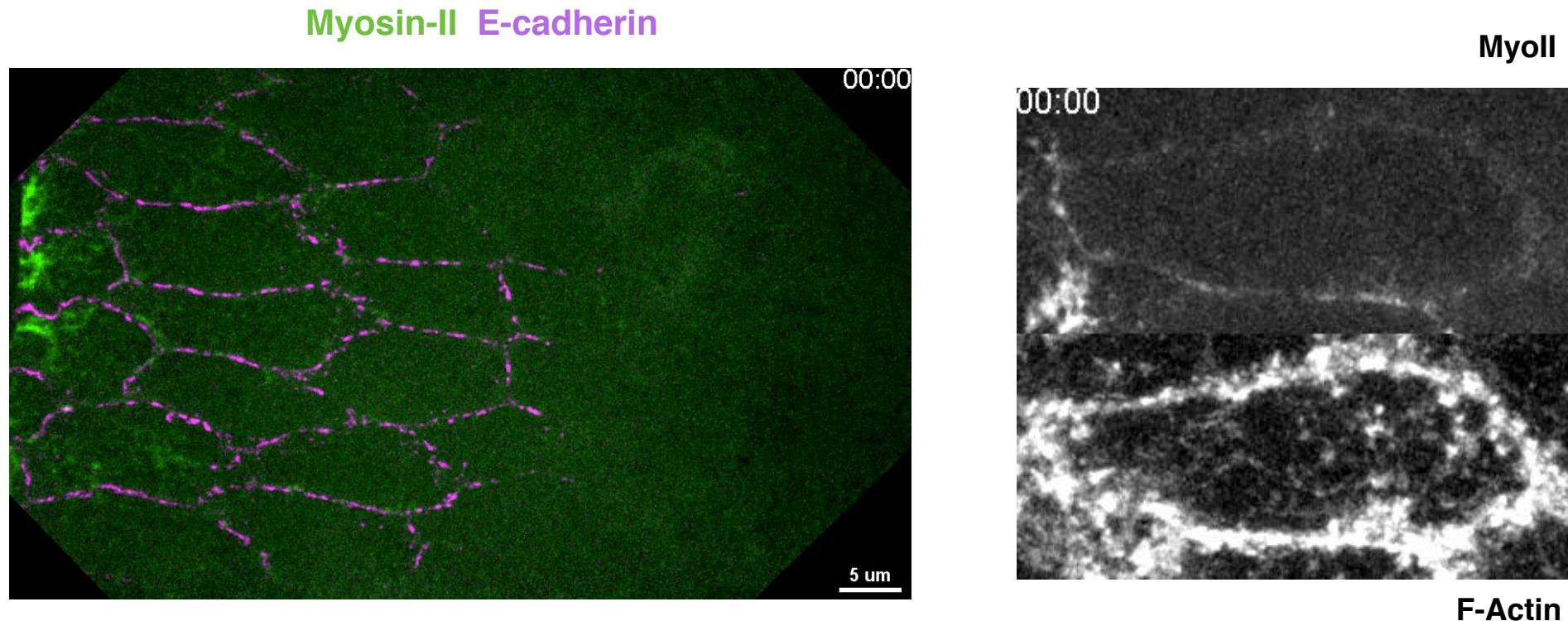
# A tissue scale wave of Myosin-II accumulation



# An anterior wave of Myosin-II contraction

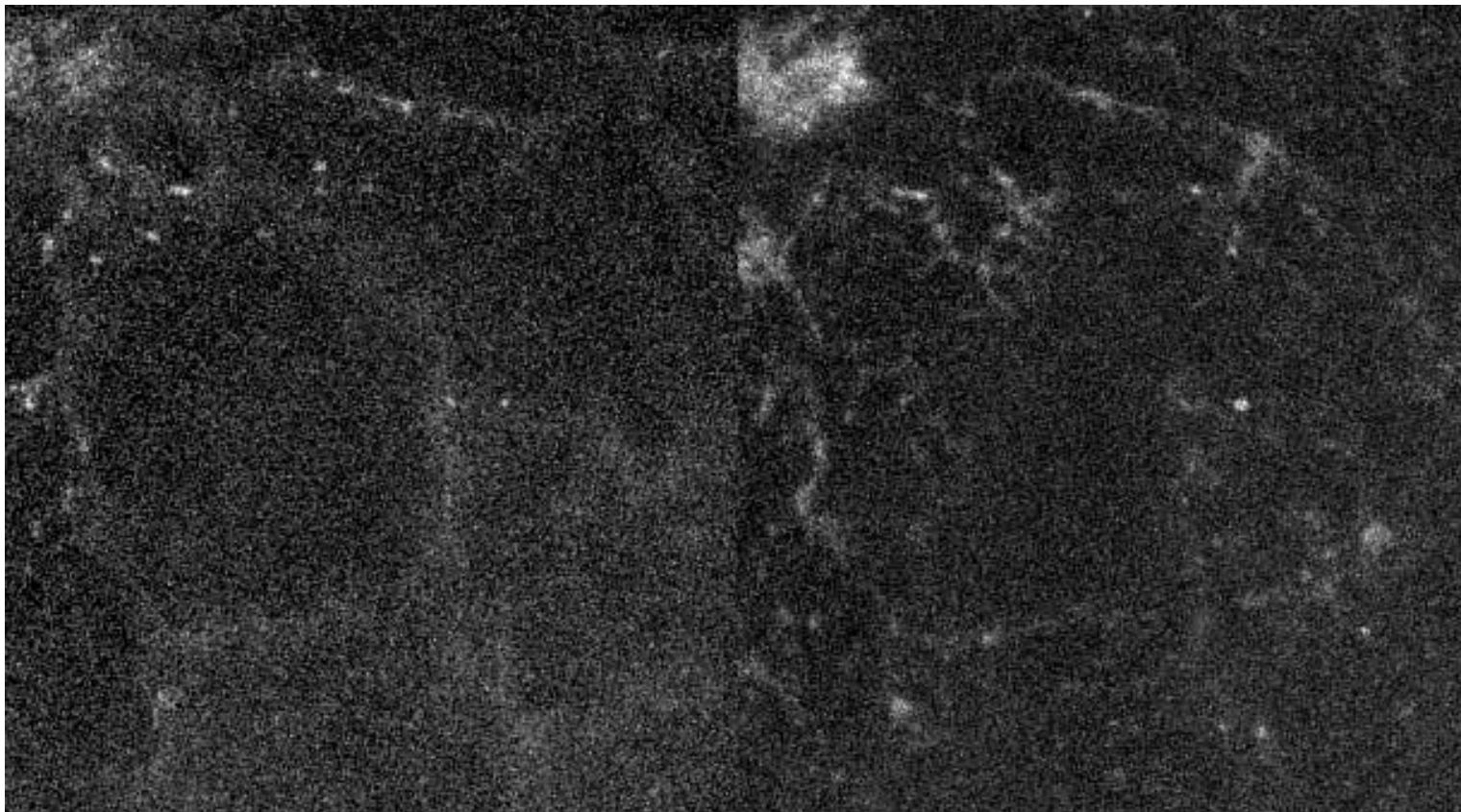


# Subcellular and tissue waves of Myosin-II activation

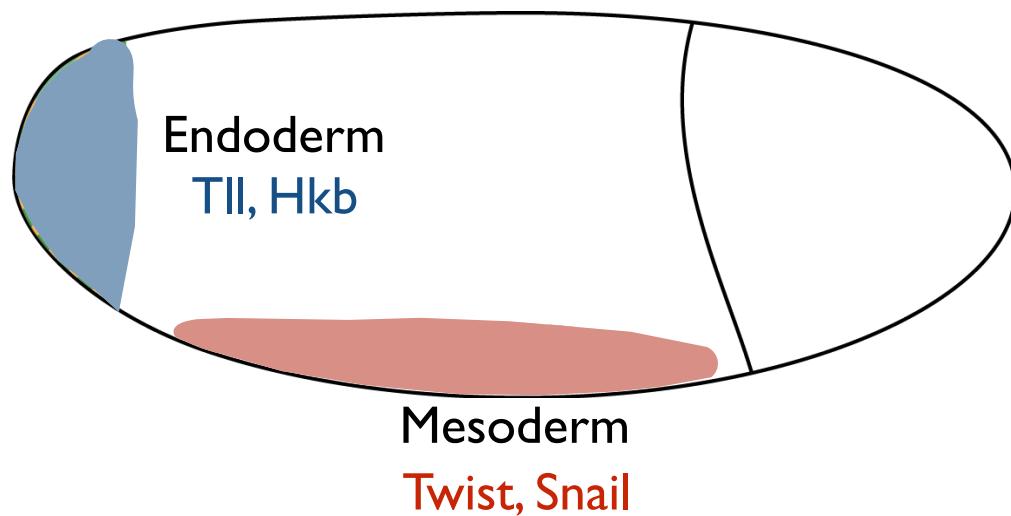


# An anterior wave of Myosin-II & Rho I-GTP

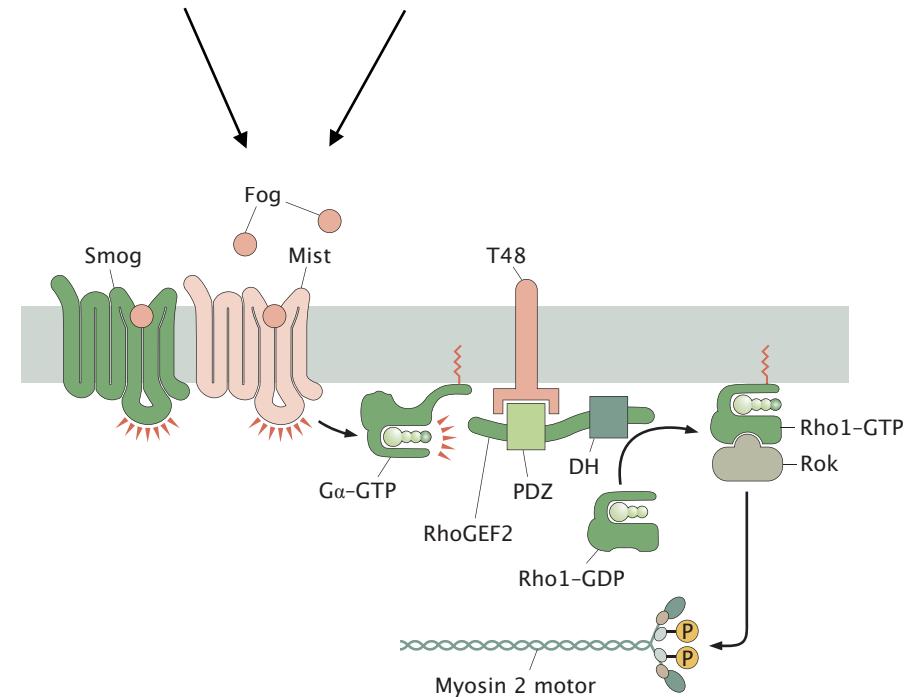
Rho1GTP Biosensor-GFP      MyoII-Cherry



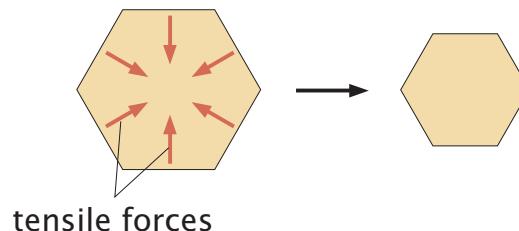
# Spatial control of MyosinII activation



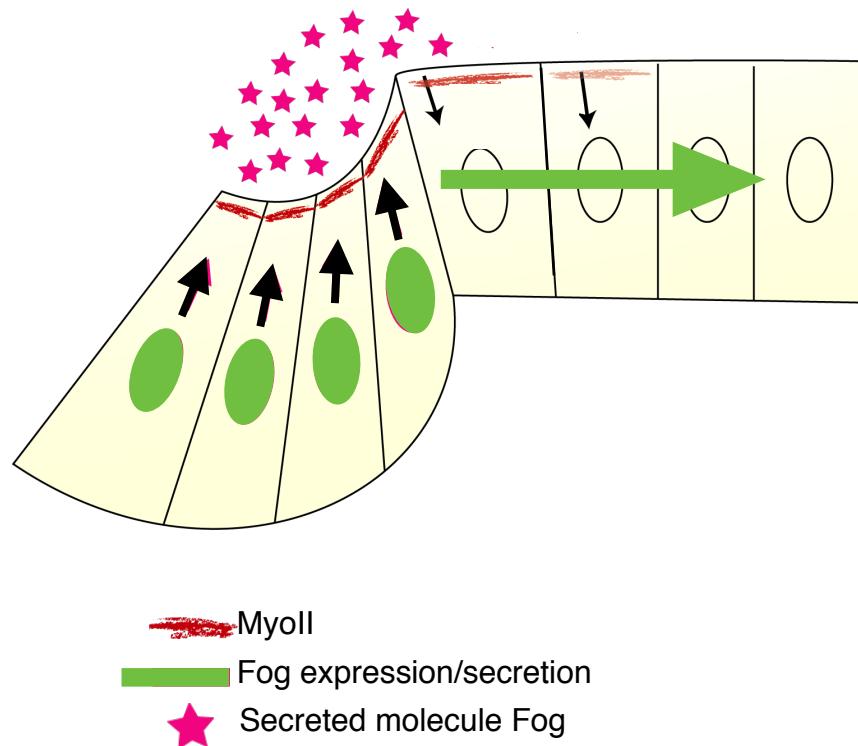
TII, Hkb   Twist, Snail



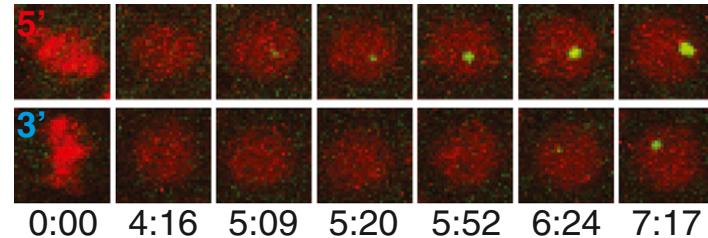
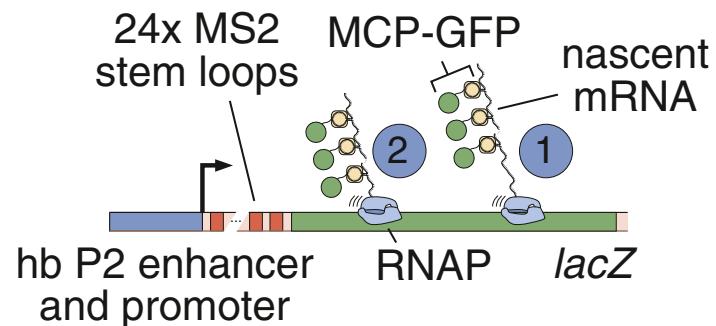
apical constriction



# Model I:Transcriptional wave of Fog expression

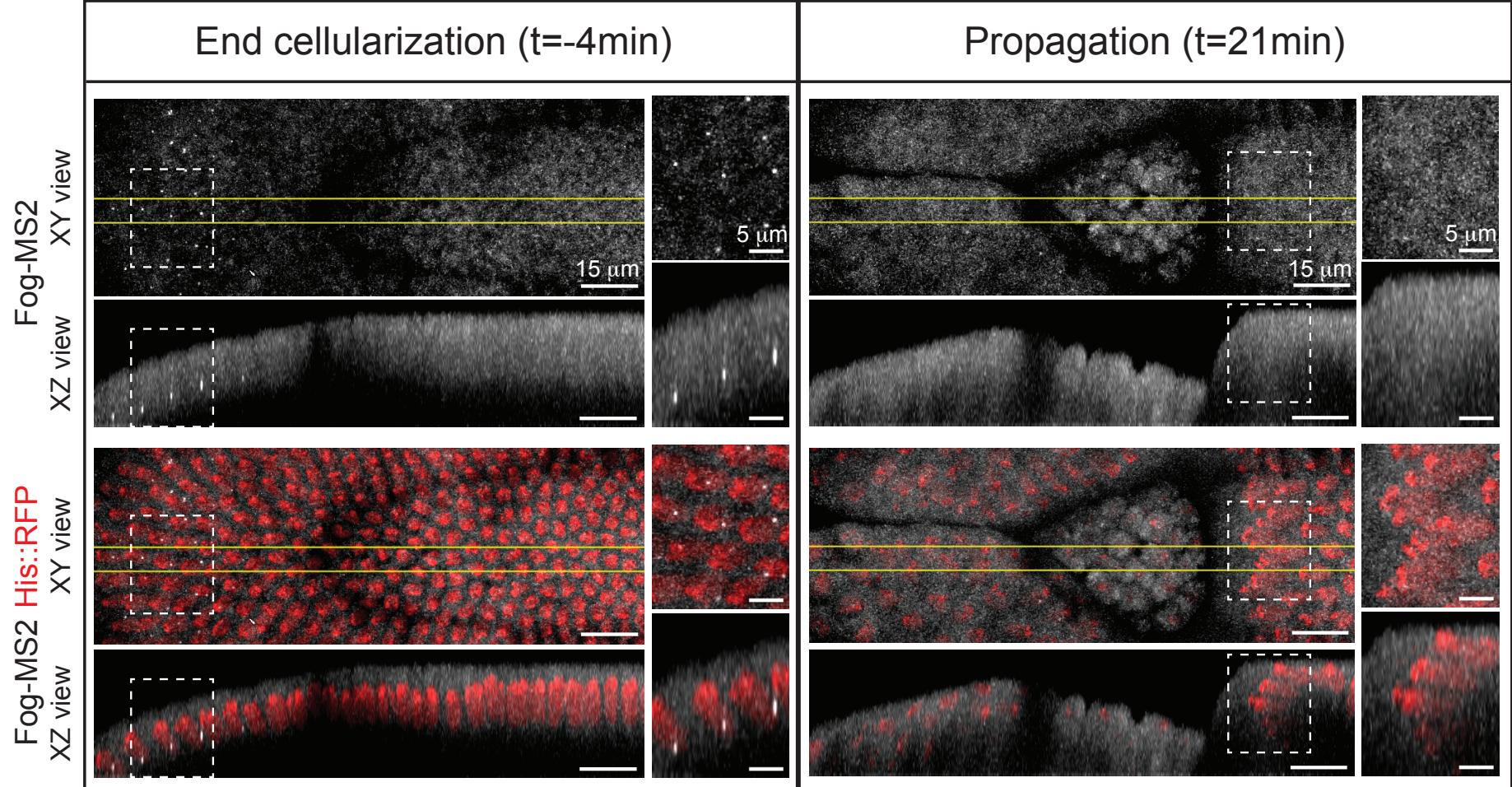


# Live Fog transcription dynamics



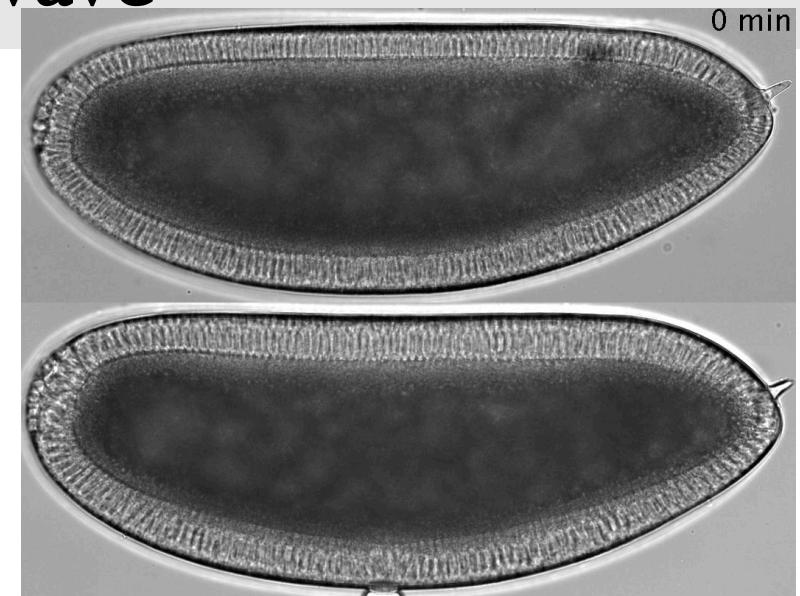
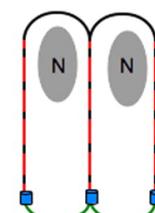
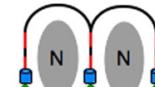
Garcia et al., 2013

# Fog is not transcribed in propagation zone

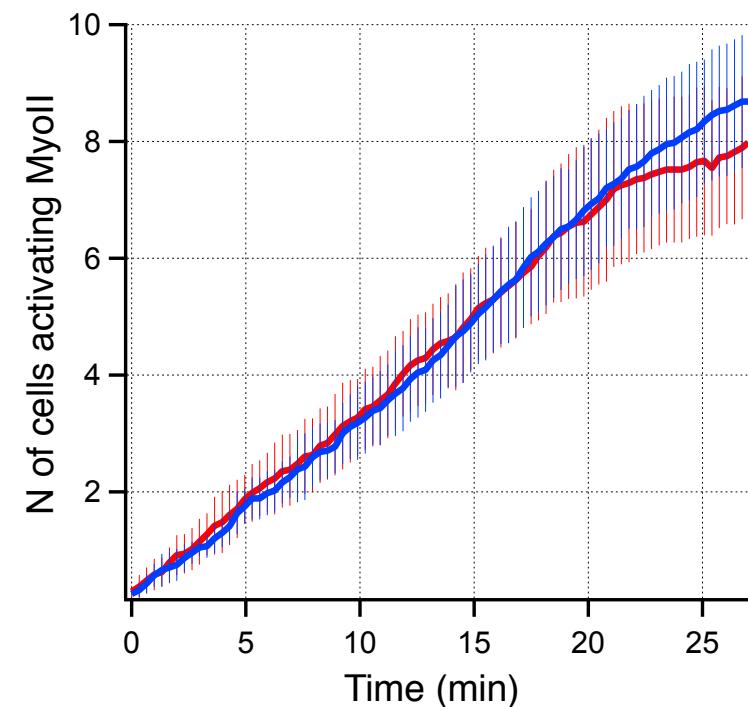


# Transcription controls Initiation but NOT propagation of wave

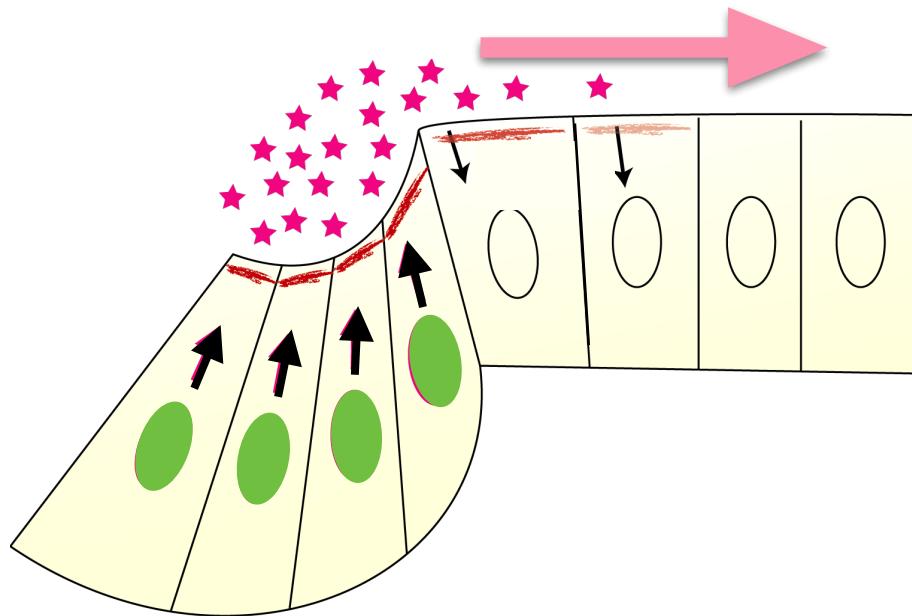
- $\alpha$ -amanitin is potent inhibitor of RNA Pol-II



— WT —  $\alpha$ -amanitin

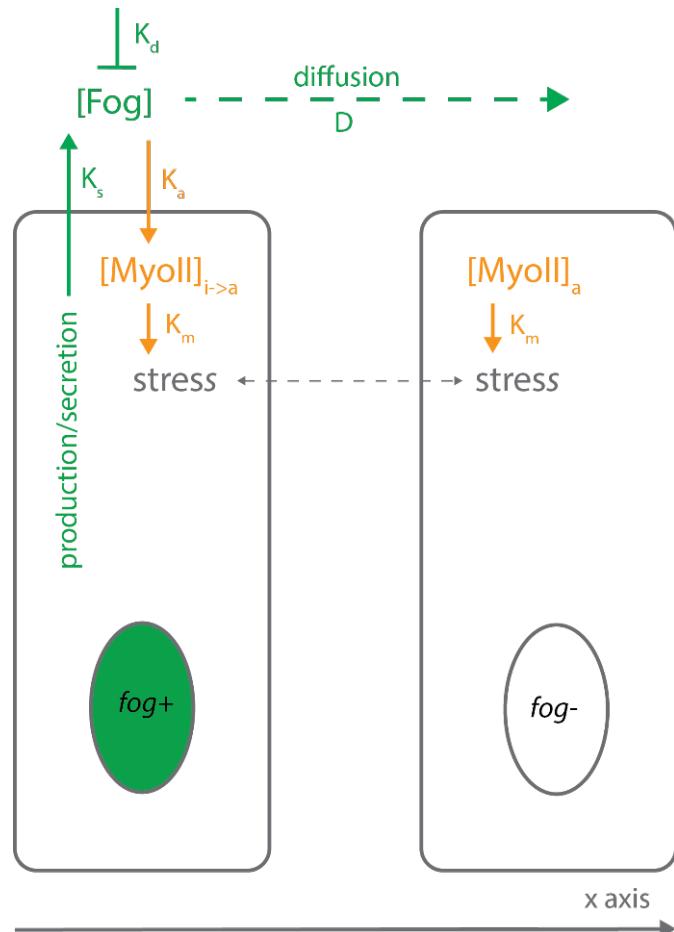


# Model 2: Diffusion-based wave: Is Fog a morphogen?

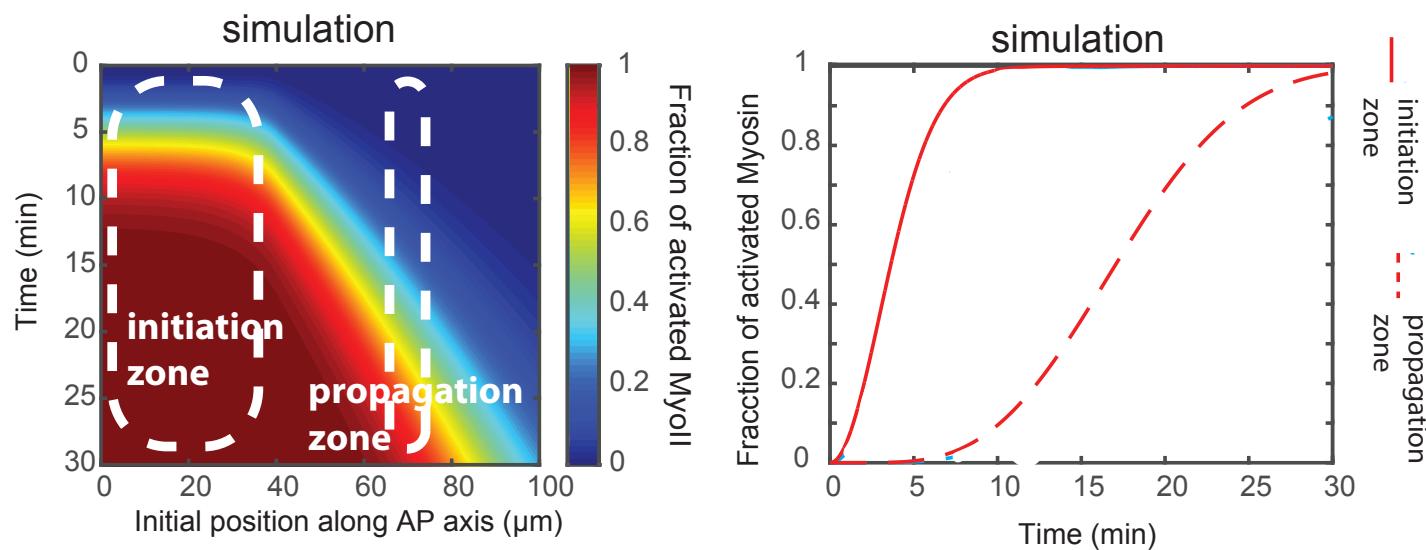


# Model 2: Diffusion-based wave: Is Fog a morphogen?

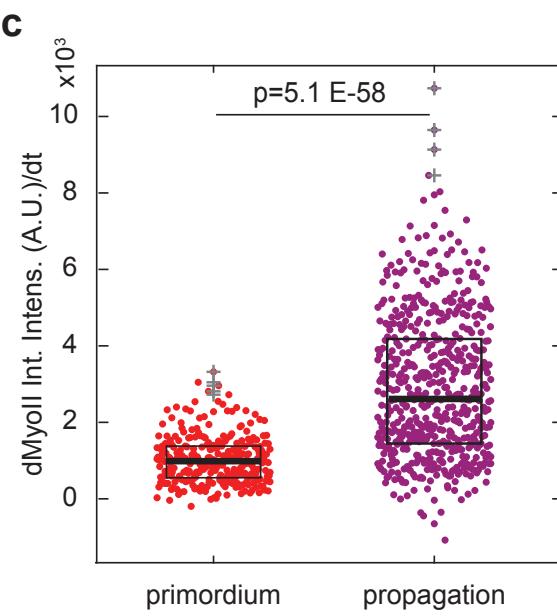
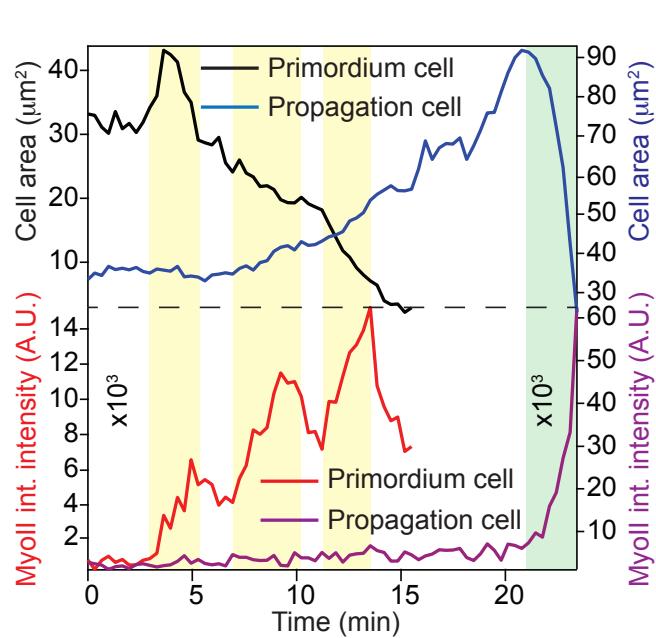
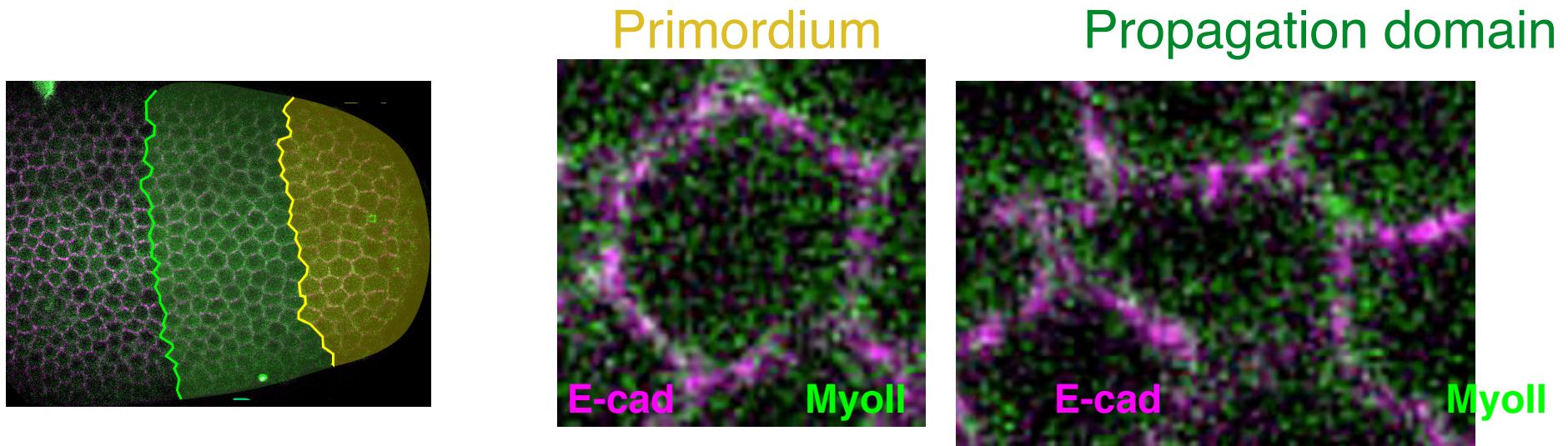
Diffusion and deformation model:



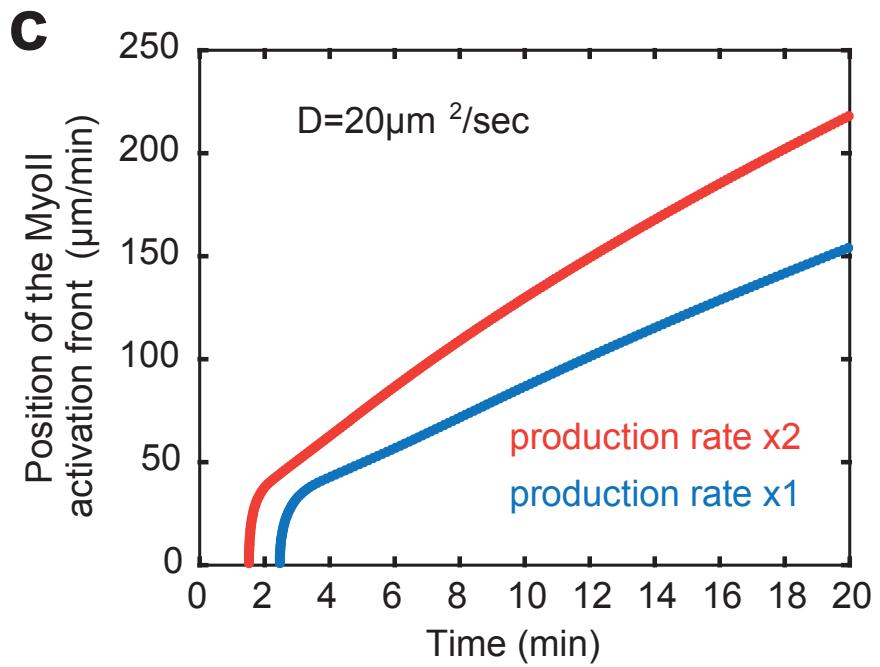
# Diffusion-based wave: Is Fog a morphogen?



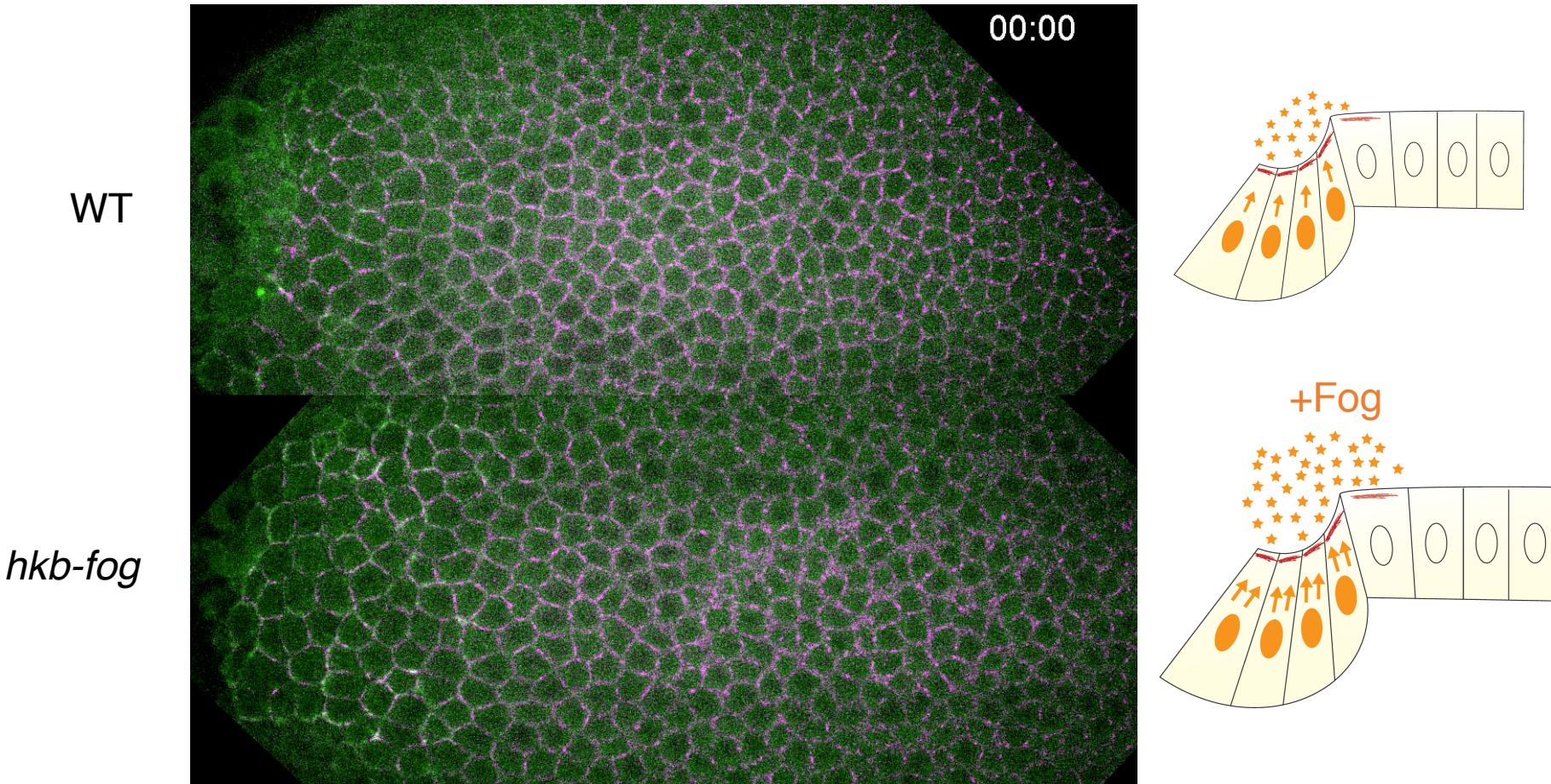
# MyoII activation does not spatially decay



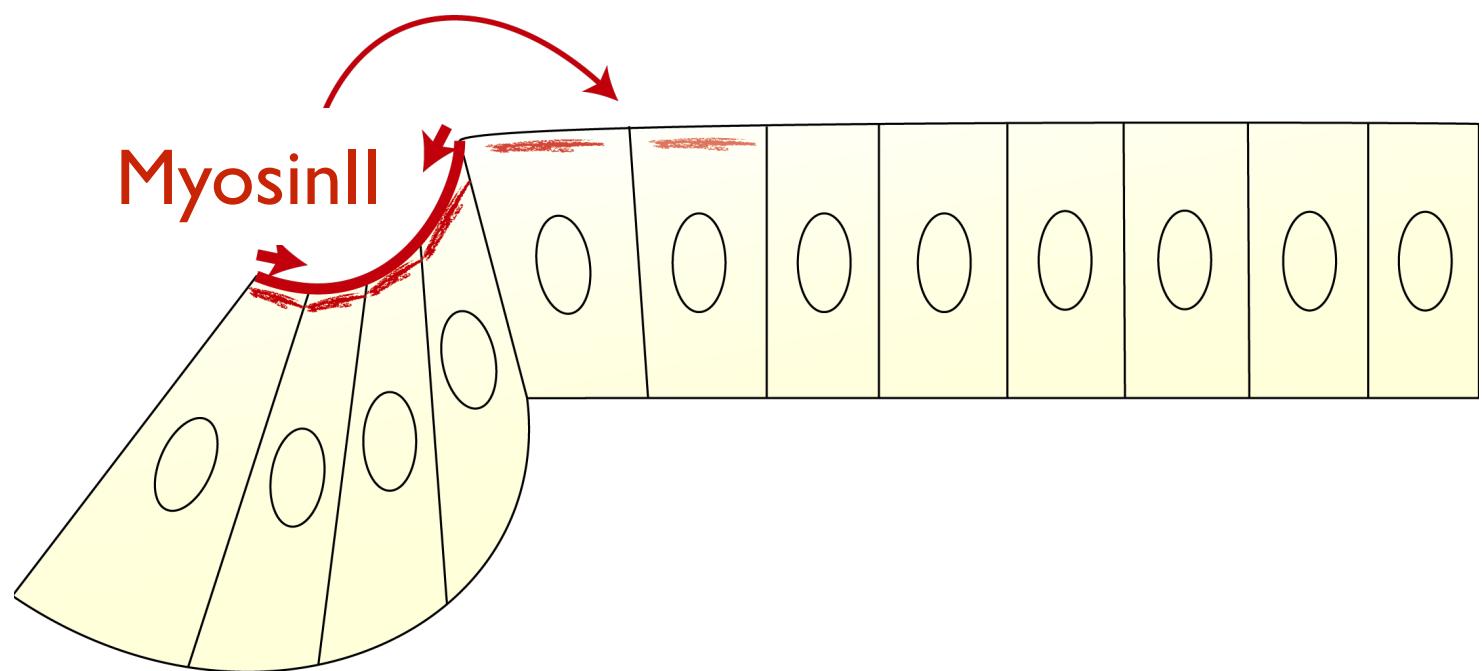
# Increasing Fog expression has no effect on wave dynamics



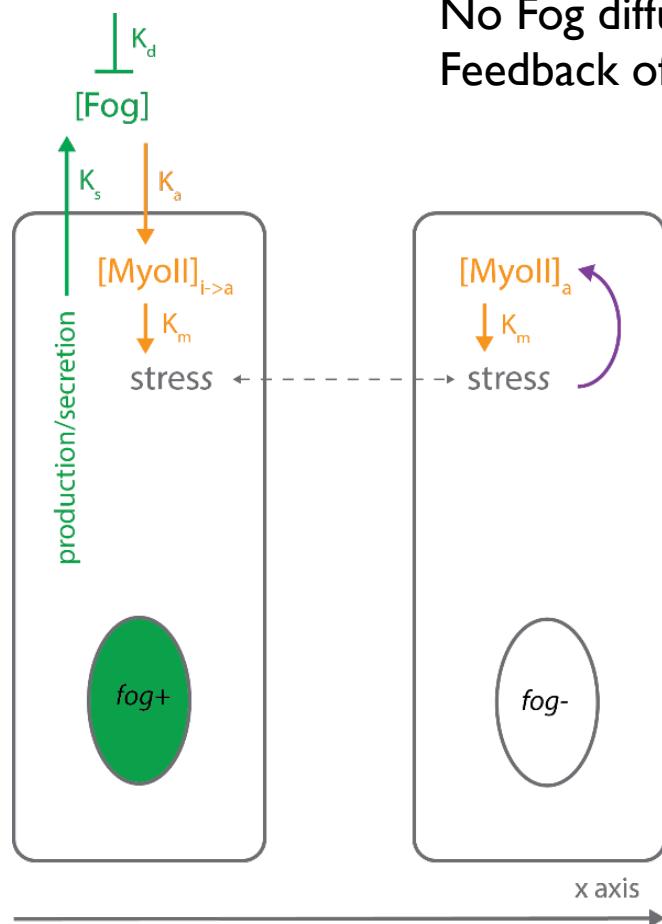
# Increasing Fog expression has no effect on wave dynamics



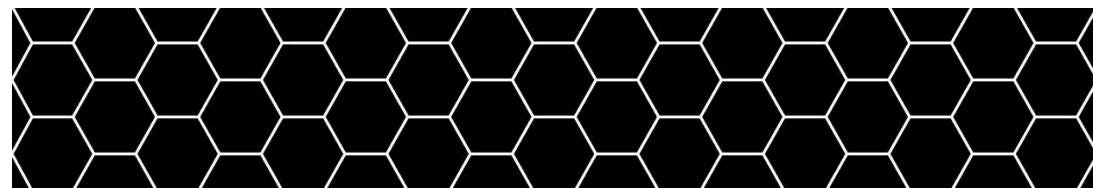
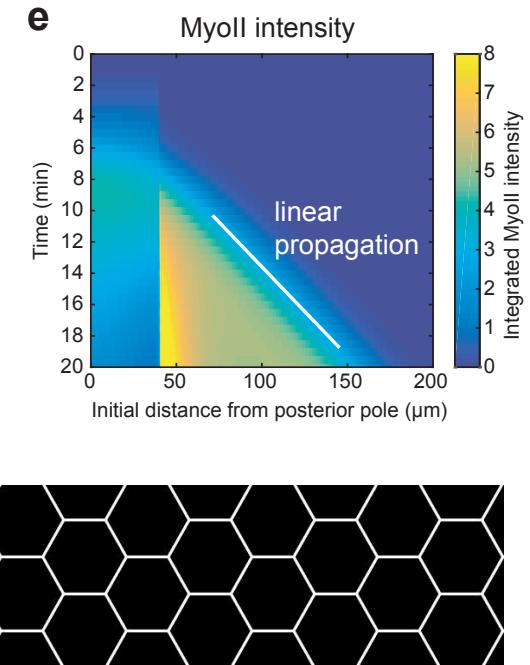
# Model 3: Self-organised mechanical propagation



# Model 3: Self-organised mechanical propagation

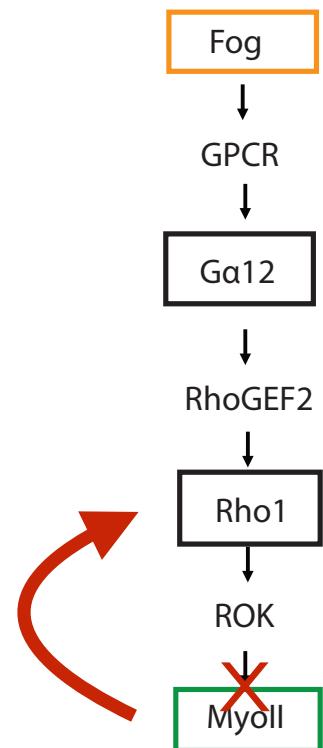


No Fog diffusion  
Feedback of stress onto Myoll activation

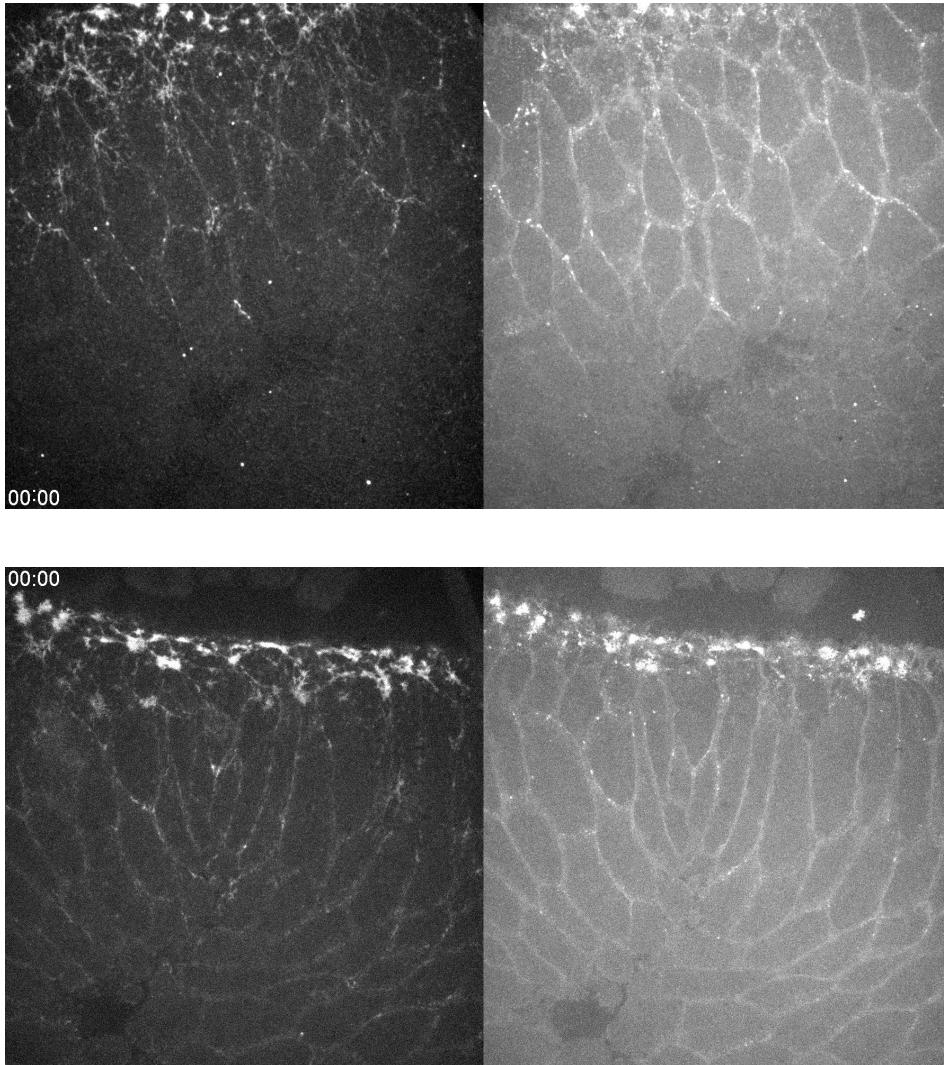


Predicts linear, sustained (un-damped)  
wave of Myoll activation

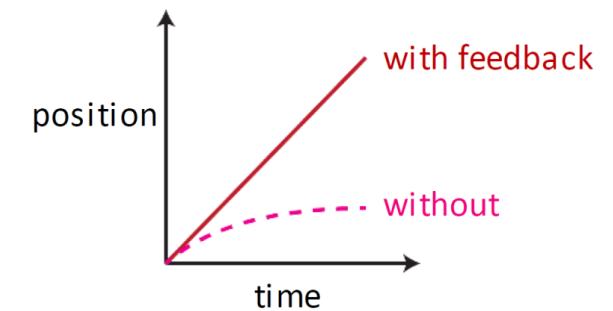
# Speed and range of RhoIGTP wave requires MyoII activation



MyoIICherry      RhoI biosensor (GFP)

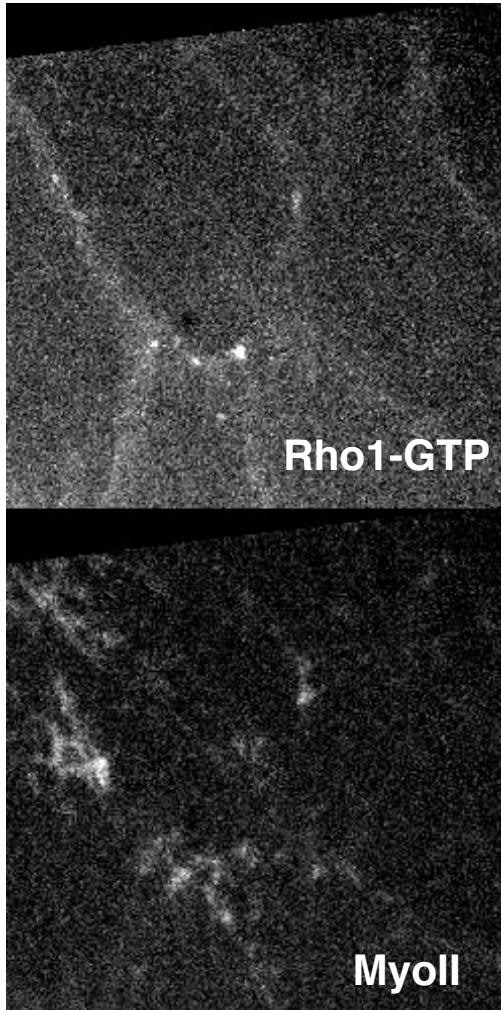


control



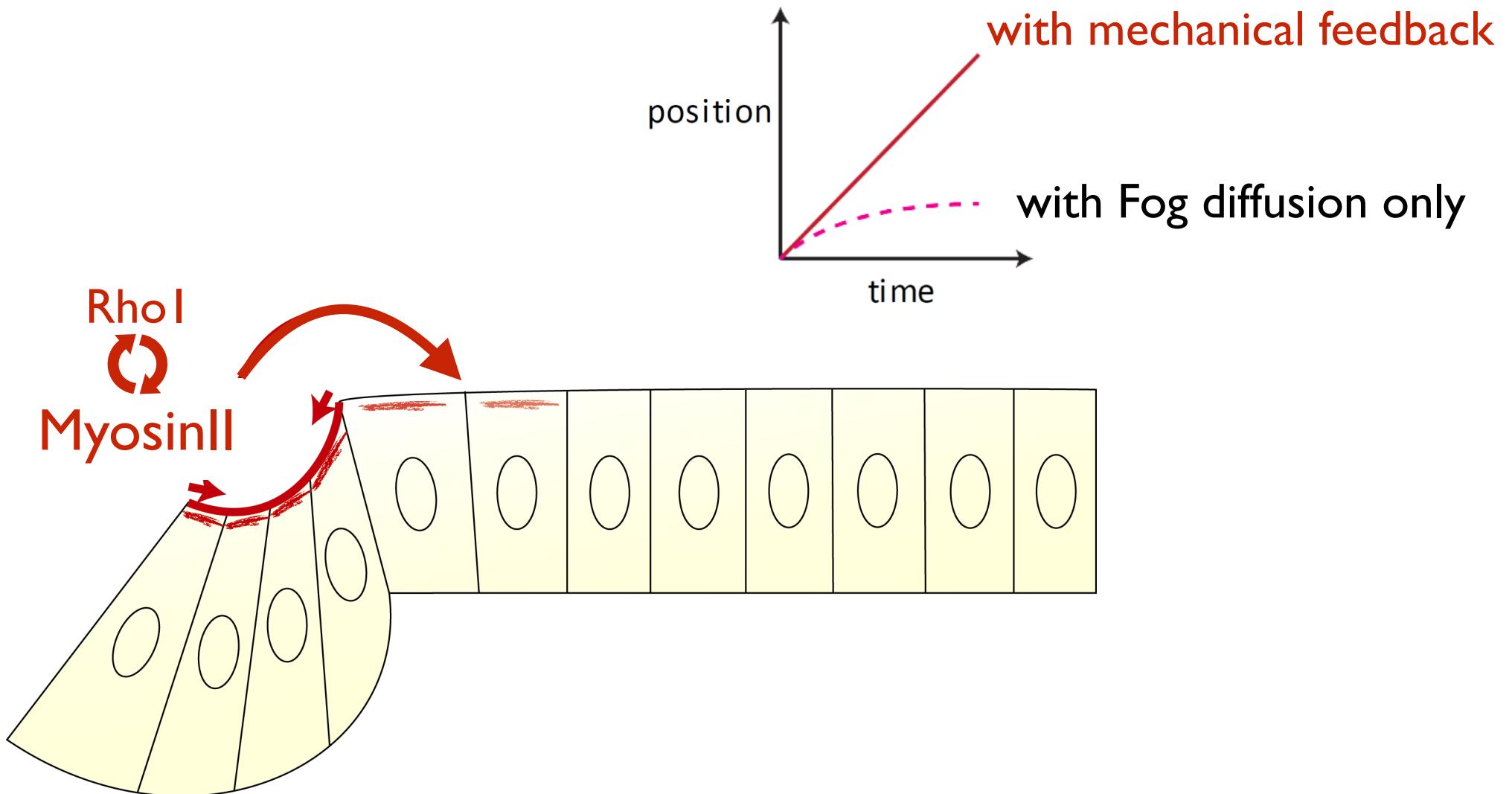
Rock  
inhibitor

# Rho1-GTP stabilisation requires MyoII activation

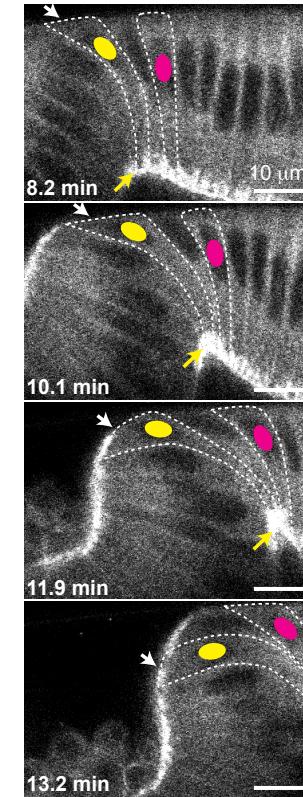
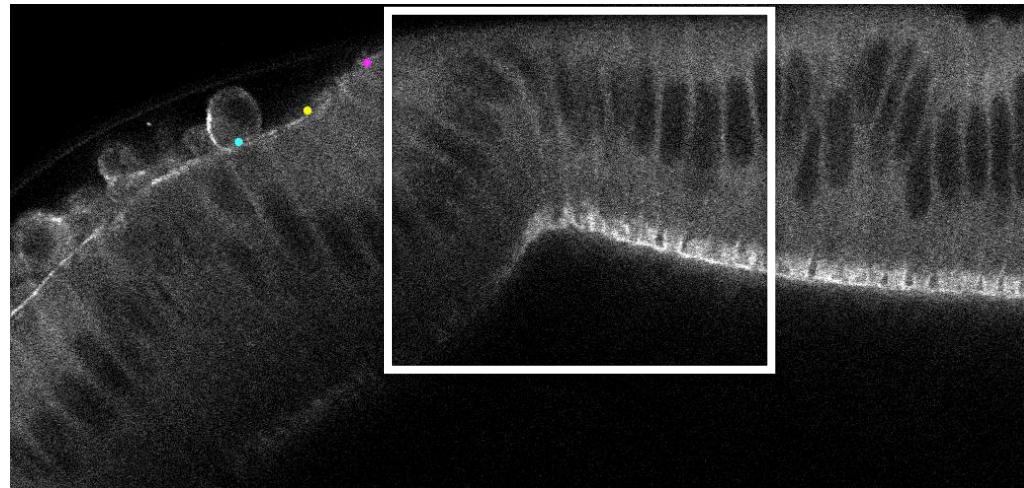


Rock  
inhibitor

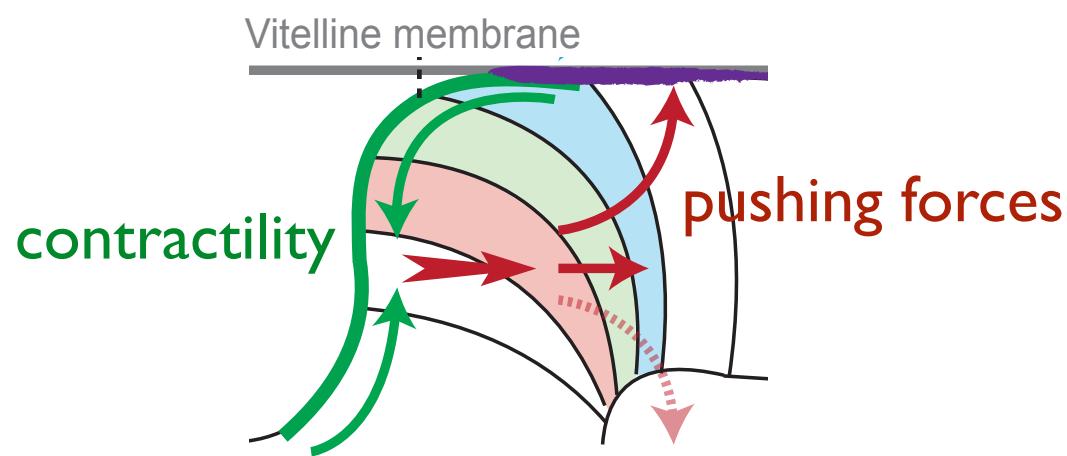
# Mechanical trigger wave: Positive feedback and spatial coupling



# 3D cell deformations associated with MyoII wave

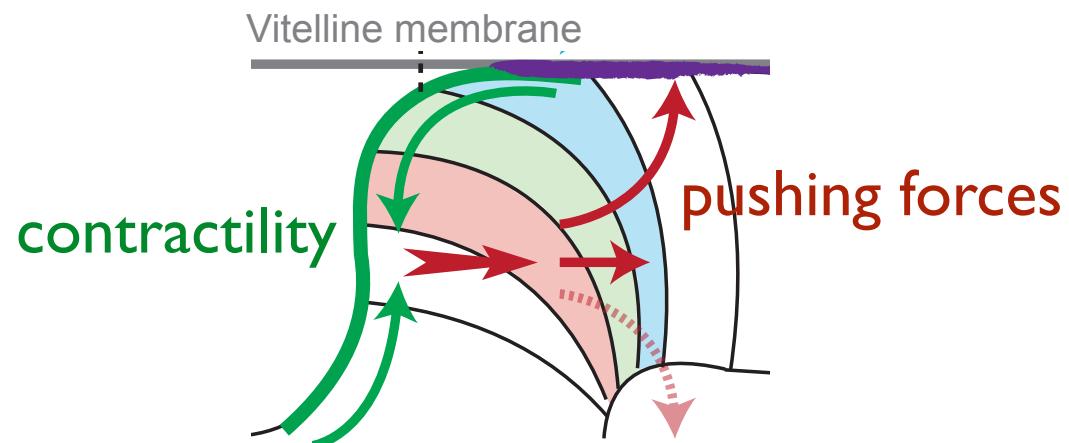
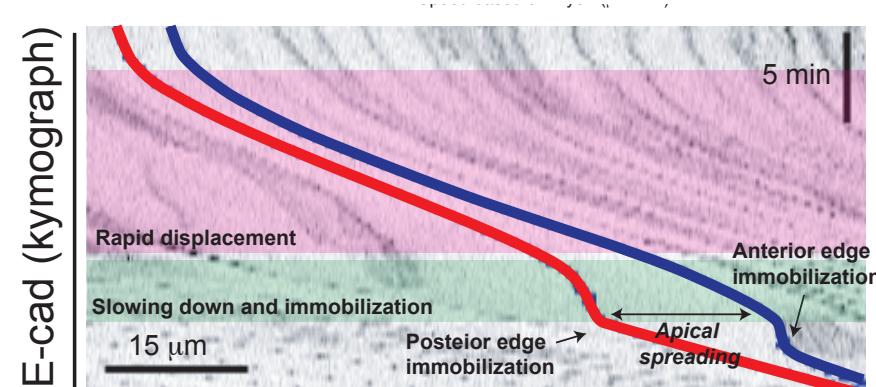
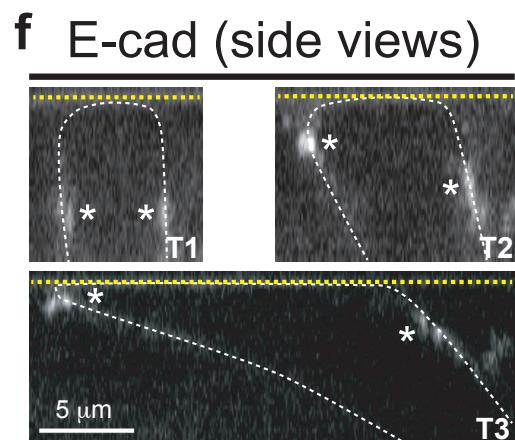


Cells are compressed and lifted  
against the vitellin membrane

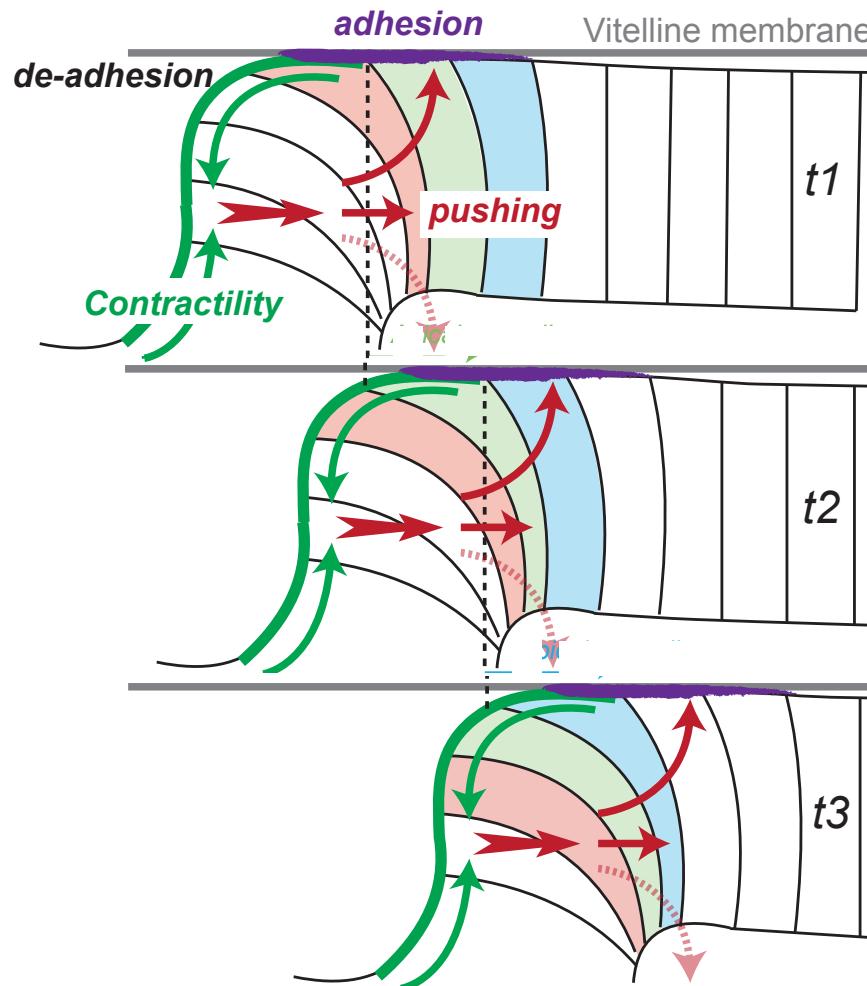


# Apical surface spreading against the vitelline membrane

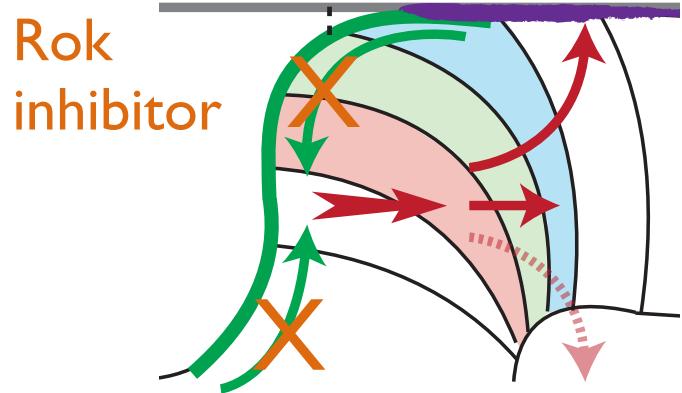
Sequential immobilisation of adherens junctions from posterior to anterior against the vitelline membrane



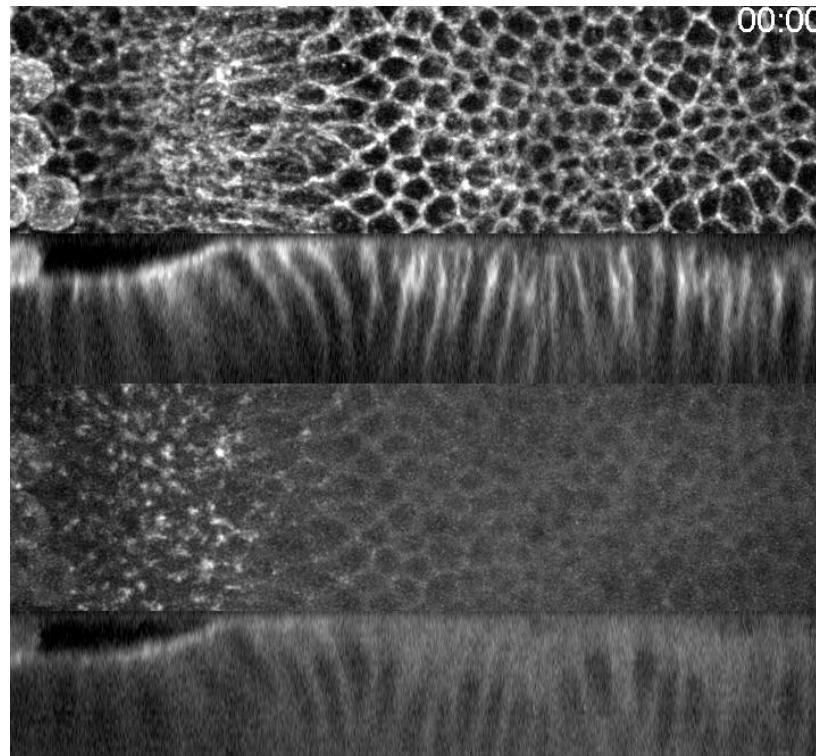
# A mechanical travelling cycle



# A mechanically driven travelling cycle



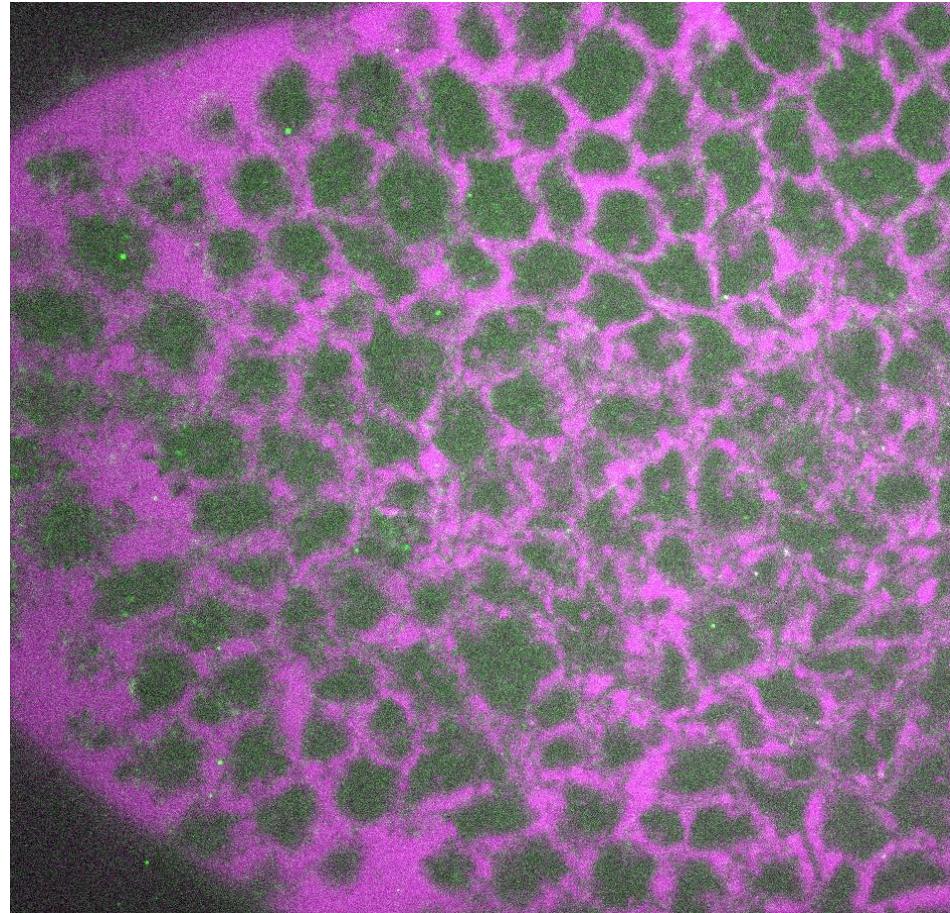
Rok Inhibition blocks cycle



# Adhesion to the vitelline membrane

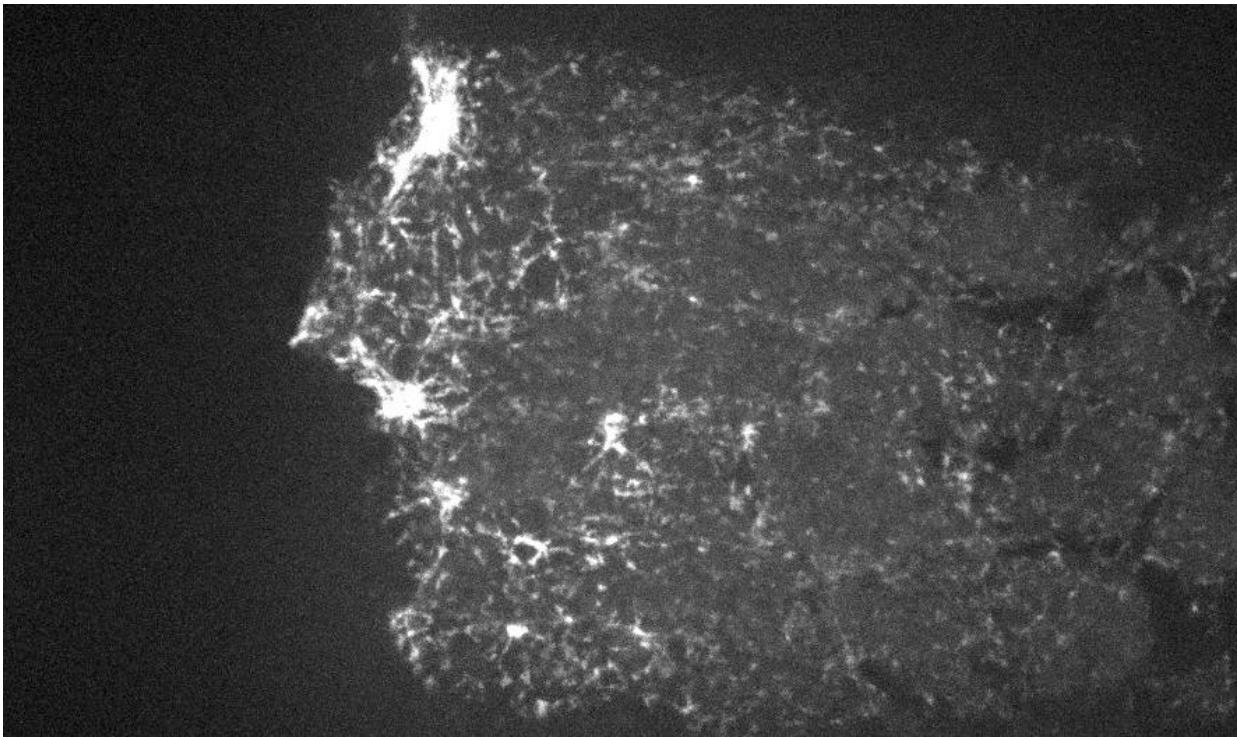
- cells just anterior to the furrow are in direct contact with the vitelline membrane

Posterior

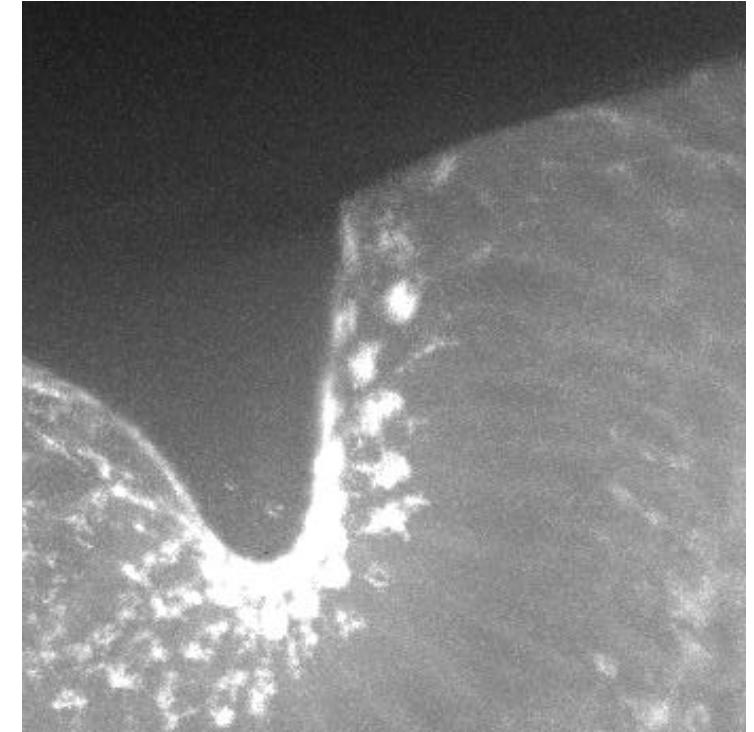


# Adhesion to the vitelline membrane

Top view

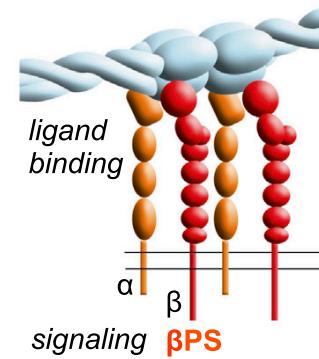
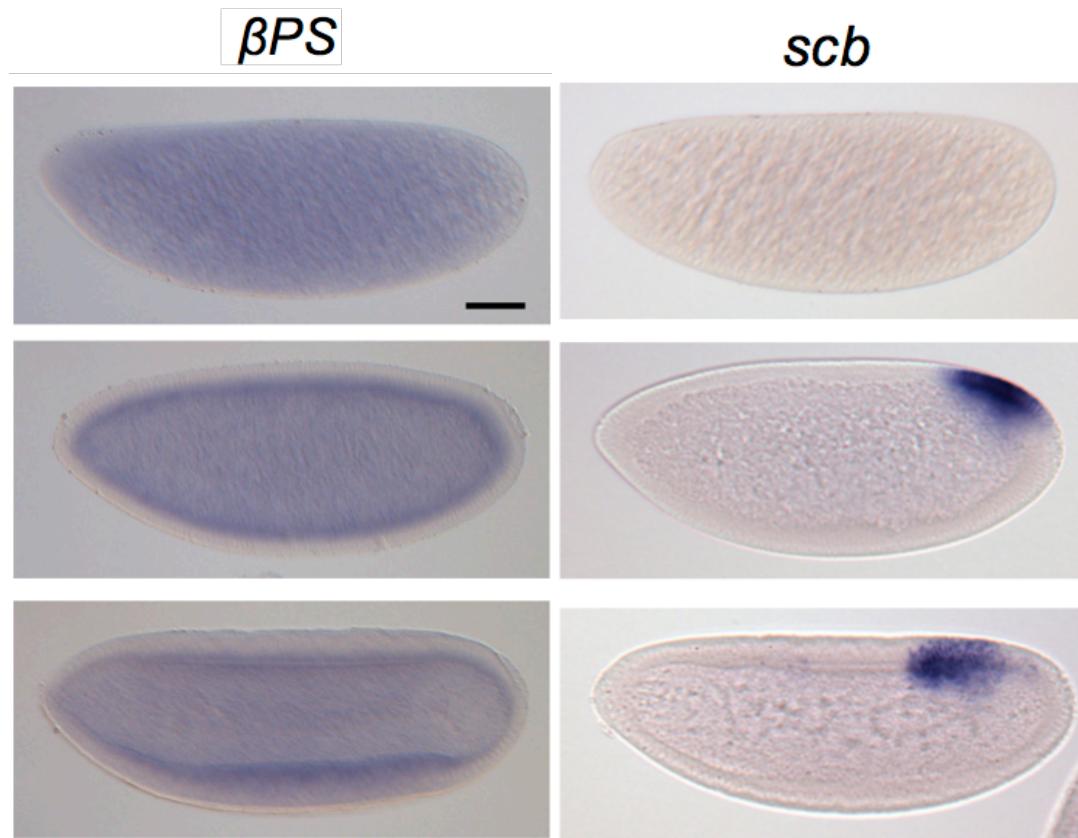


Side view



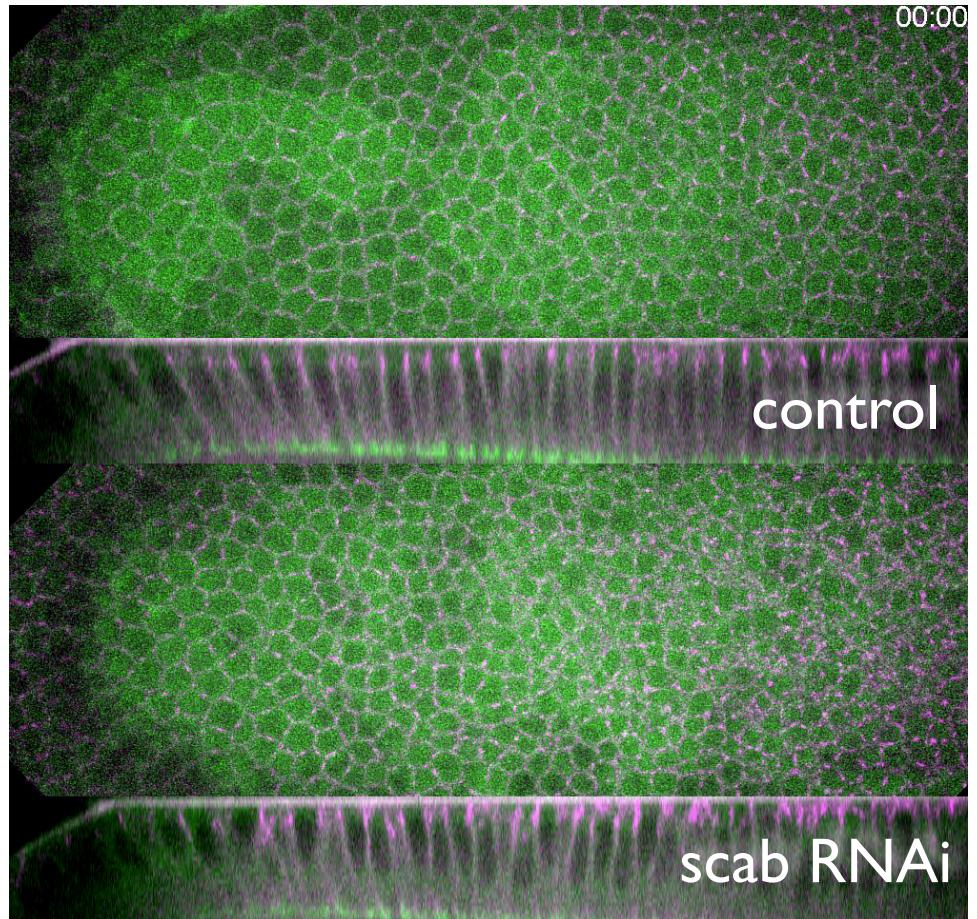
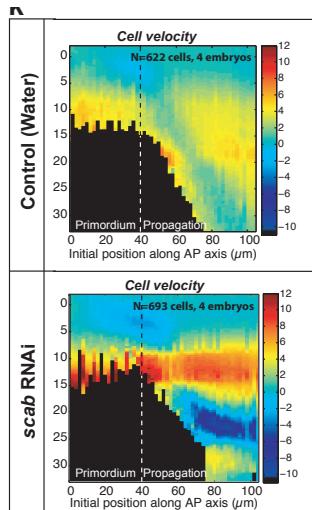
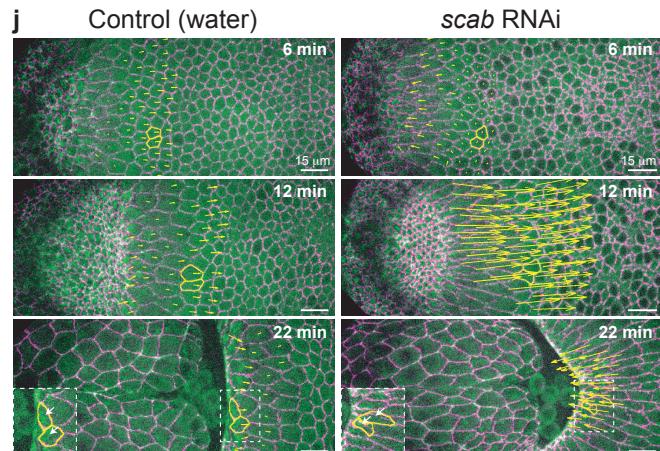
# Adhesion to the vitelline membrane requires Integrins

alpha PS3 Integrin (*Scab*) is expressed in the dorsal posterior ectoderm (ie. the propagation zone)



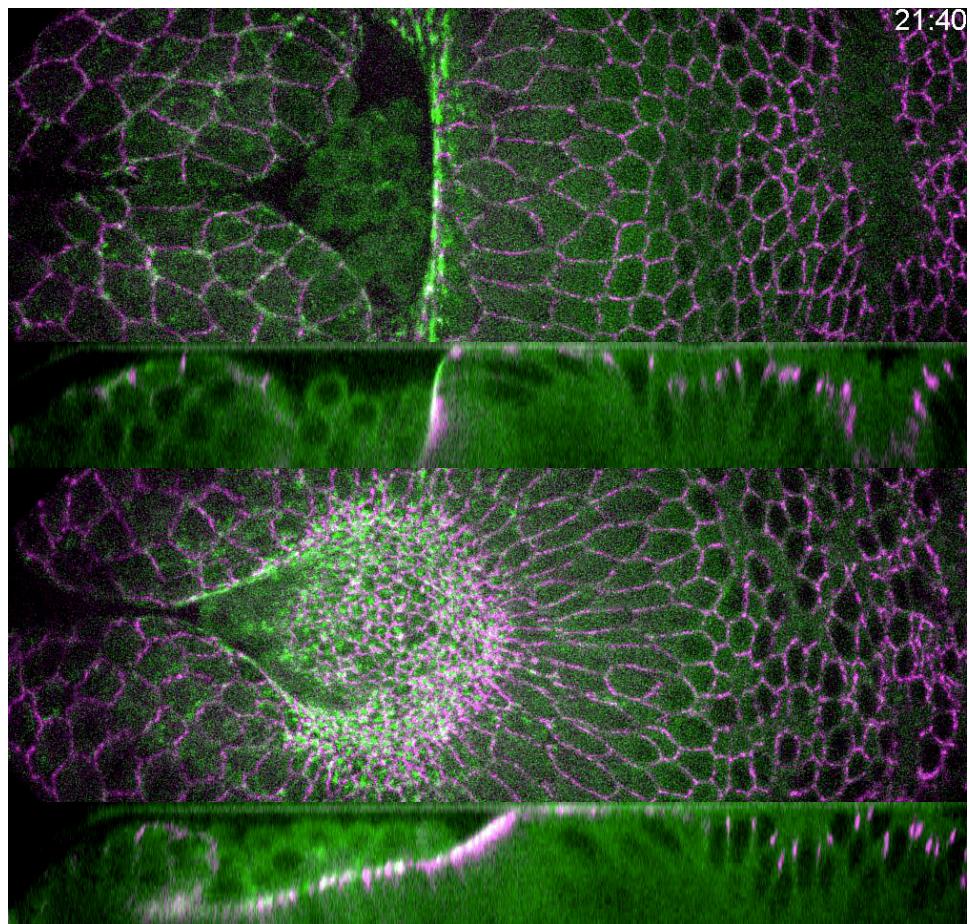
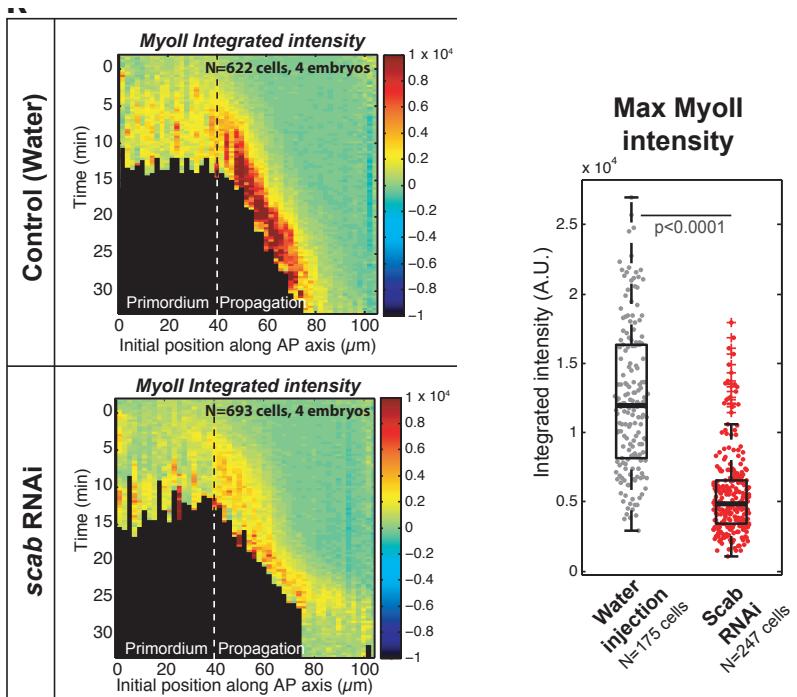
# Adhesion to the vitelline membrane requires Integrins

- Travelling mechanical cycle is blocked in aPS3 integrin RNAi:
- Biphasic extension: fast then blocked
- Delayed invagination

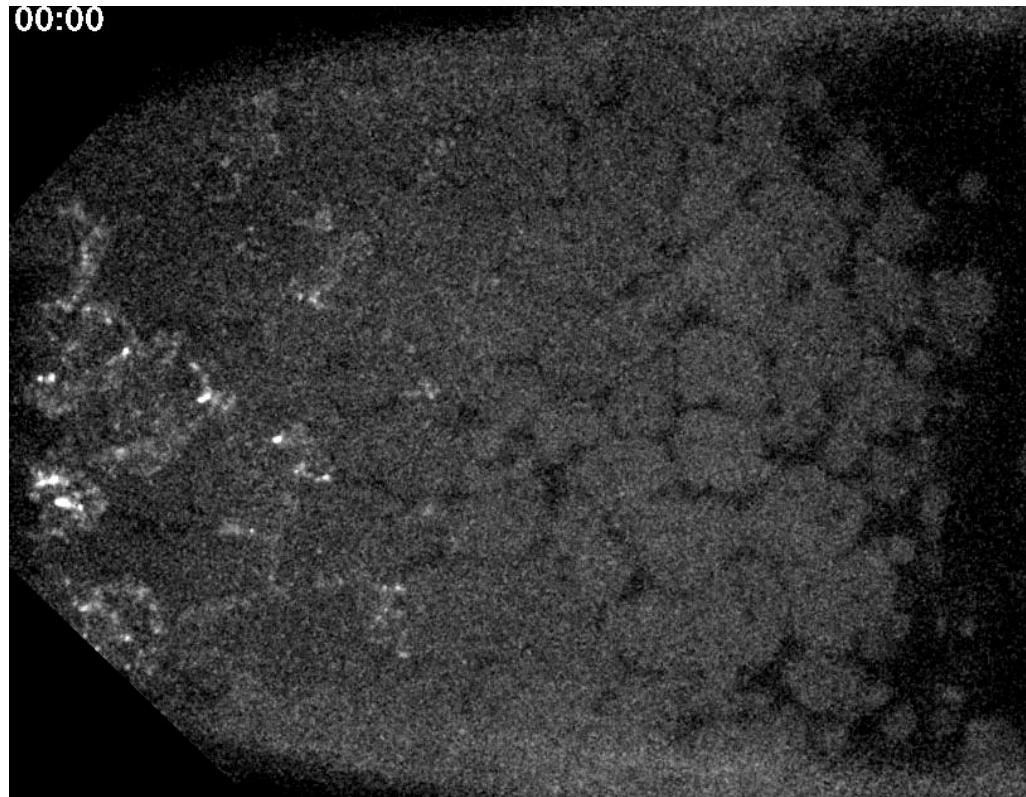


# Integrin signalling is required for MyoII activation wave

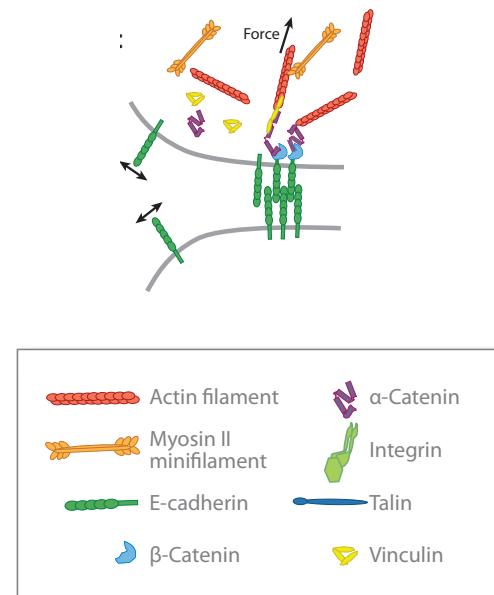
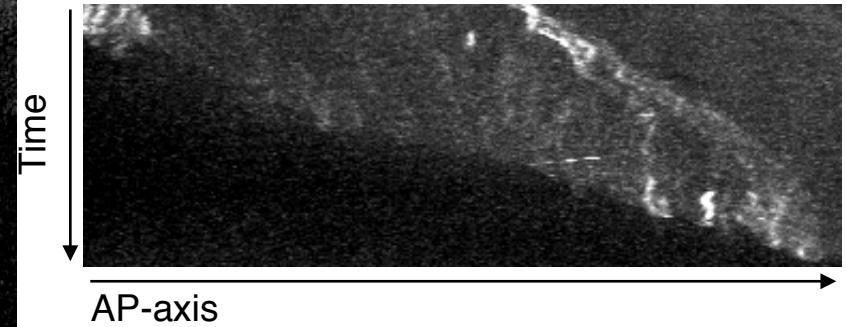
- Myosin-II activation is reduced
- wave propagation of high MyoII activation is blocked



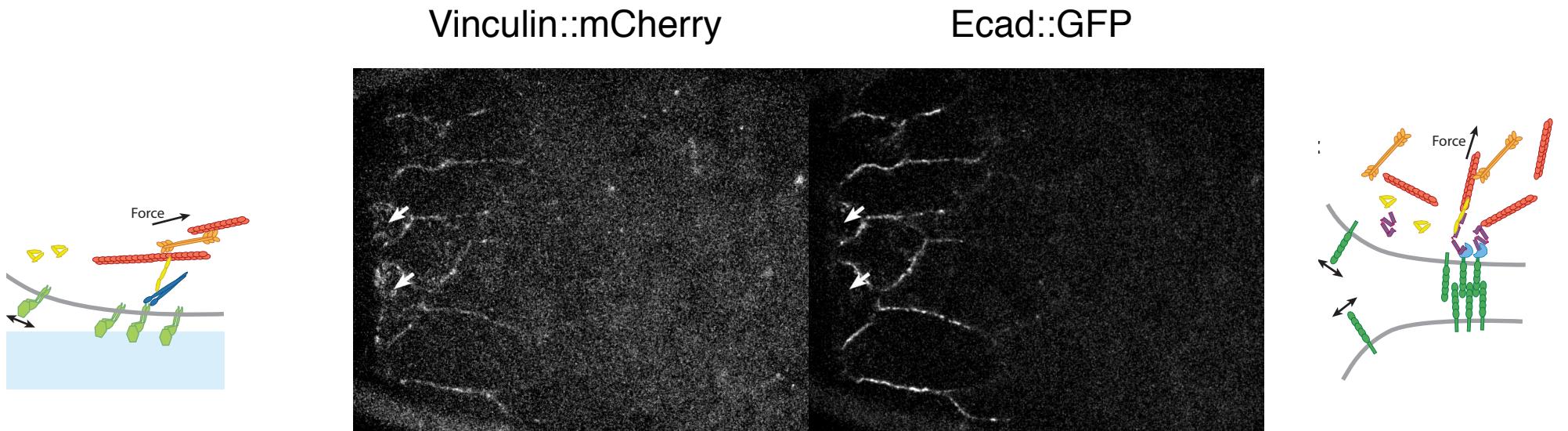
# Talin is recruited at the apical cell surface contacting the vitelline membrane



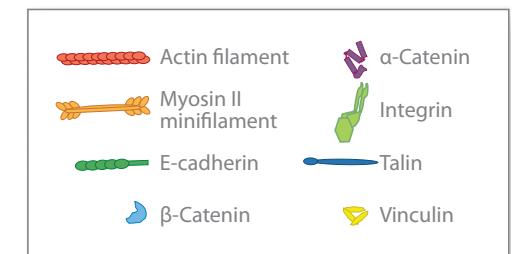
endo Talin::YFP



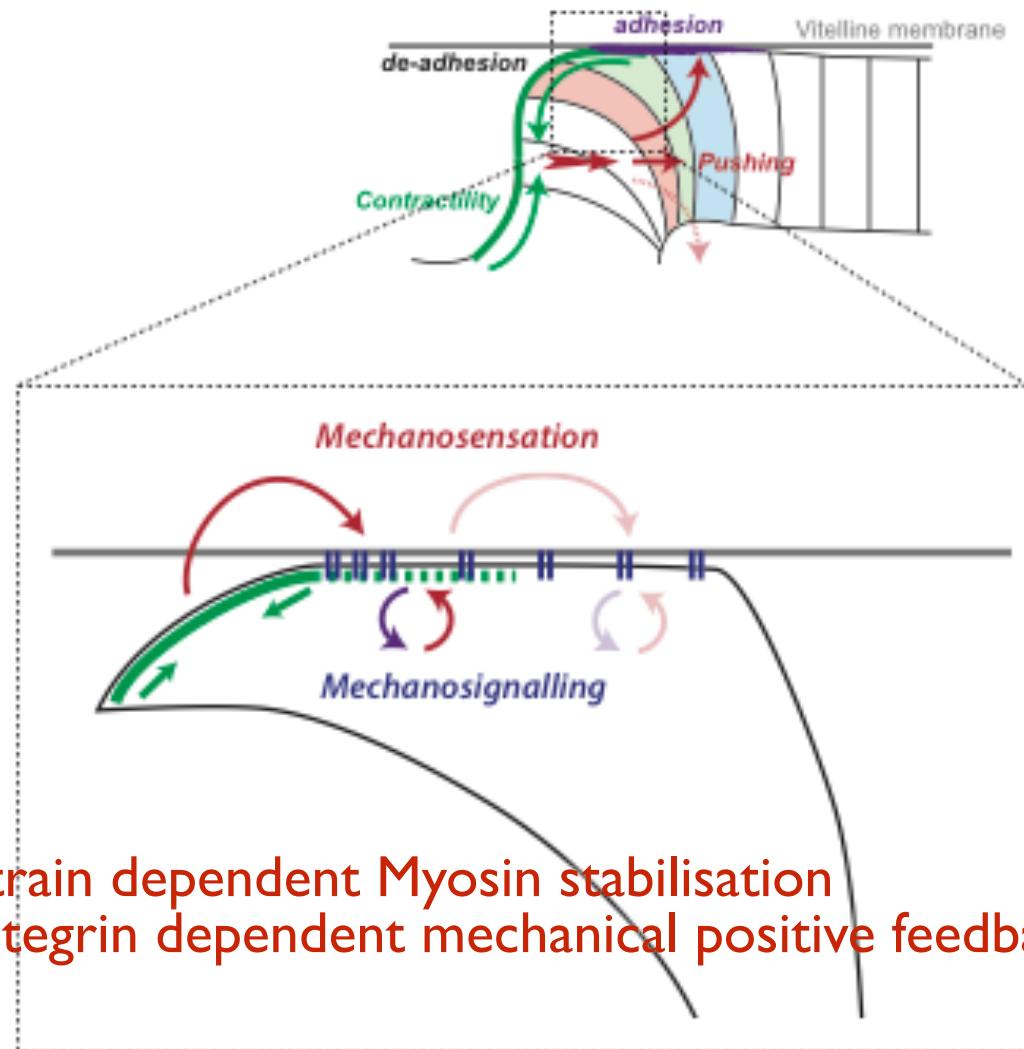
# Vinculin is recruited at the apical cell surface in contact to the vitelline membrane



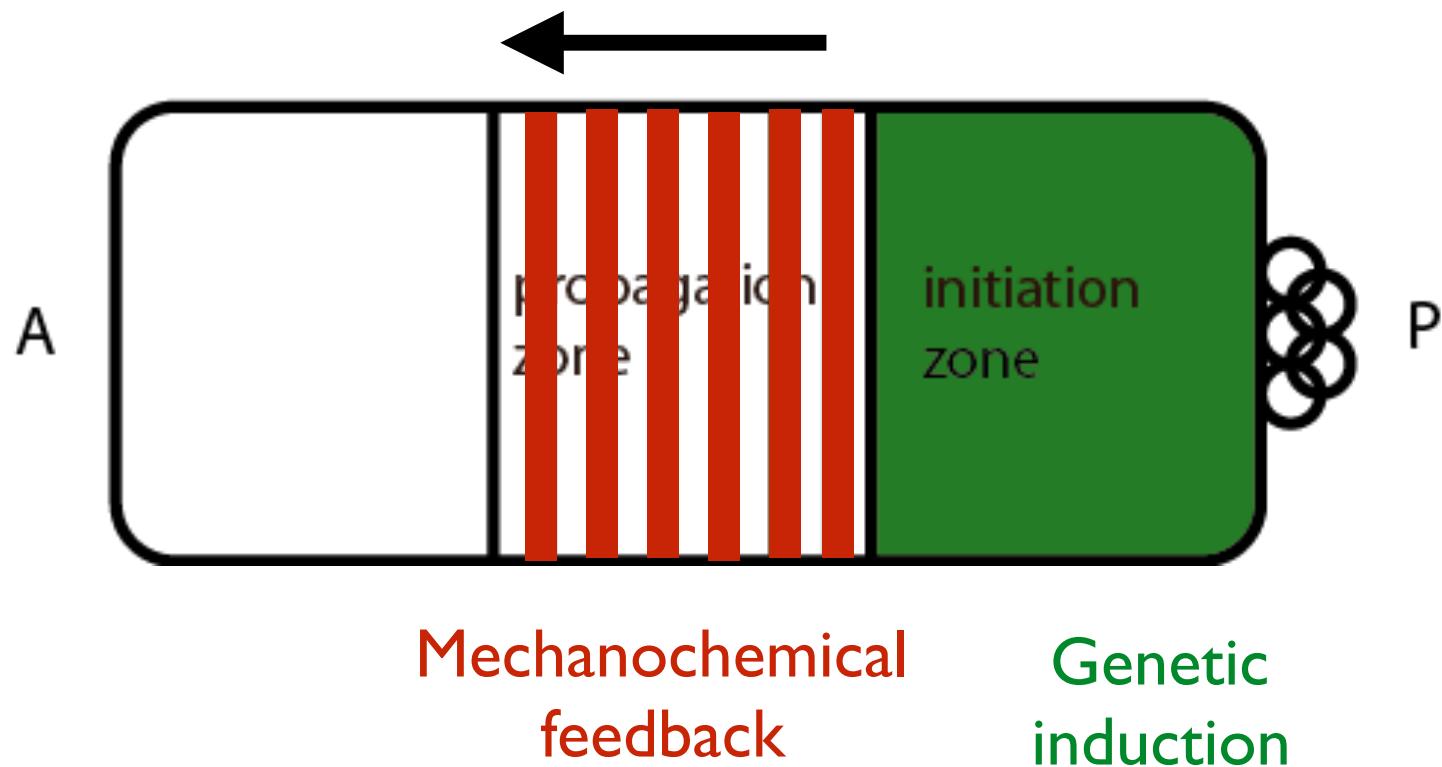
Vinculin is normally recruited at focal adhesion under mechanical load



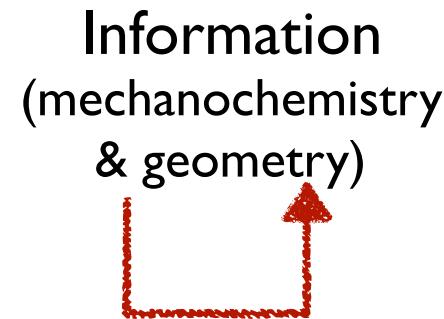
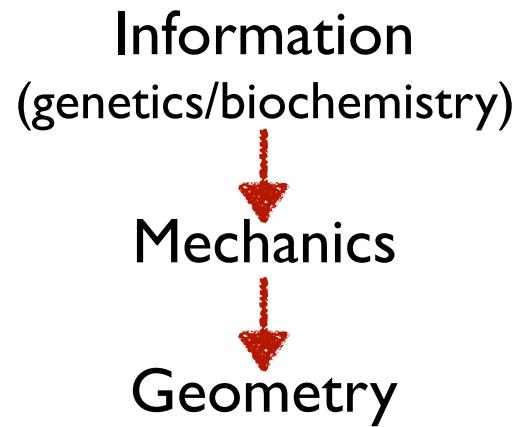
# Working model for MyoII activation wave



# Genetic induction and mechanochemical propagation of a morphogenetic wave

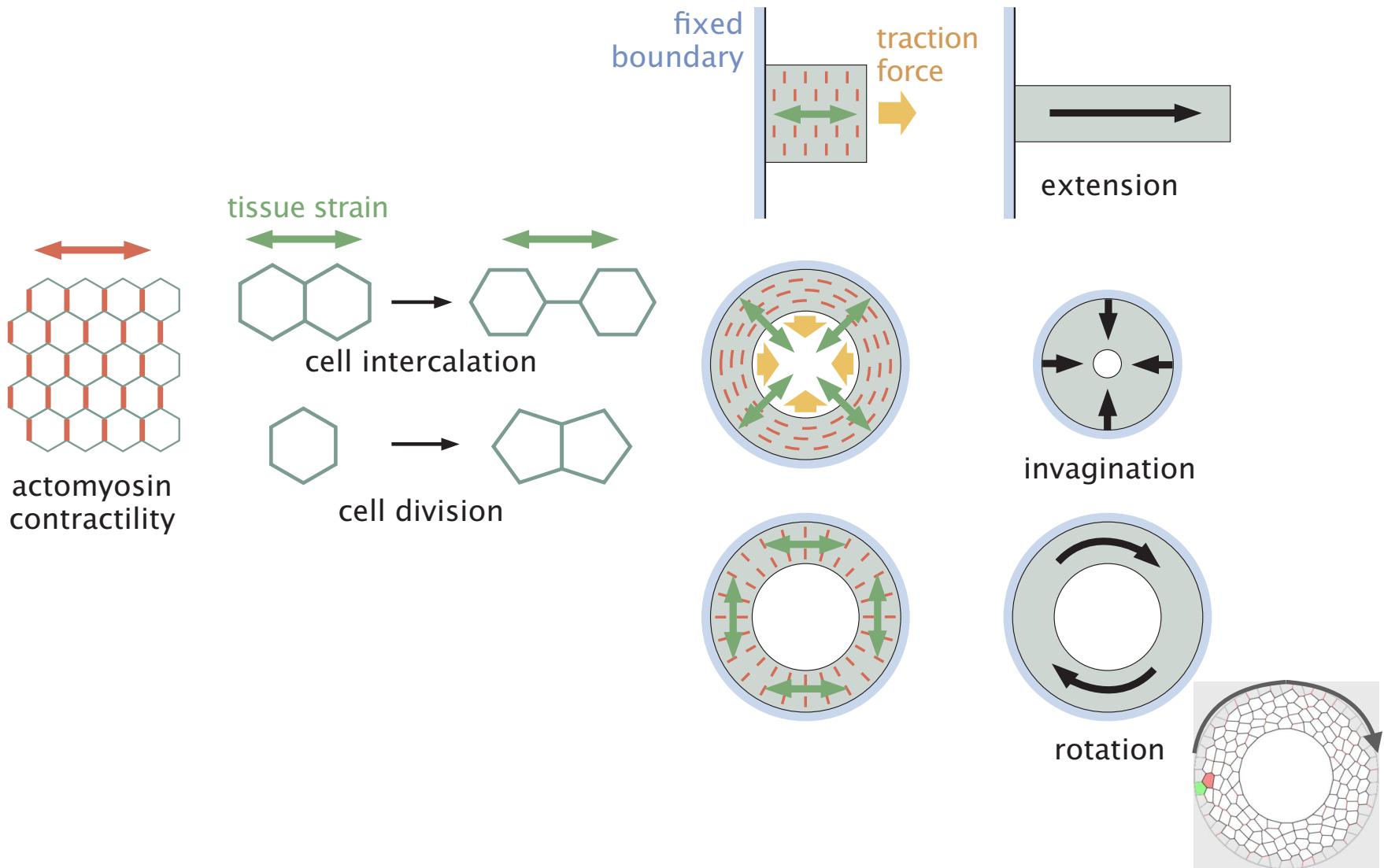


# Self-organisation with mechano-chemical information

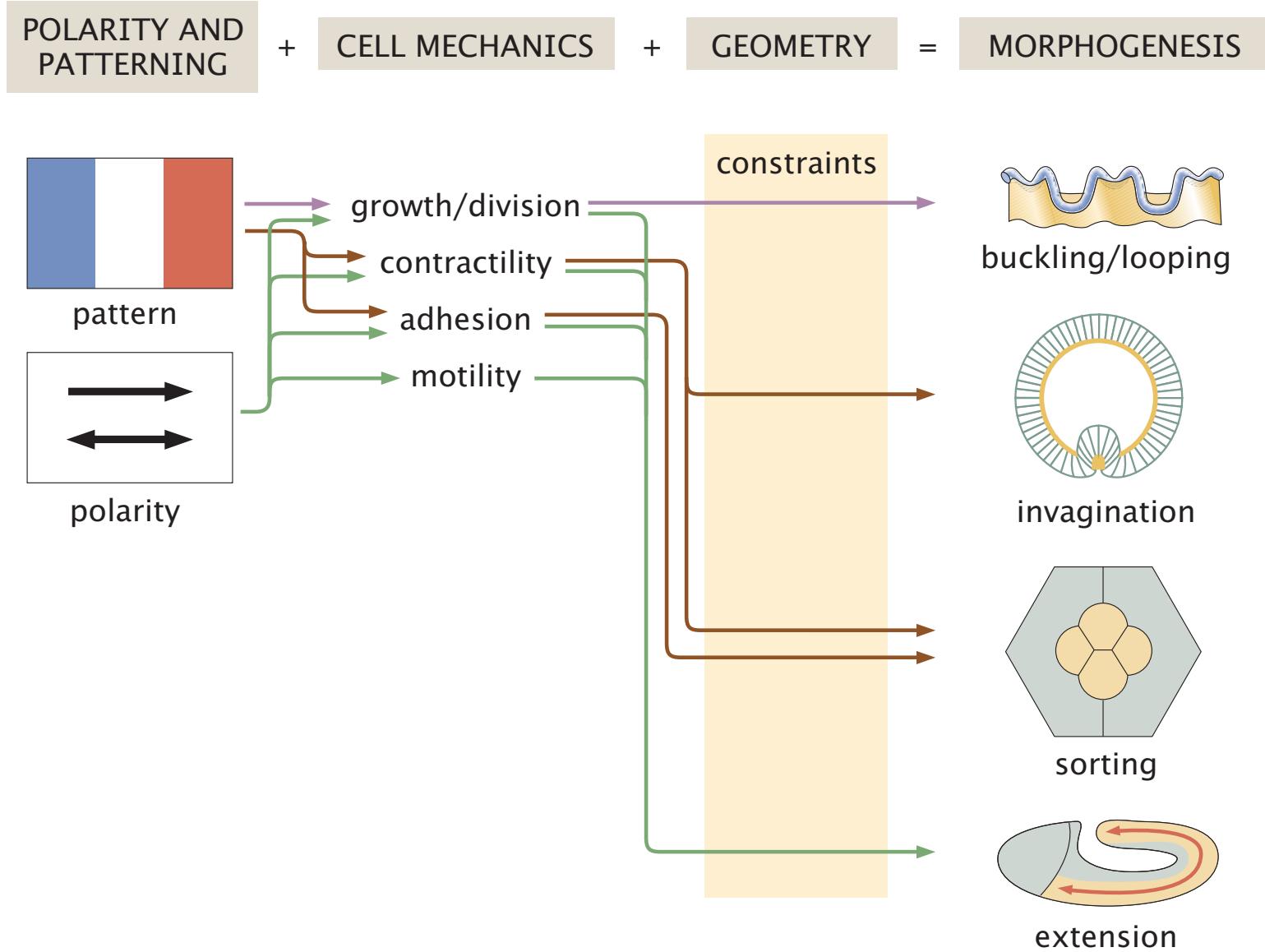


# General conclusion

$$\text{POLARITY} + \text{CELL MECHANICS} + \text{GEOMETRY} = \text{MORPHOGENESIS}$$



# General conclusion





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**Anaïs Bailles**  
Claire Bertet  
Bandan Chakraporty  
**Claudio Collinet**  
Benoit Dehapiot  
Alain Garcia de las Bayonas  
Emily Gehrels  
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Steve Kerridge  
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Qiyan Mao (@ F Schnorrer)  
Benoit Dehapiot (Turing Center)



Collaborators:

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Matthias Merkel (CPT & Turing Center)  
**Ed Munro** (Chicago)  
Madan Rao (NCBS)  
Jitu Mayor (NCBS)



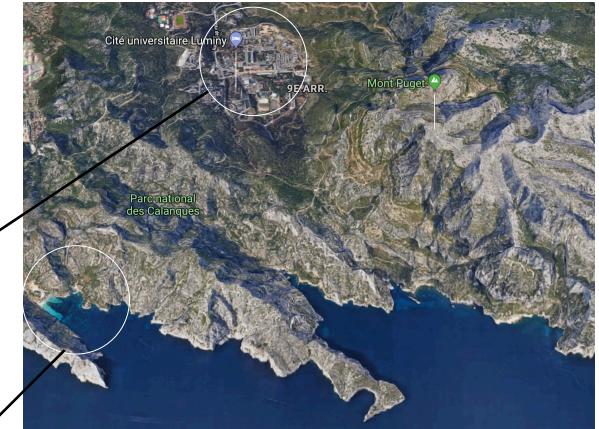


# CENTURI

TURING CENTRE  
FOR LIVING SYSTEMS



Aix-Marseille University: Luminy Campus



Calanques