

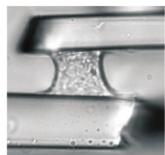
the actomyosin drive in morphogenesis

Jocelyn Étienne

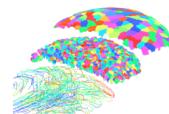
LIPHY, CNRS–Univ. Grenoble Alpes



Dynamics of pulsatile apicomедial myosin in early embryo development



Jonathan Fouchard
Démosthène Mitrossilis
Nathalie Bufl
Pauline Durand-Smet
Atef Asnacios
MSC, CNRS–Univ. Paris-Diderot



Guy Blanchard

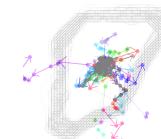
PDN, Univ. Cambridge

Pedro Machado
Alfonso Martinez Arias

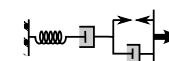
Genetics, Univ. Cambridge

Julia Duque
Nicole Gorfinkiel

CIB, CSIC, Madrid



Nilankur Dutta



Jocelyn Étienne

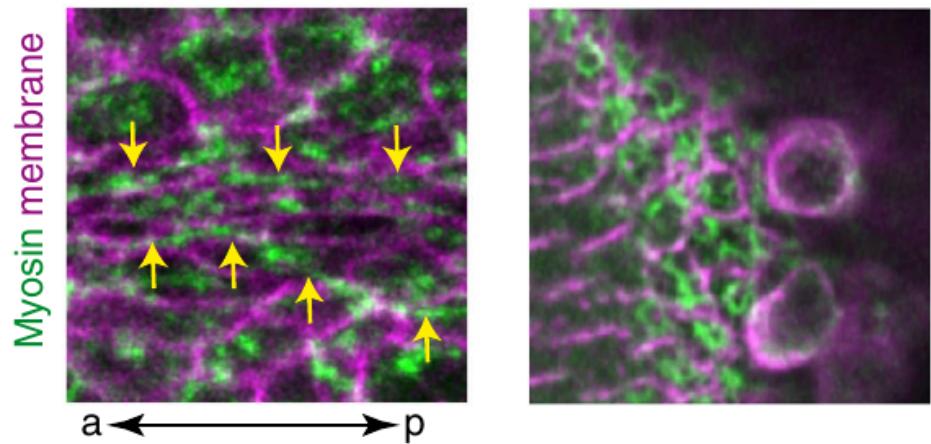
LIPHY, CNRS–Univ. Grenoble Alpes



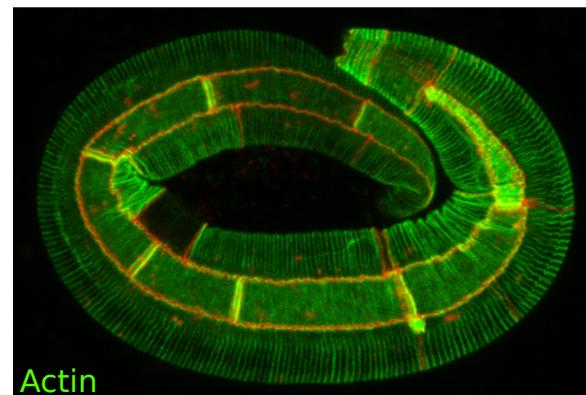
PARIS
DIDEROT



Actomyosin in its diversity

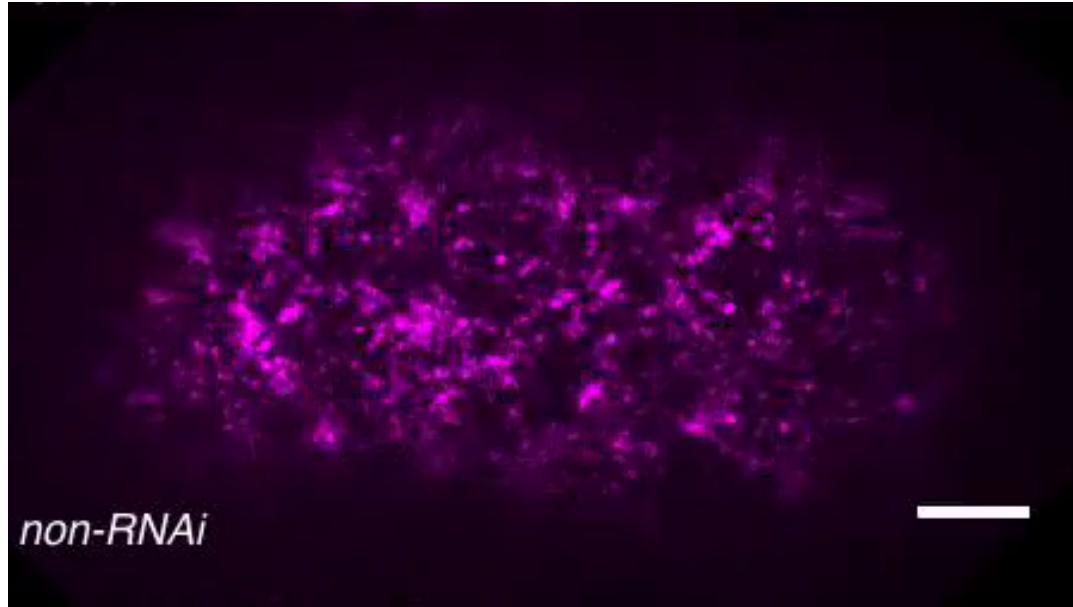


Drosophila mesoderm & PMG
[Chanet et al, 2017]

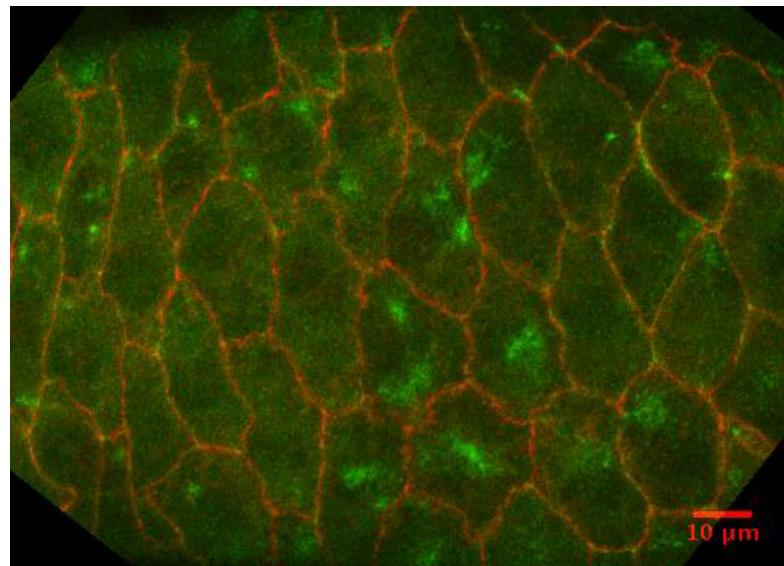


C elegans
[G. Michaux, Rennes]

Pulsatility of actomyosin

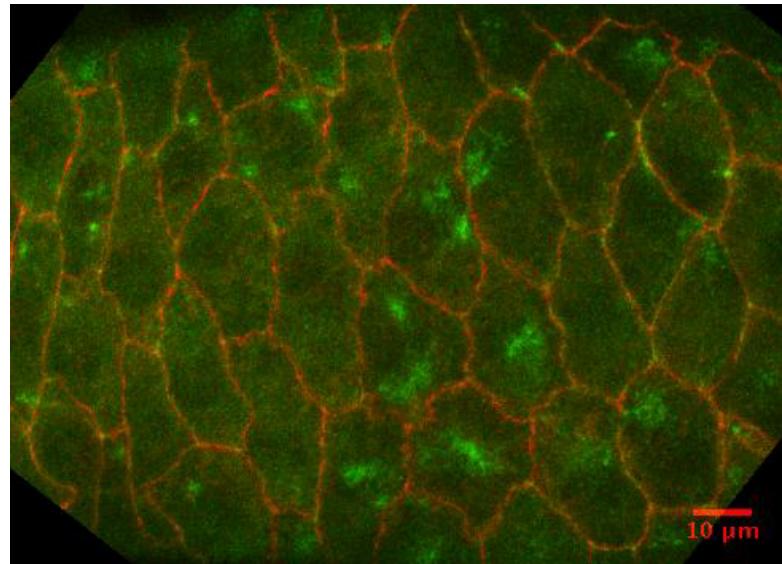
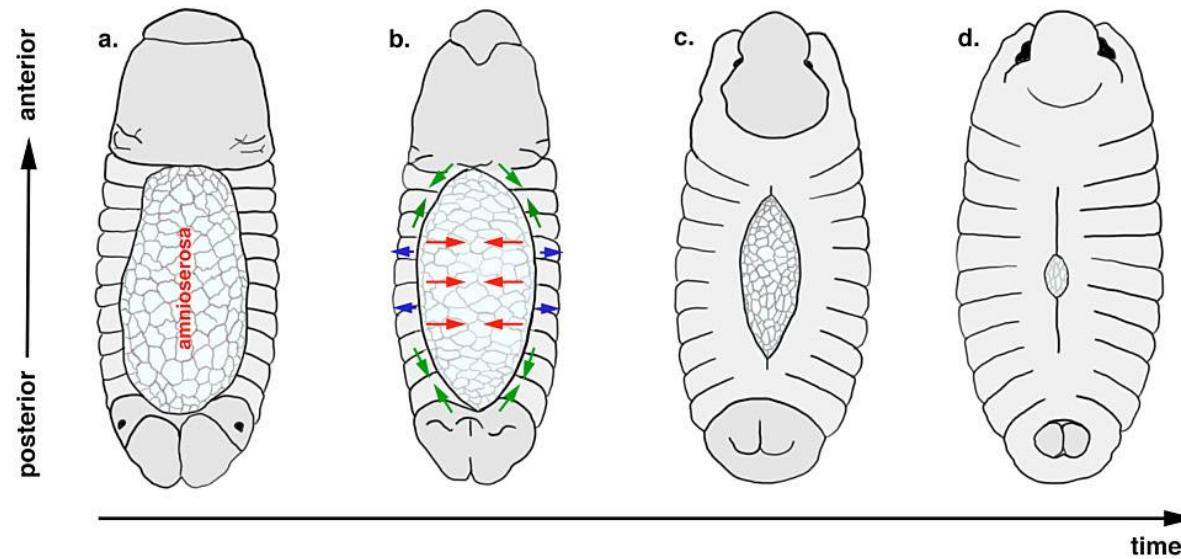


C elegans zygote [Nishikawa et al, 2017]



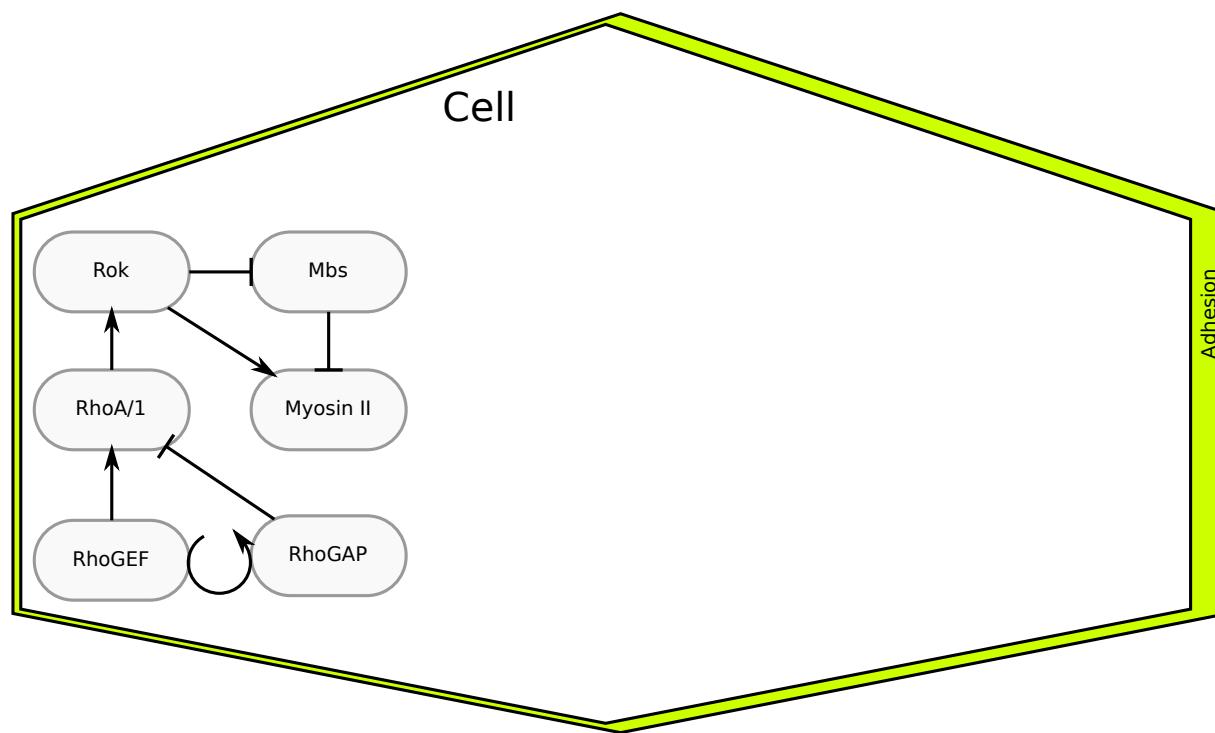
Drosophila amnioserosa during dorsal closure [Fischer et al, 2014]

Pulsatility of actomyosin and dorsal closure



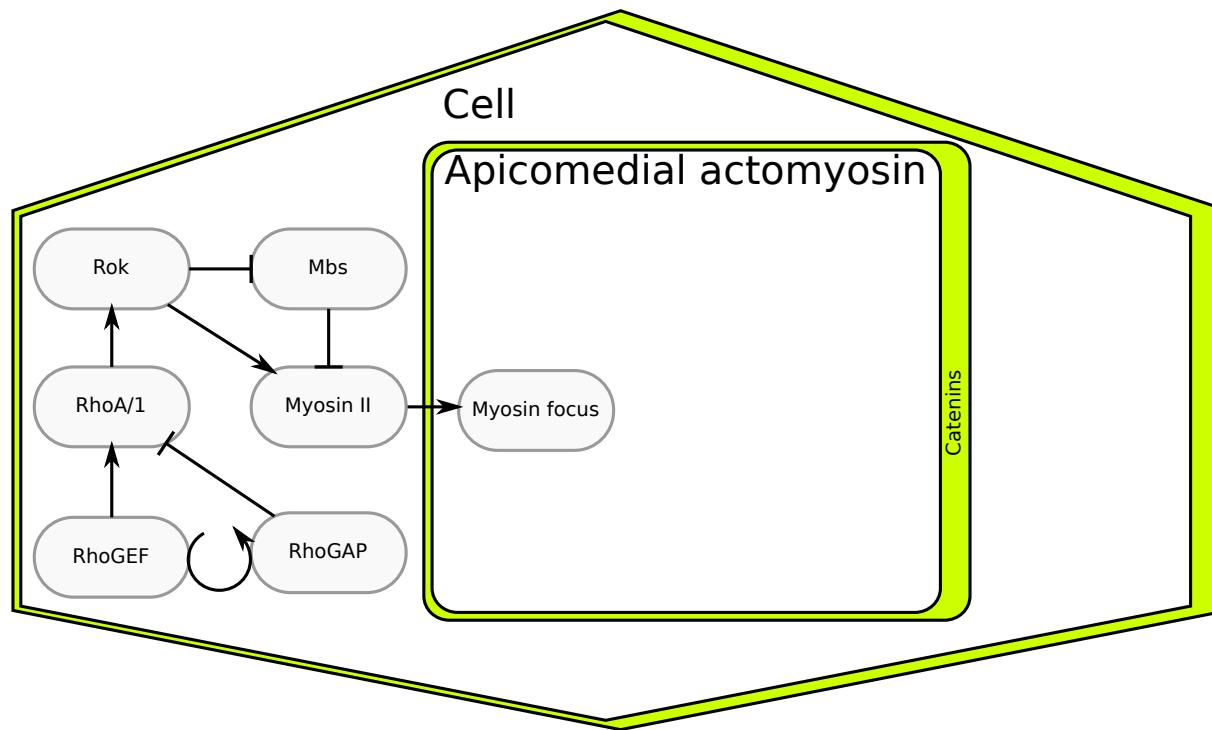
Drosophila amnioserosa during dorsal closure [Fischer et al, 2014]

What I can't tell you about pulsatility



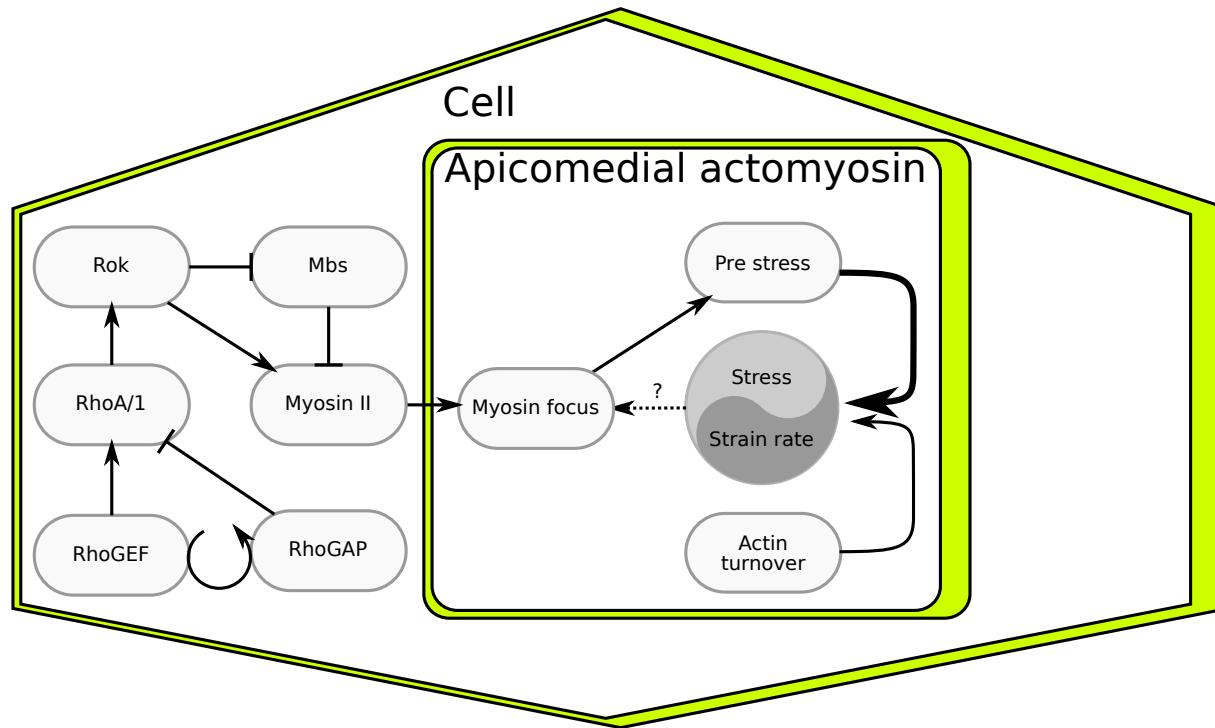
Blanchard, Etienne and Gorfinkiel, *Cur Op Gen Dev* 2018

What I can't tell you about pulsatility



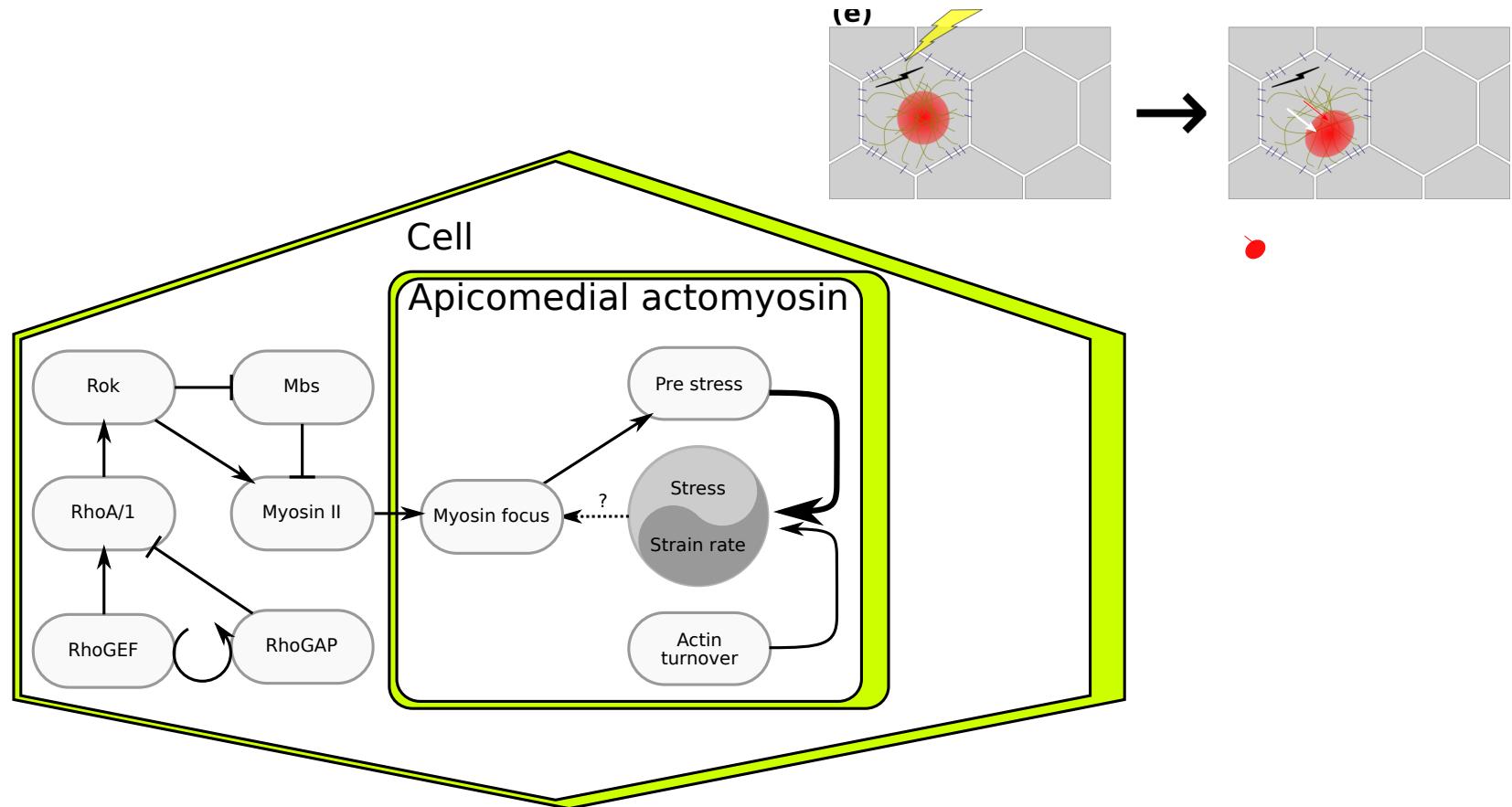
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What I can tell you about pulsatility



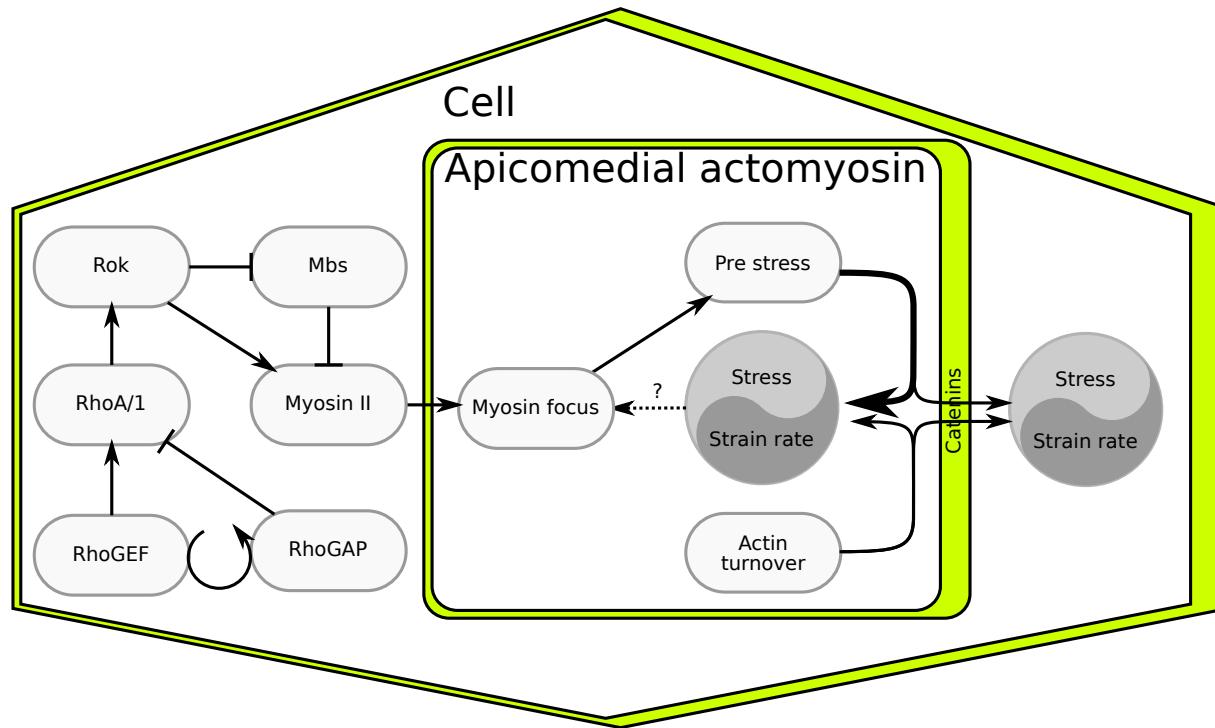
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What I can tell you about pulsatility



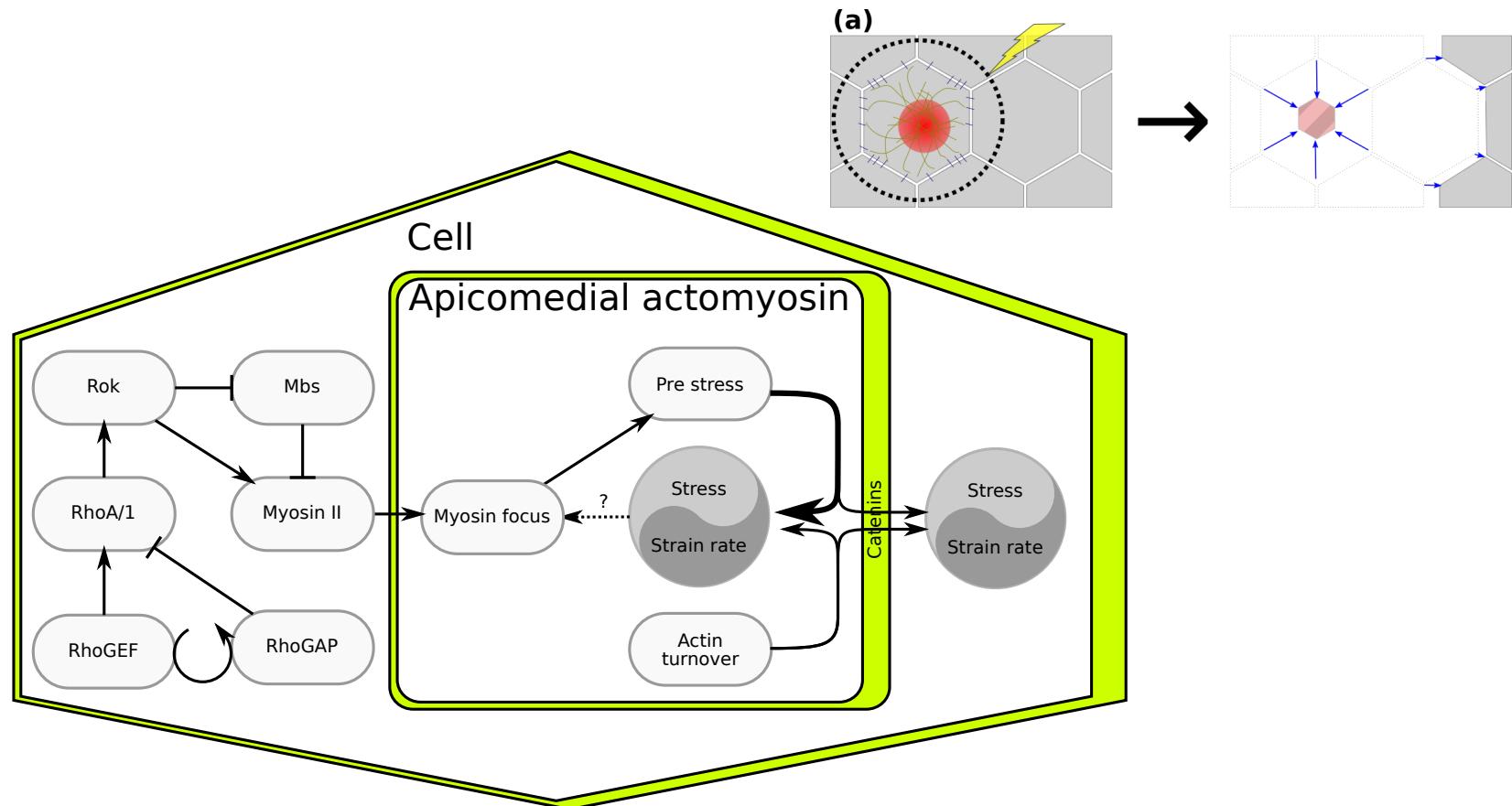
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What I can tell you about pulsatility



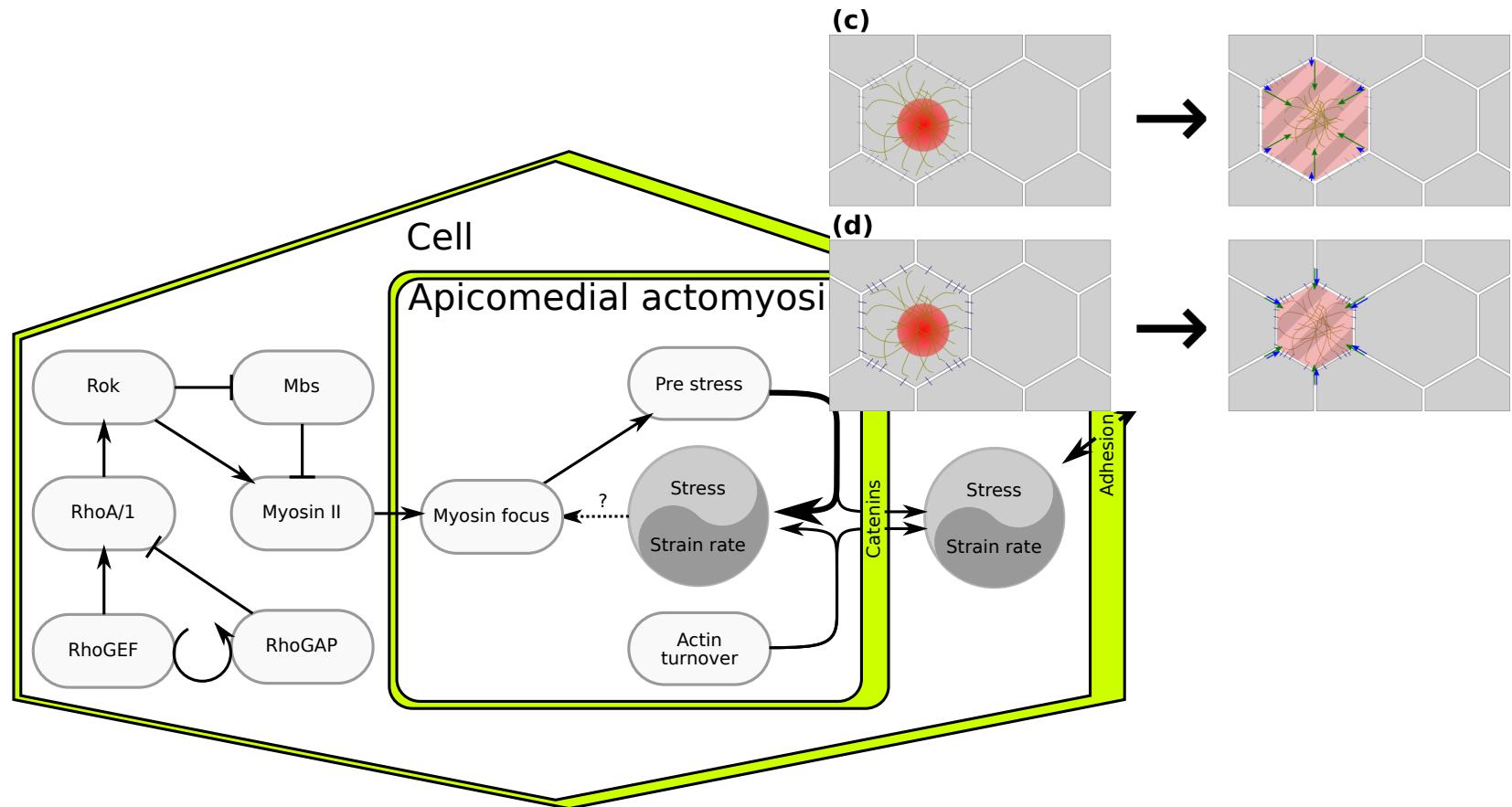
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What I can tell you about pulsatility



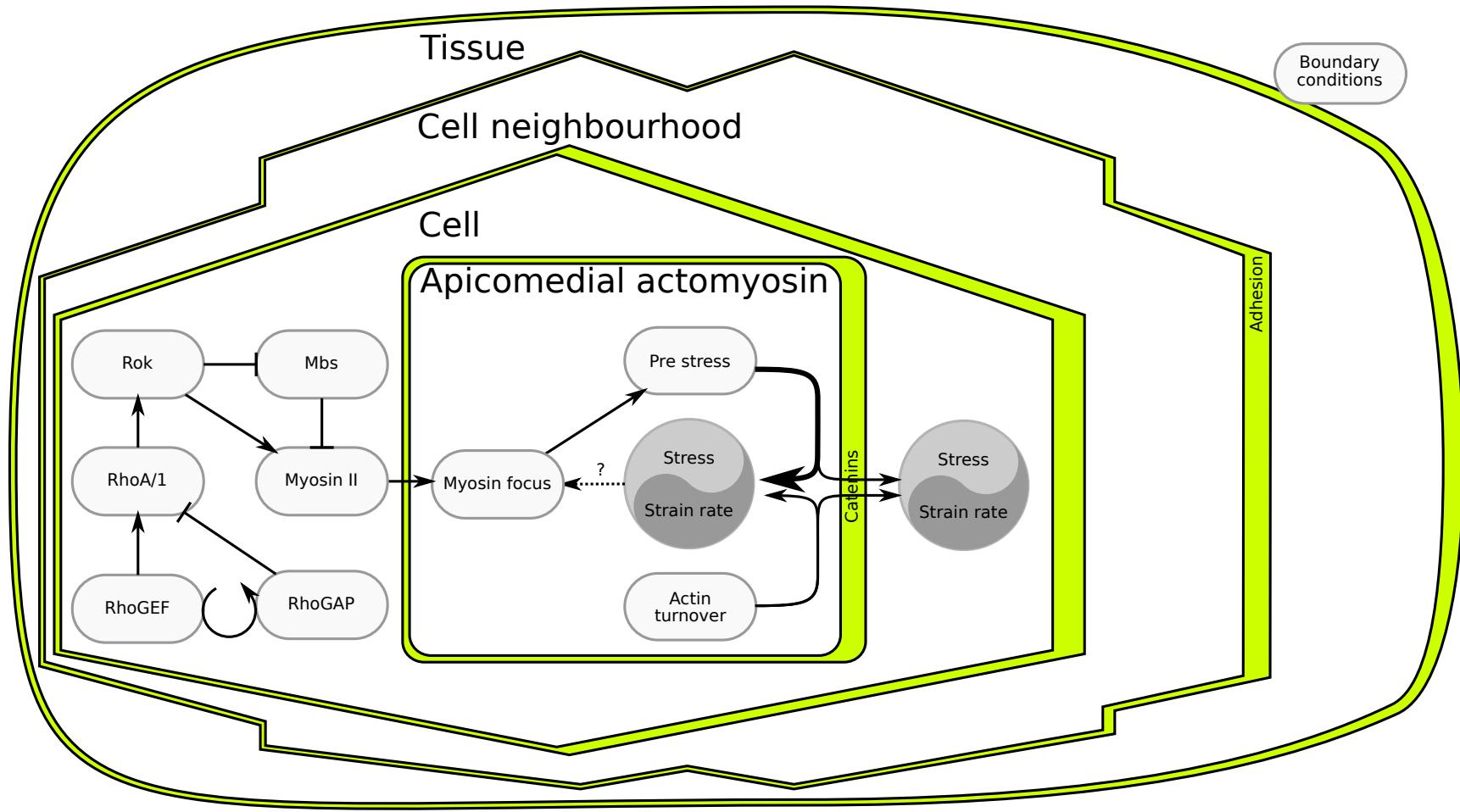
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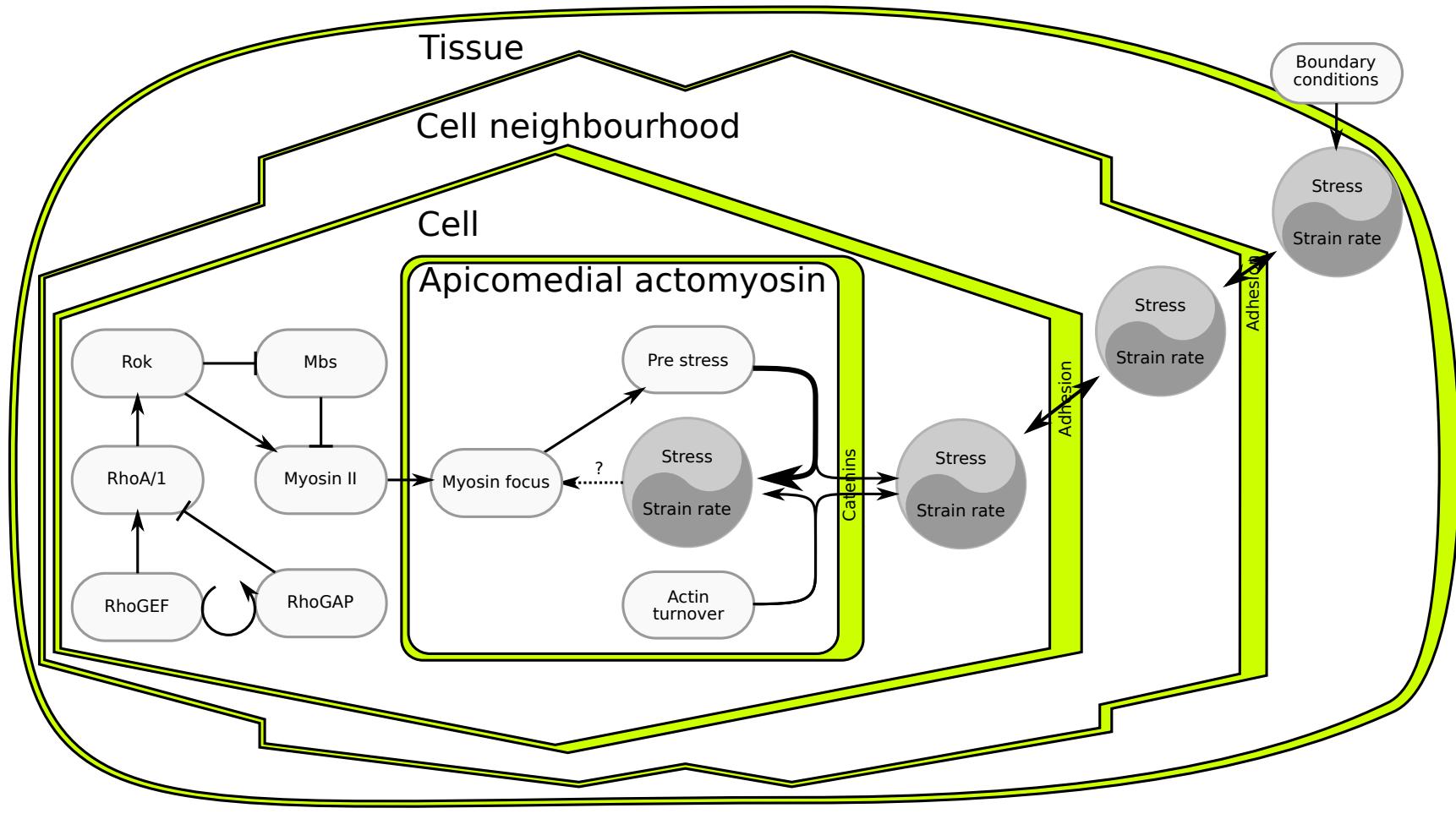
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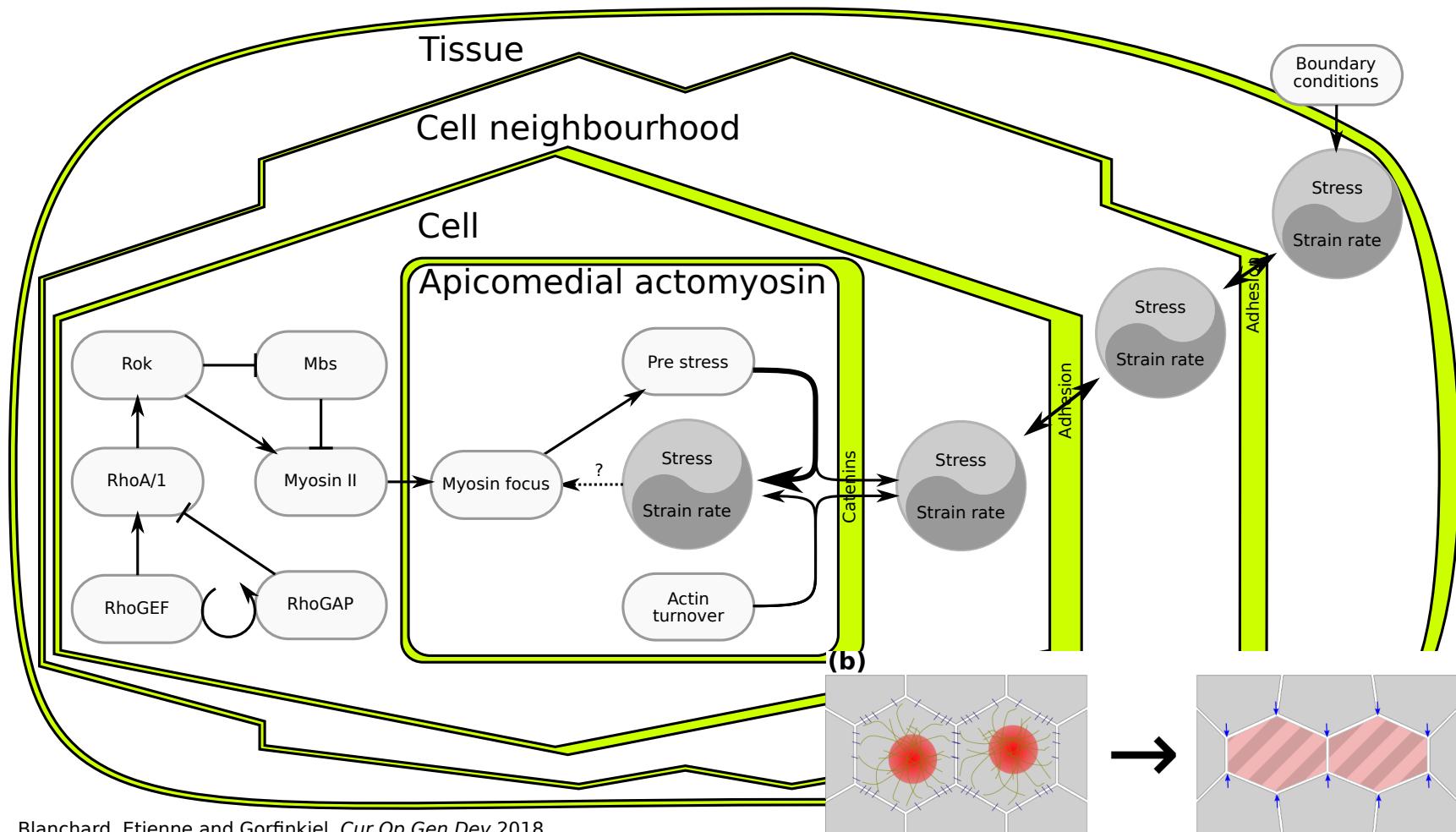


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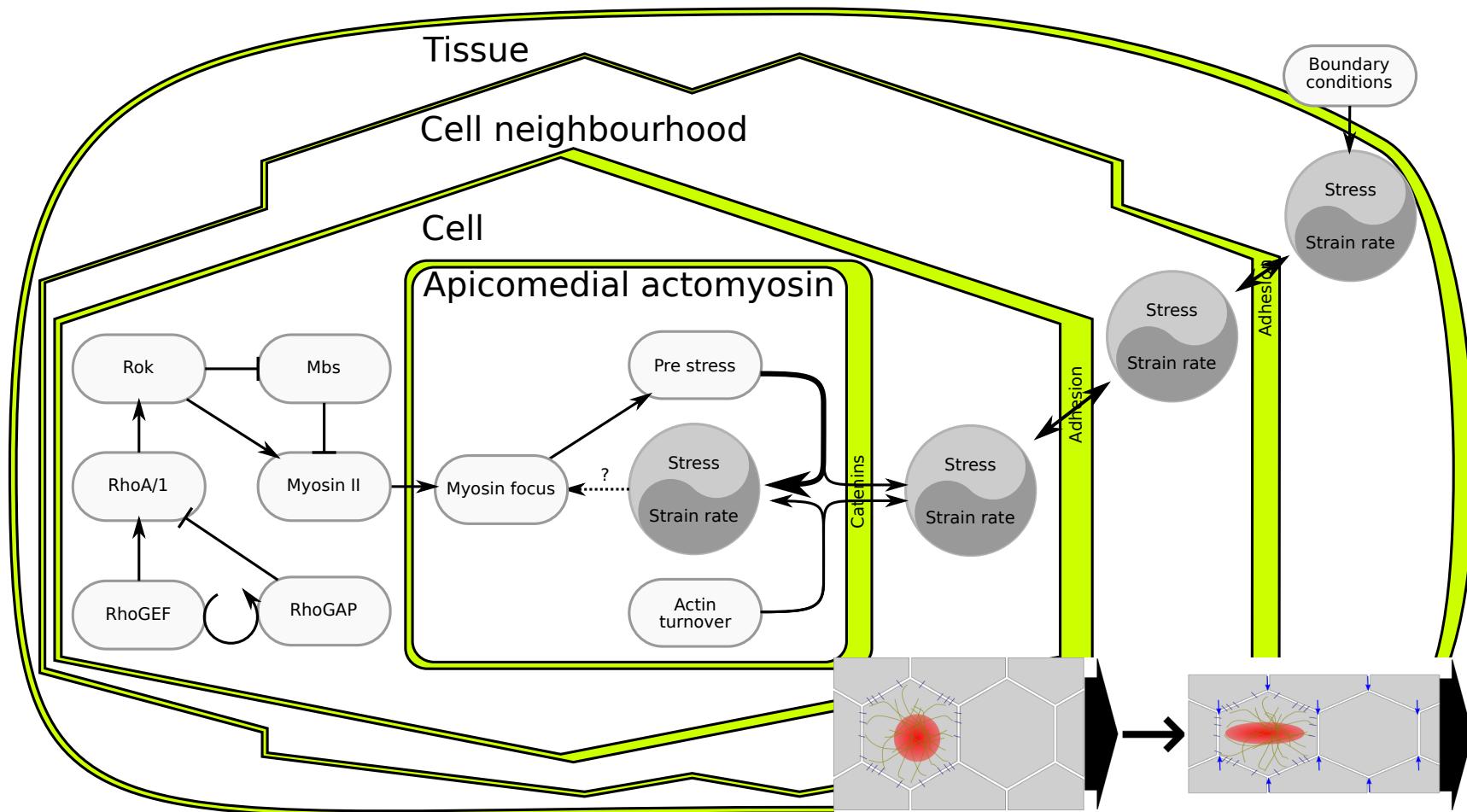
What I can tell you about pulsatility



What I can tell you about pulsatility

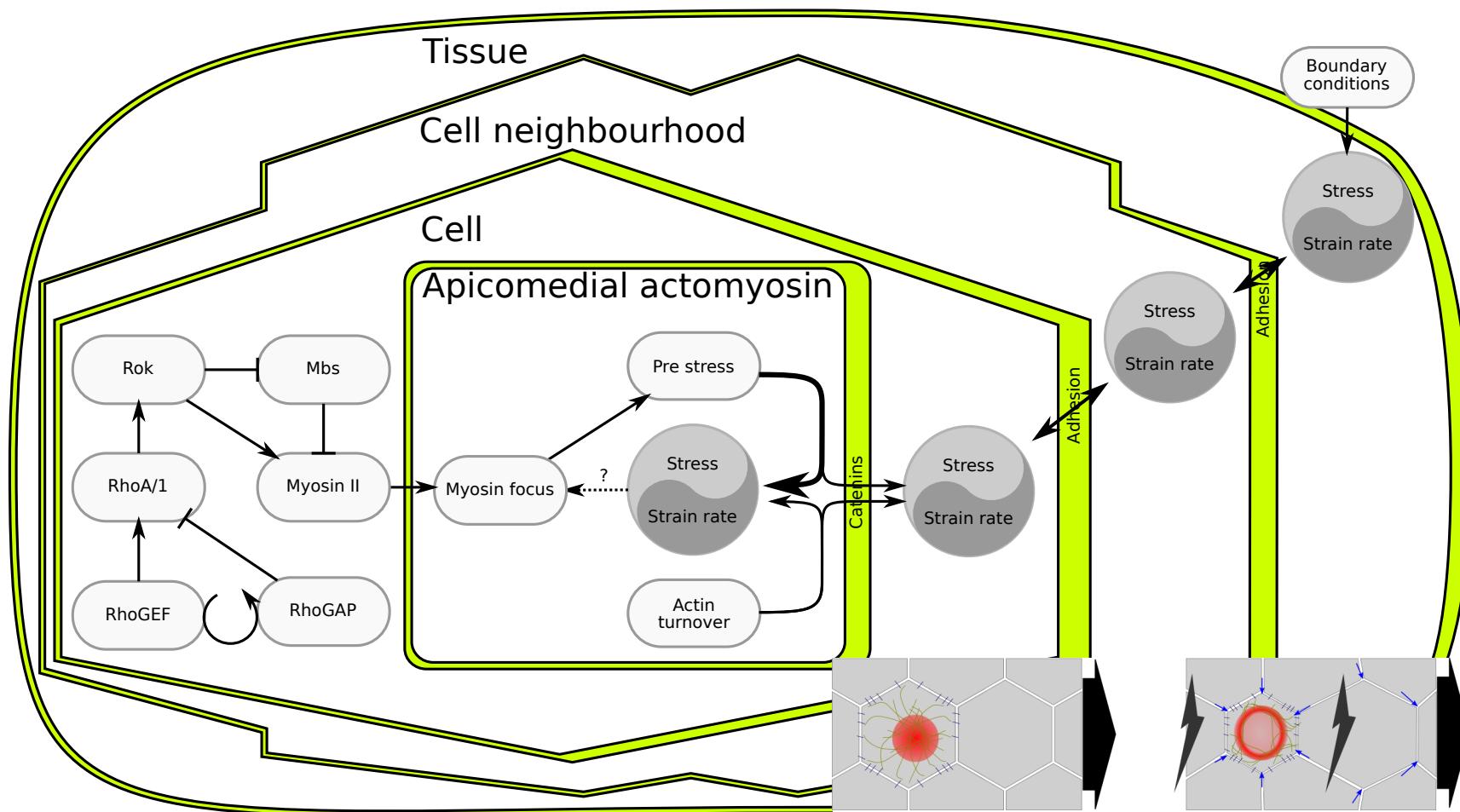


What I can tell you about pulsatility



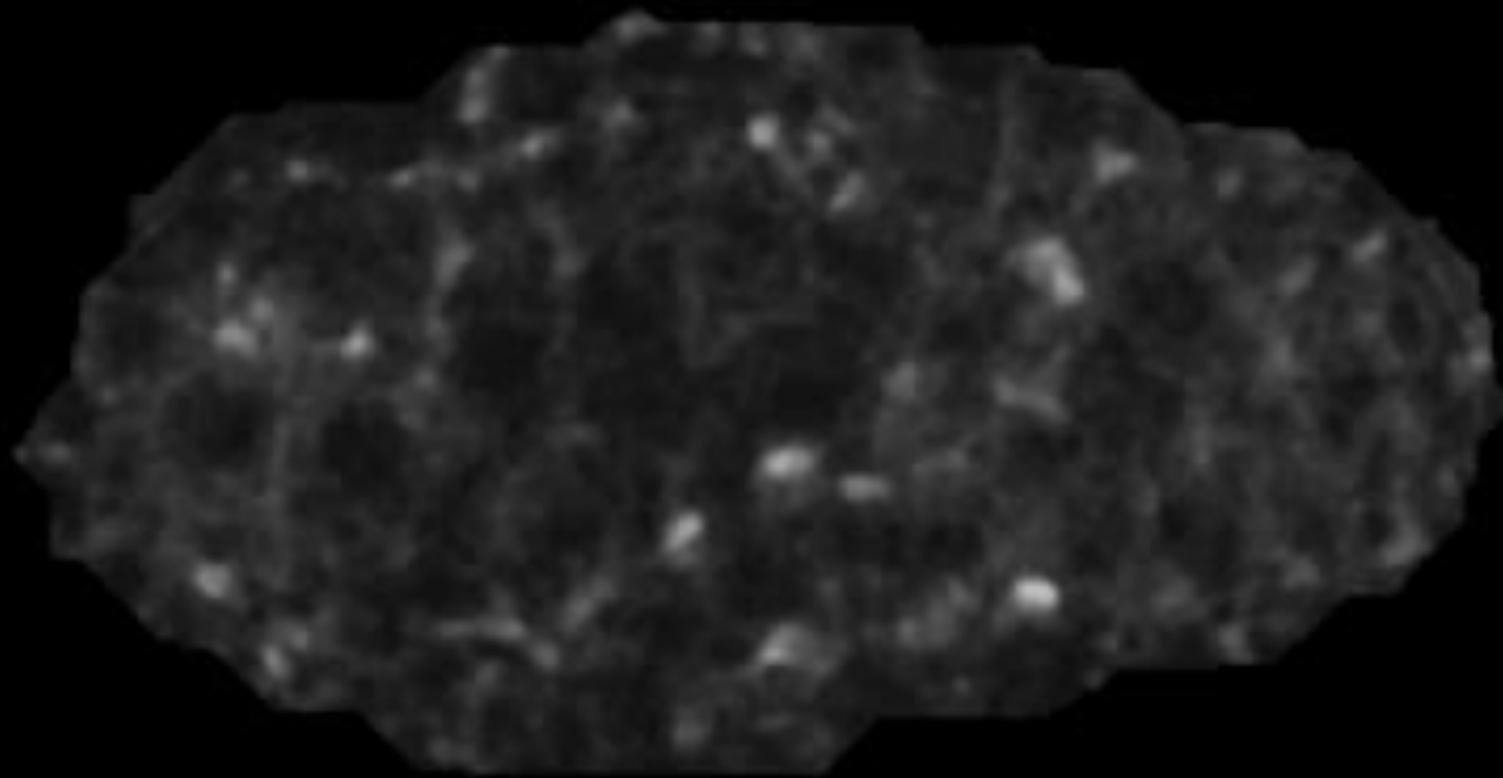
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What I can tell you about pulsatility



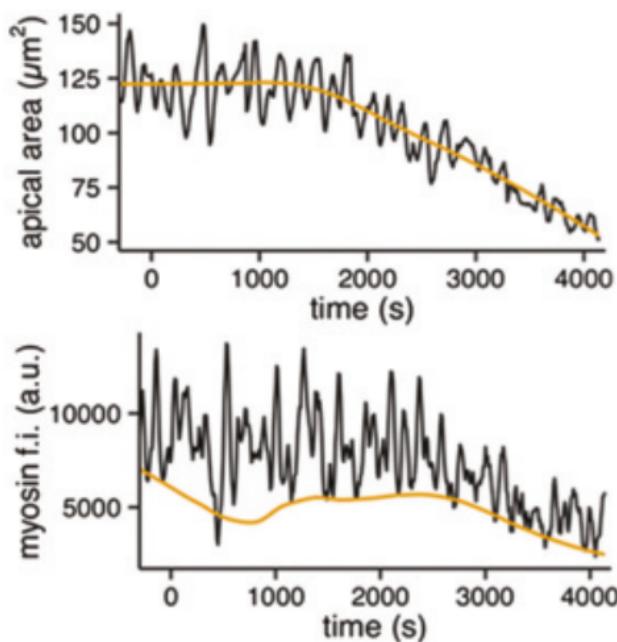
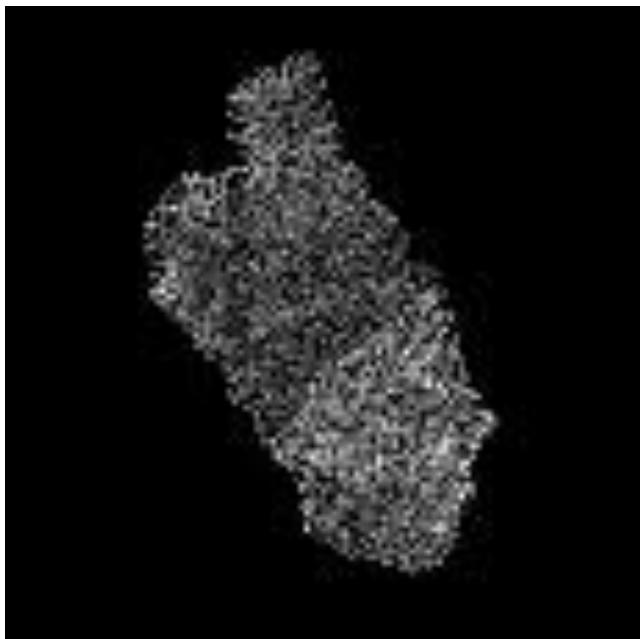
Blanchard, Etienne and Gorfinkel, Cur Op Gen Dev 2018

Myosin pulsations in dorsal closure



Myosin pulsations in dorsal closure

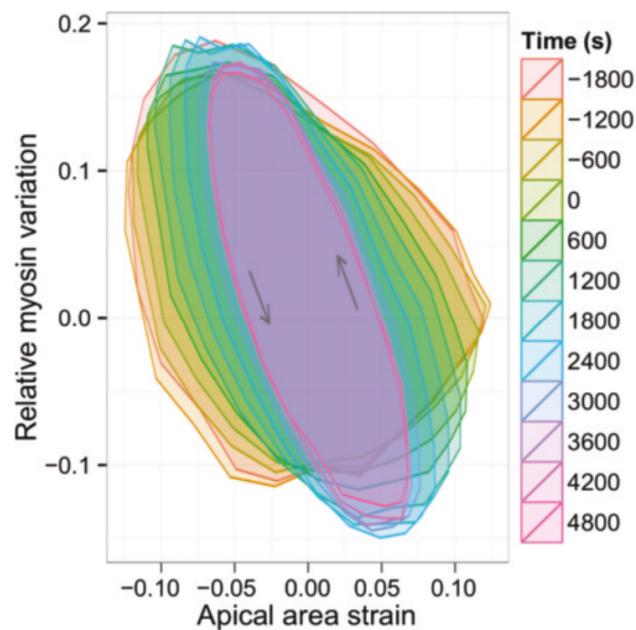
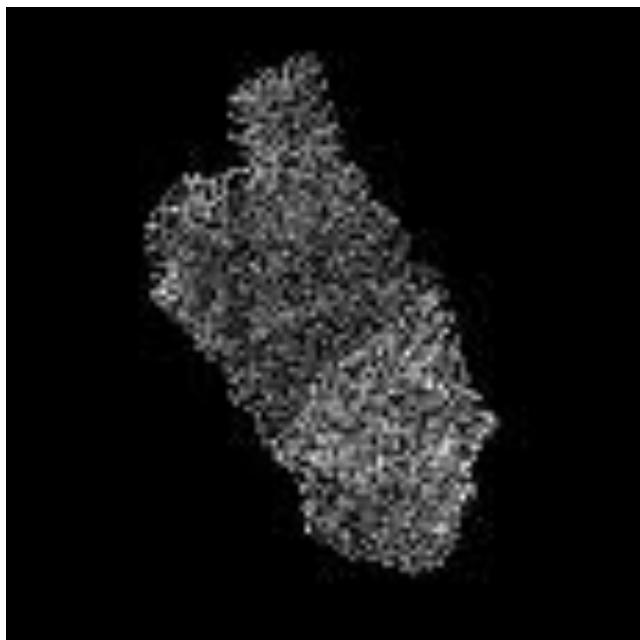
with Guy Blanchard, Alfonso Martinez-Arias (Cambridge) and Nicole Gorfinkiel (Madrid)



Machado et al, *BMC Biol* 2015

Myosin pulsations in dorsal closure

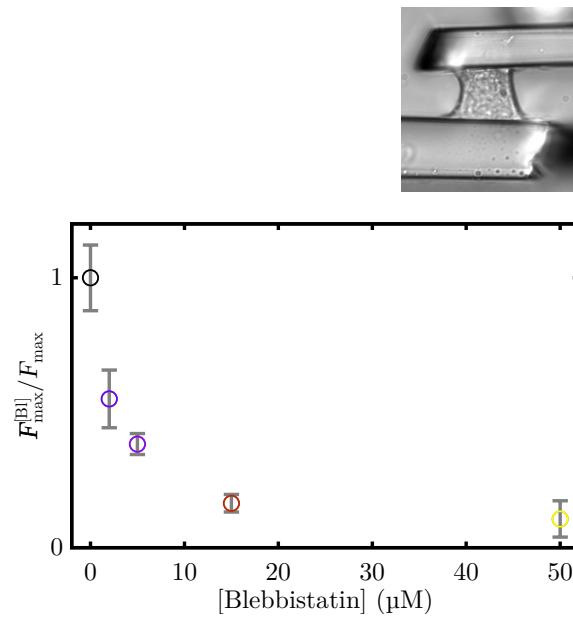
with Guy Blanchard, Alfonso Martinez-Arias (Cambridge) and Nicole Gorfinkiel (Madrid)



Machado et al, *BMC Biol* 2015

Can we use Myosin as a proxy for stress?

with Atef Asnacios, MSC Paris 7

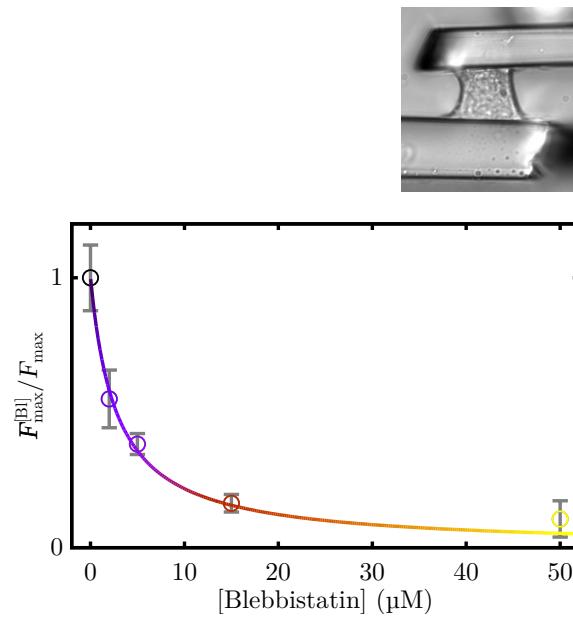


[Mitrossilis et al, *PNAS* 2009]



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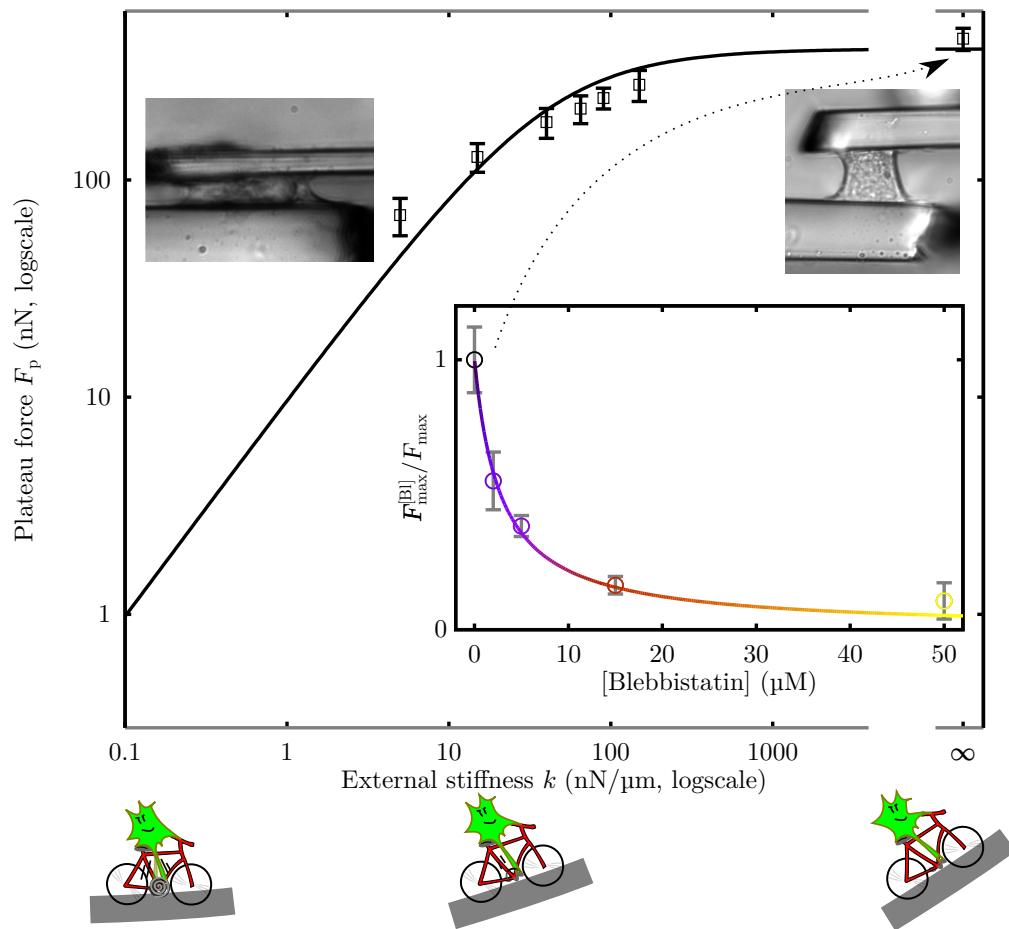


[Mitrossilis et al, *PNAS* 2009]



Can we use Myosin as a proxy for stress?

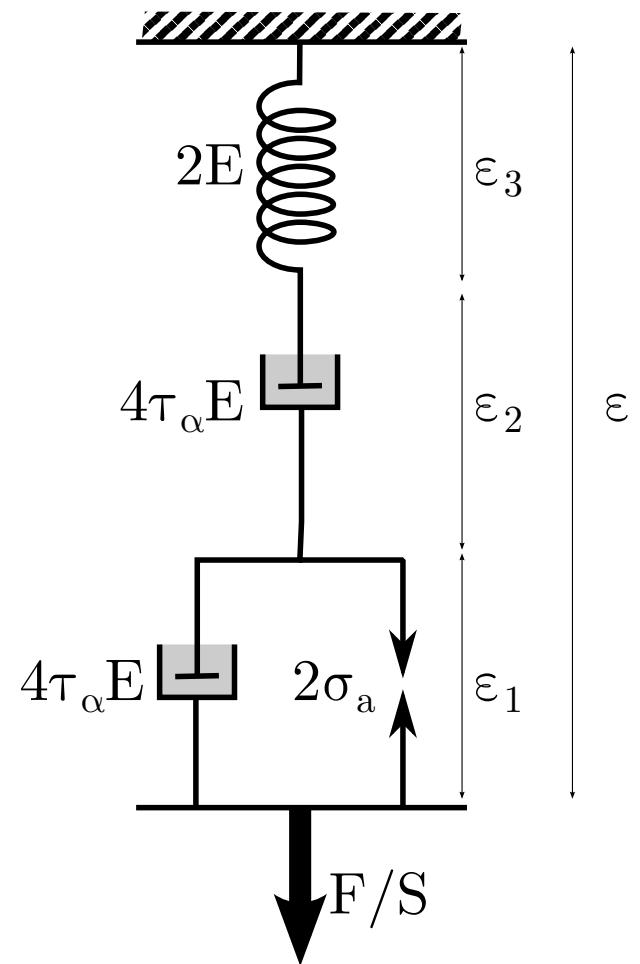
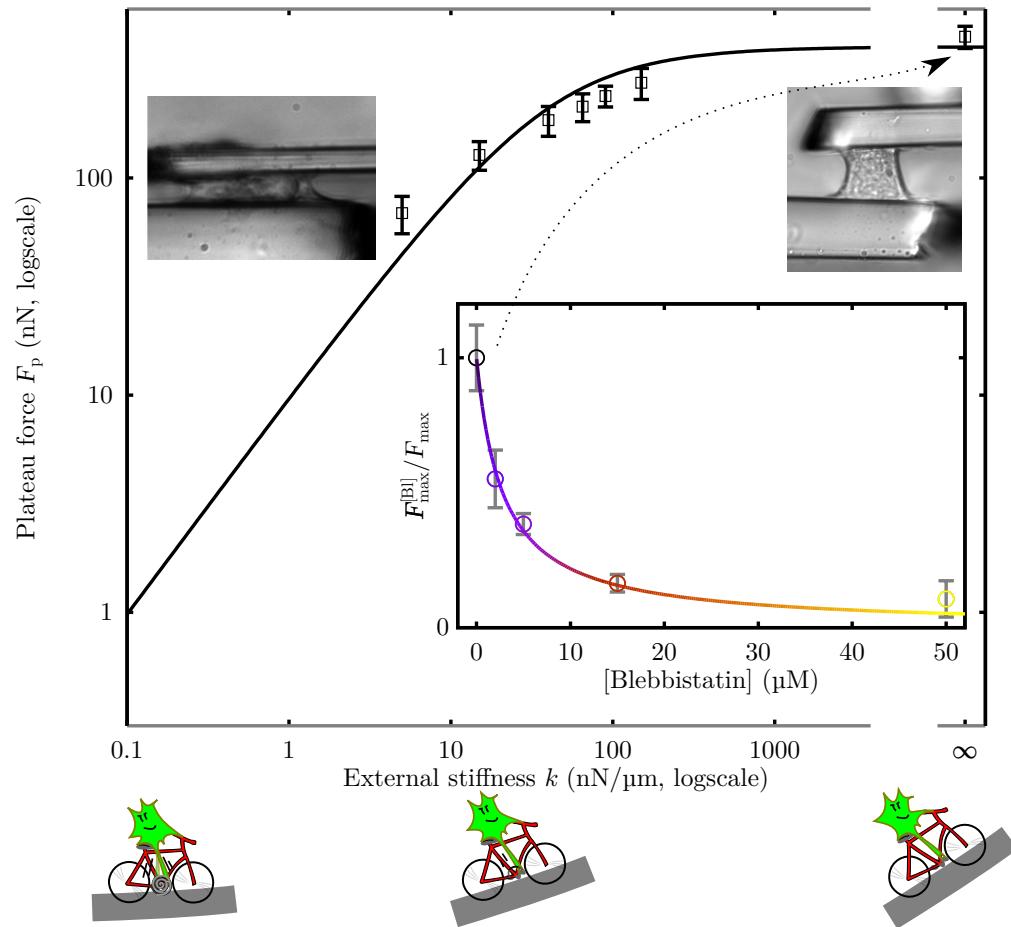
with Atef Asnacios, MSC Paris 7



[Mitrossilis et al, *PNAS* 2009]

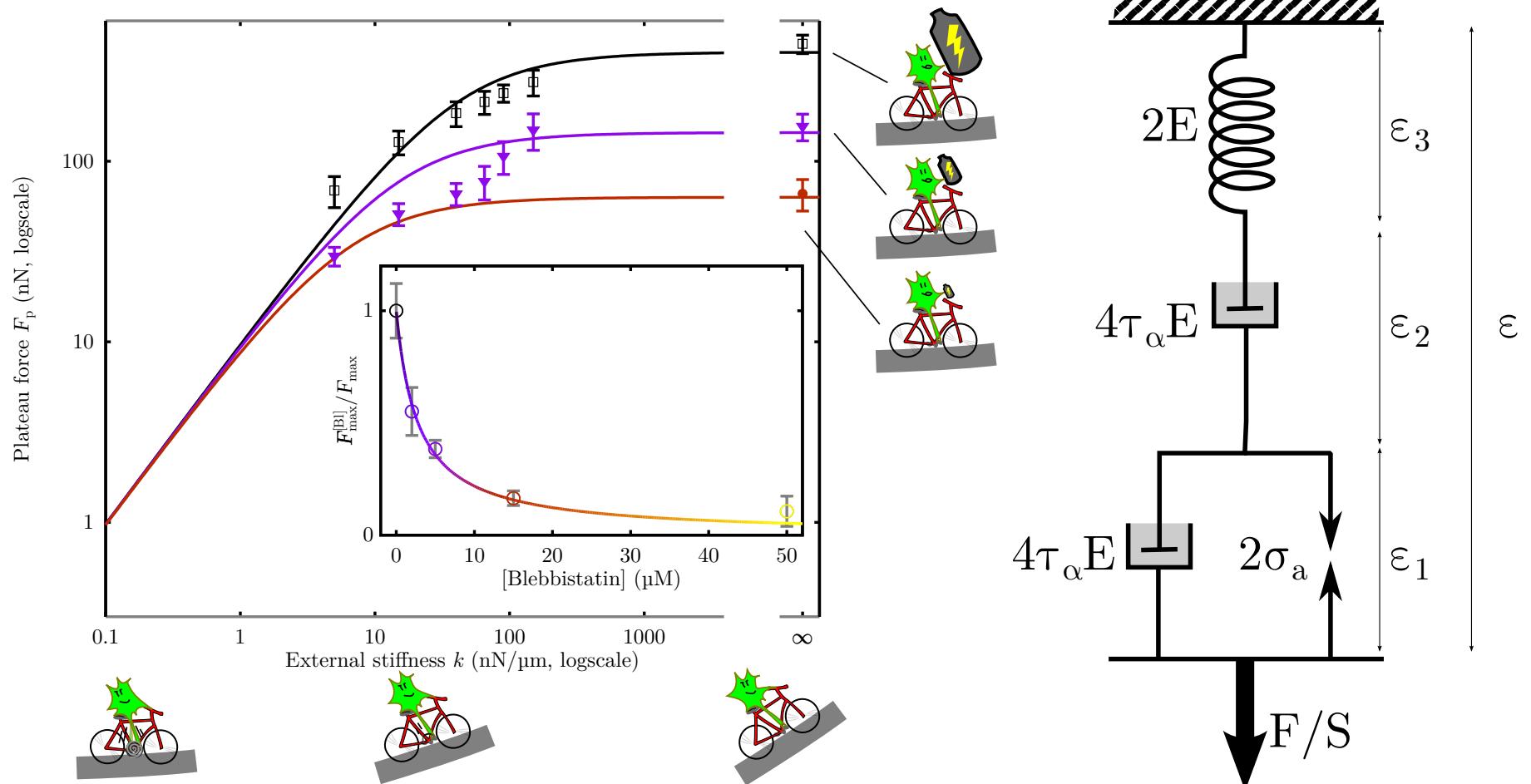


Can we use Myosin as a proxy for stress? not really



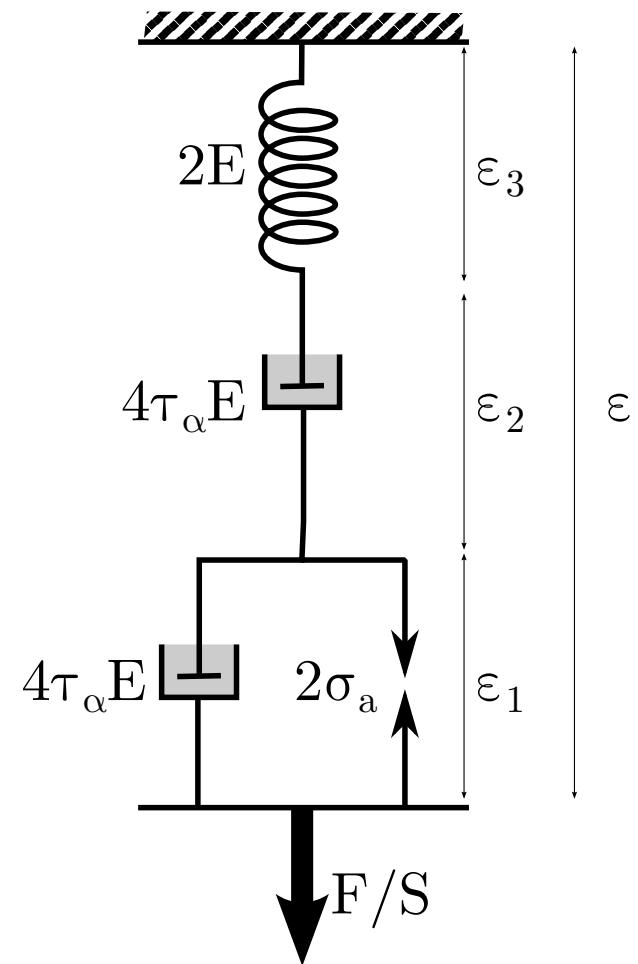
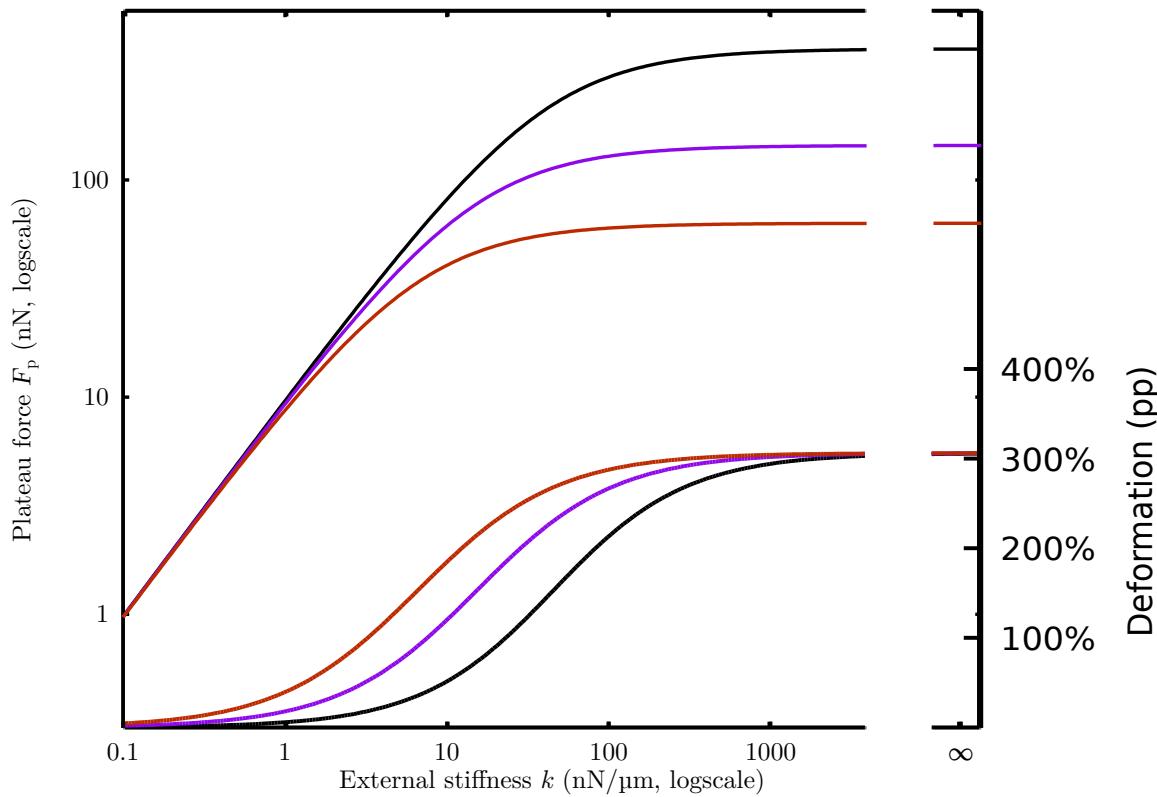
[Mitrossilis et al, *PNAS* 2009] , [Étienne et al, *PNAS* 2015]

Can we use Myosin as a proxy for stress? not really



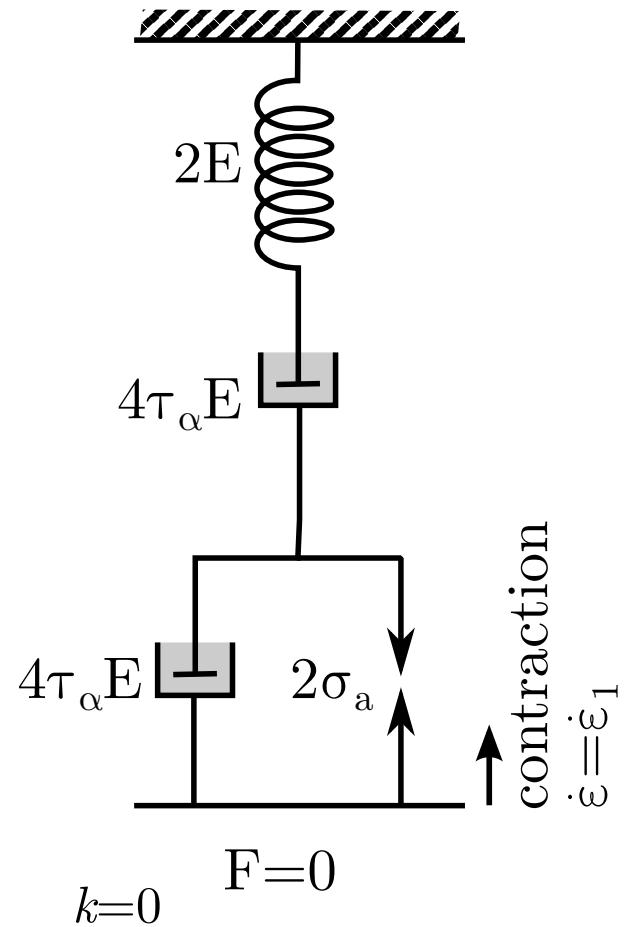
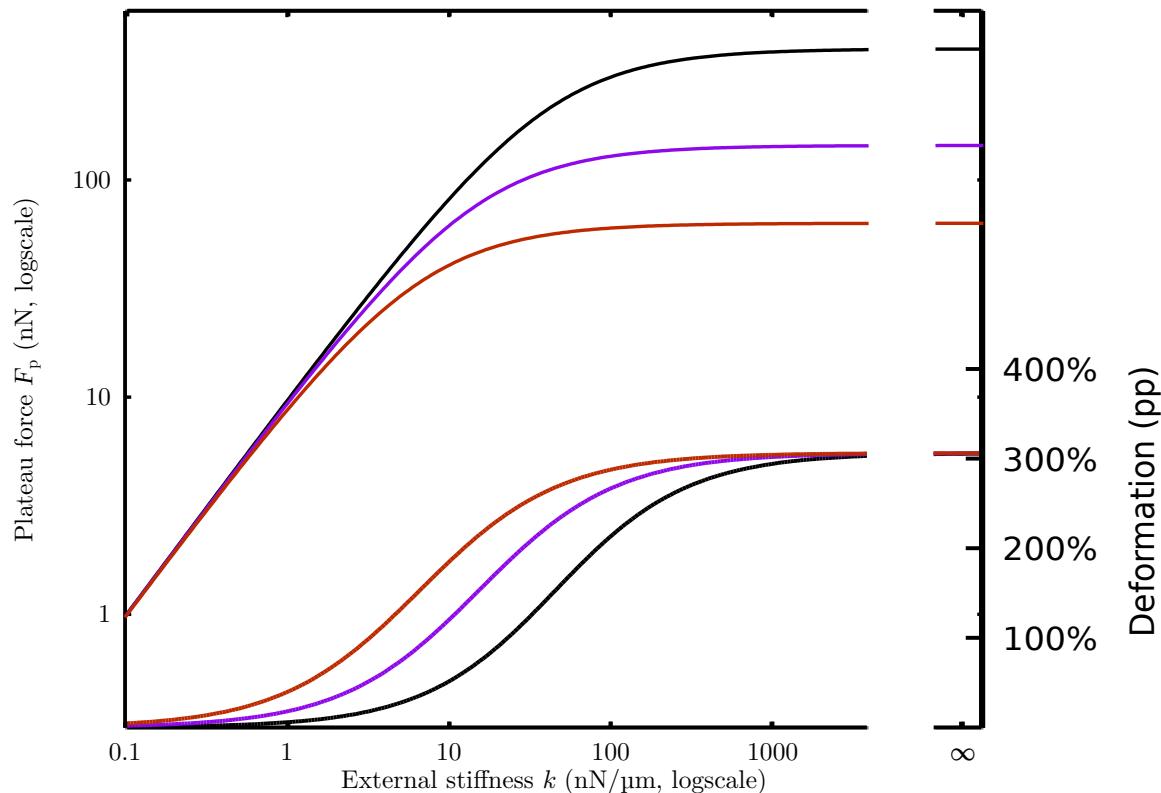
[Mitrossilis et al, *PNAS* 2009], [Étienne et al, *PNAS* 2015]

Can we use Myosin as a proxy for stress? not really



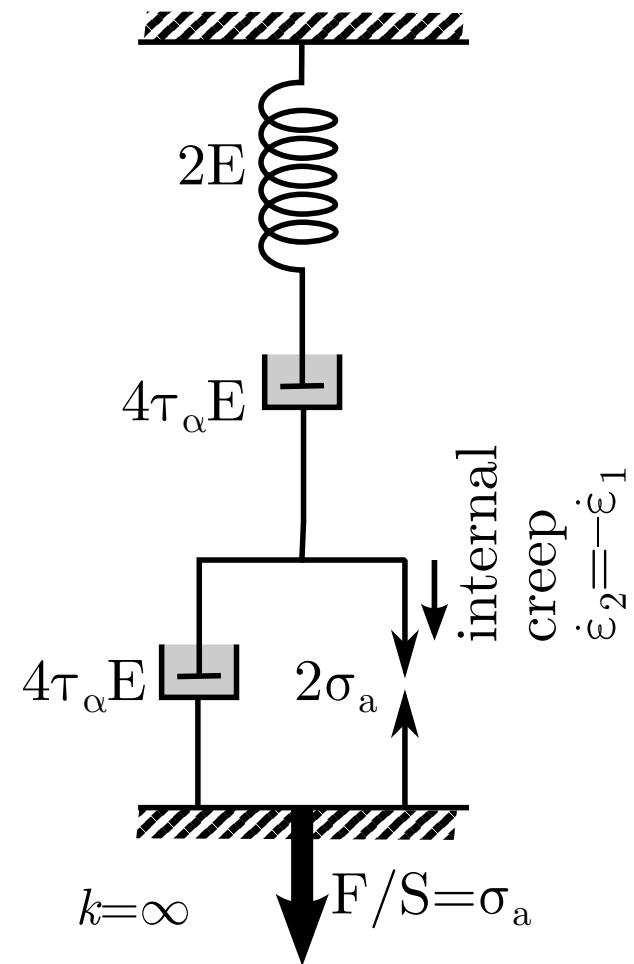
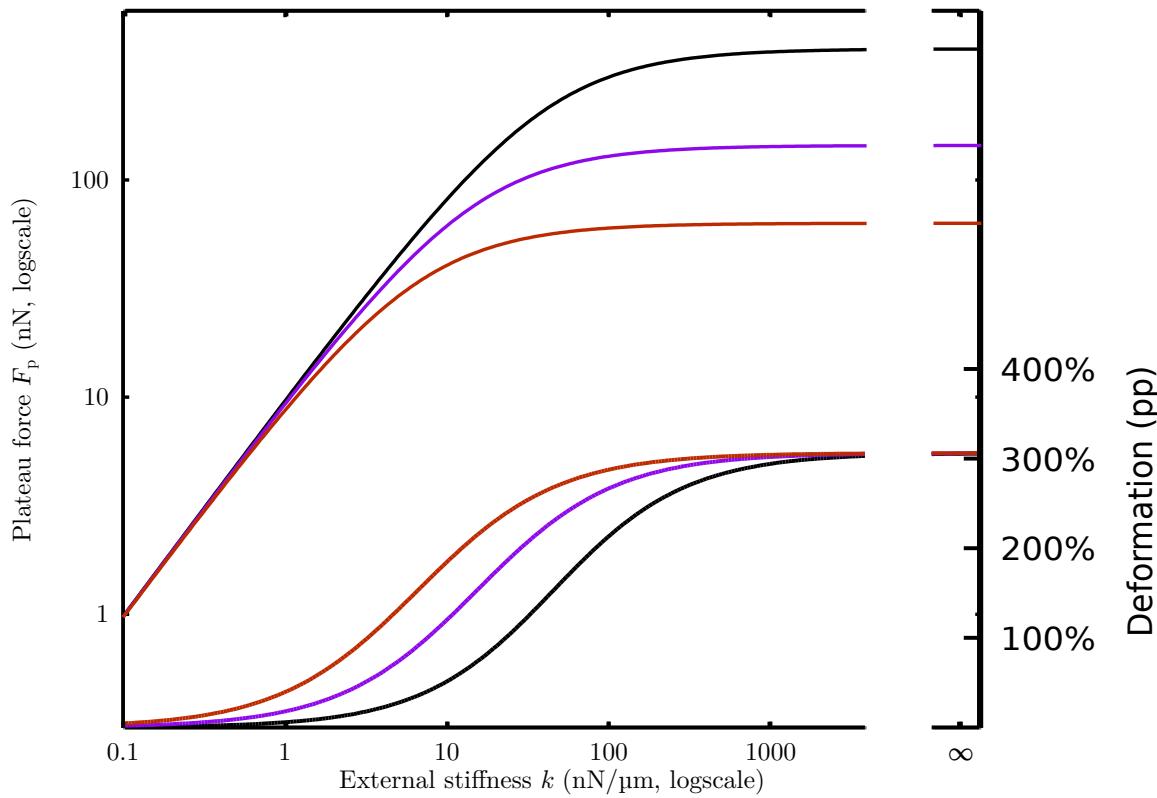
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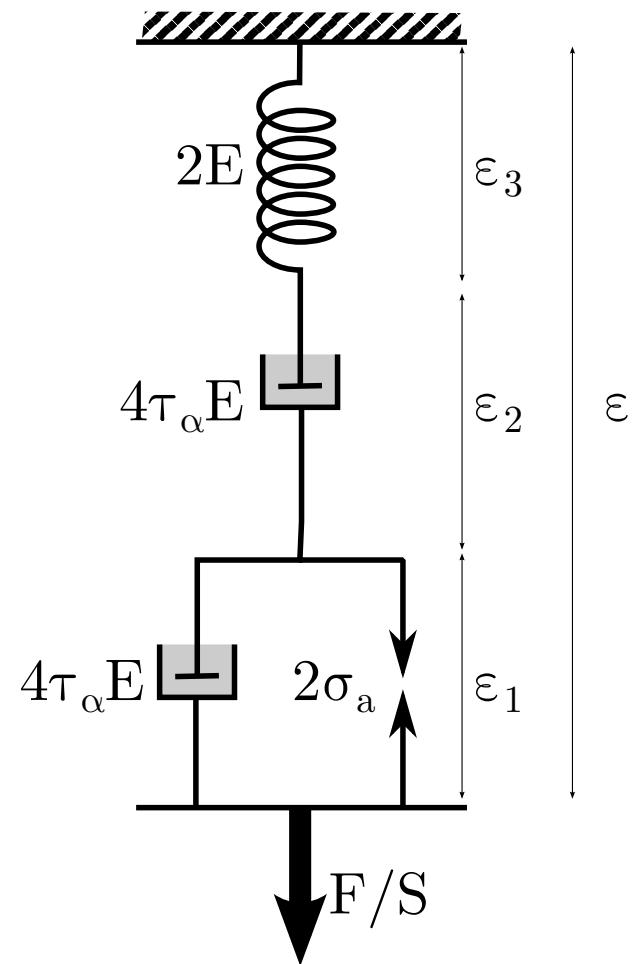
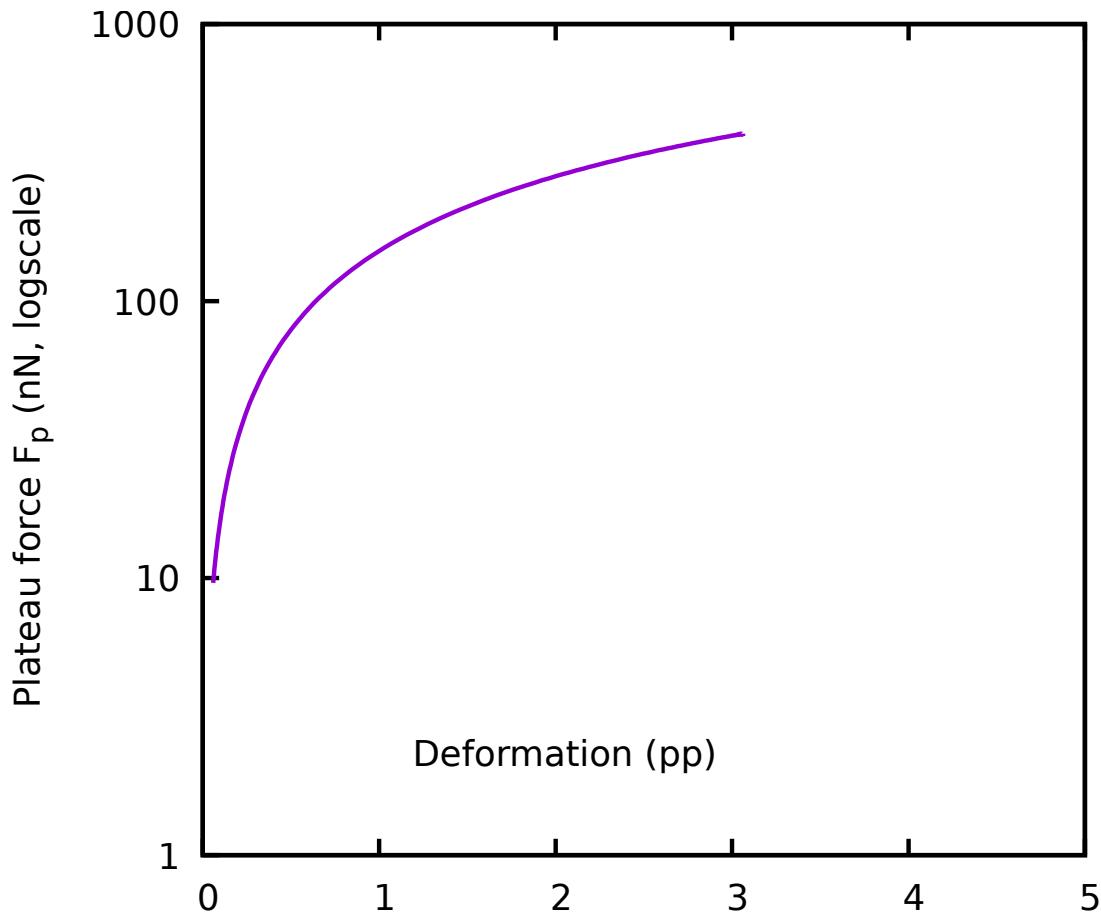
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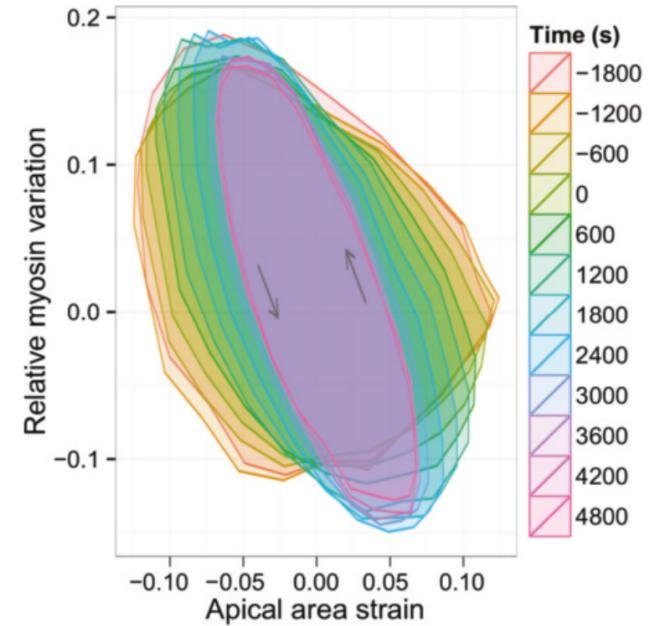
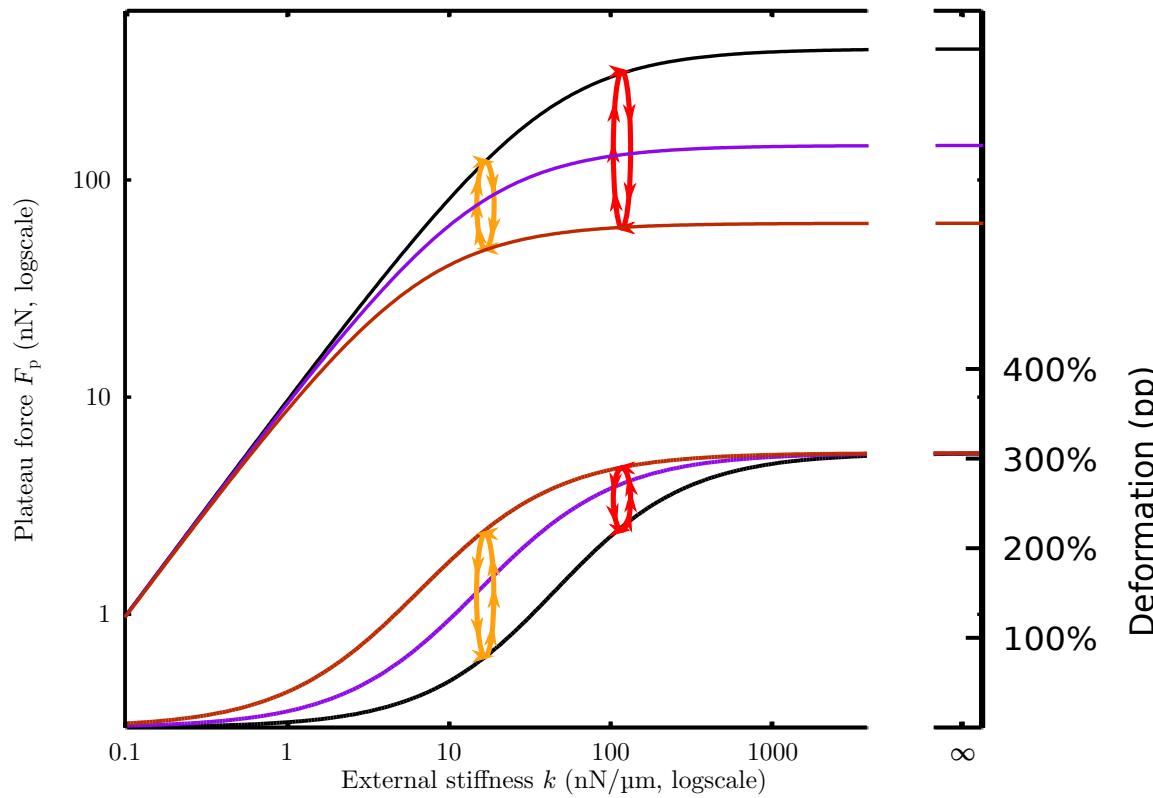


[Mitrossilis et al, *PNAS* 2009] , [Étienne et al, *PNAS* 2015]

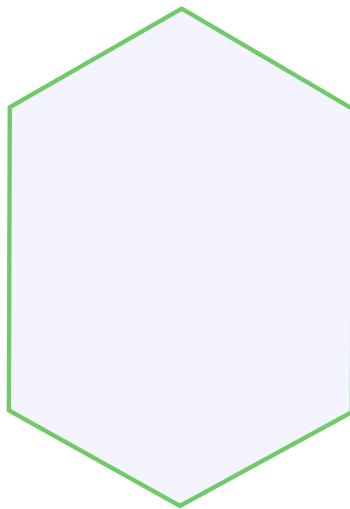
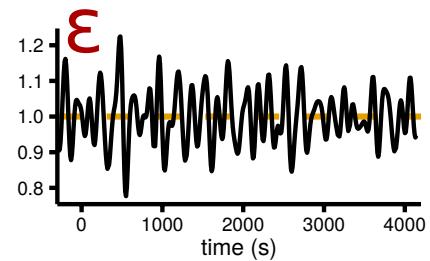
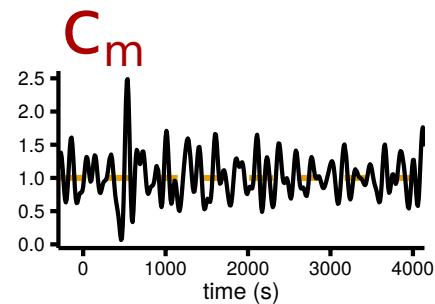
Can we use Myosin as a proxy for stress? not really



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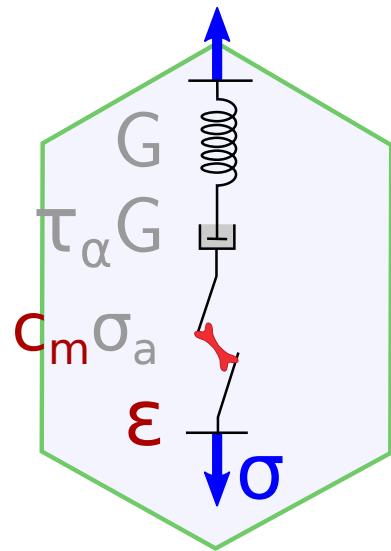
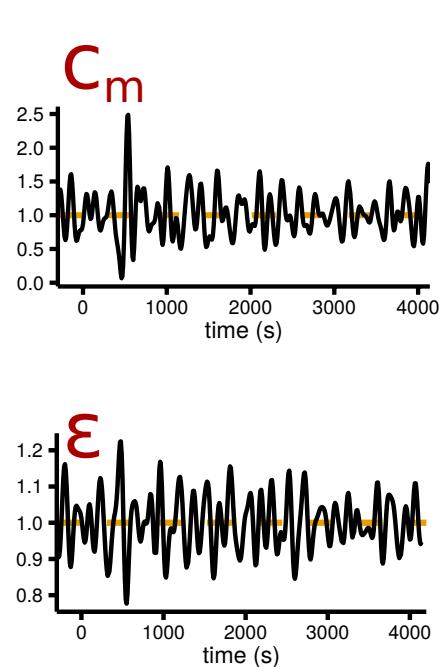
Stress inference combining myosin, strain and model



[Machado et al, *BMC Biol* 2015]

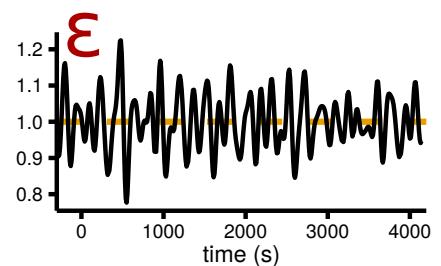
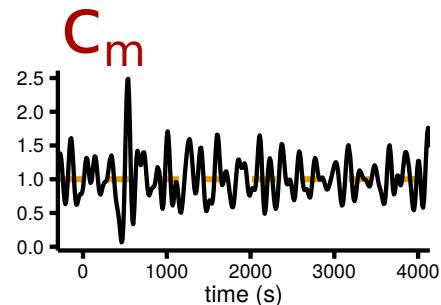


Stress inference combining myosin, strain and model



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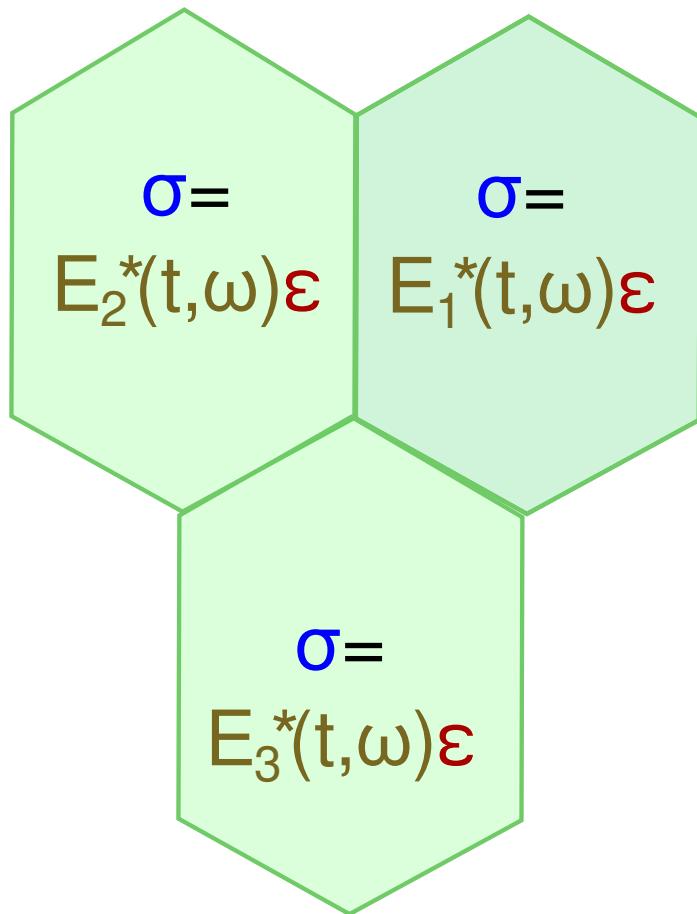
Stress inference combining myosin, strain and model



$$\sigma = E_1^*(t, \omega) \epsilon$$

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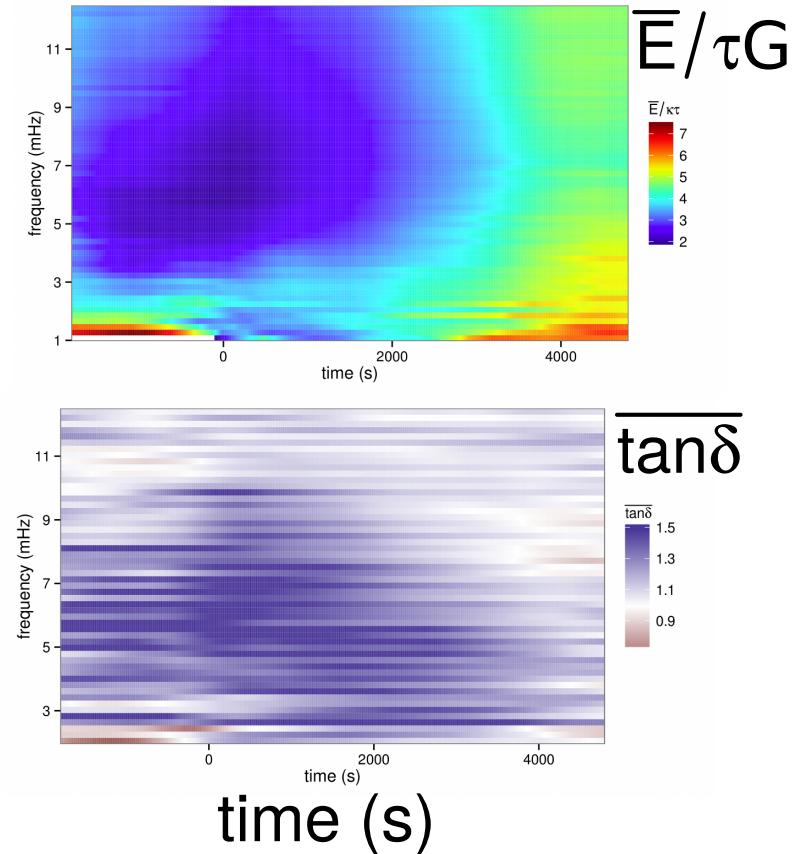
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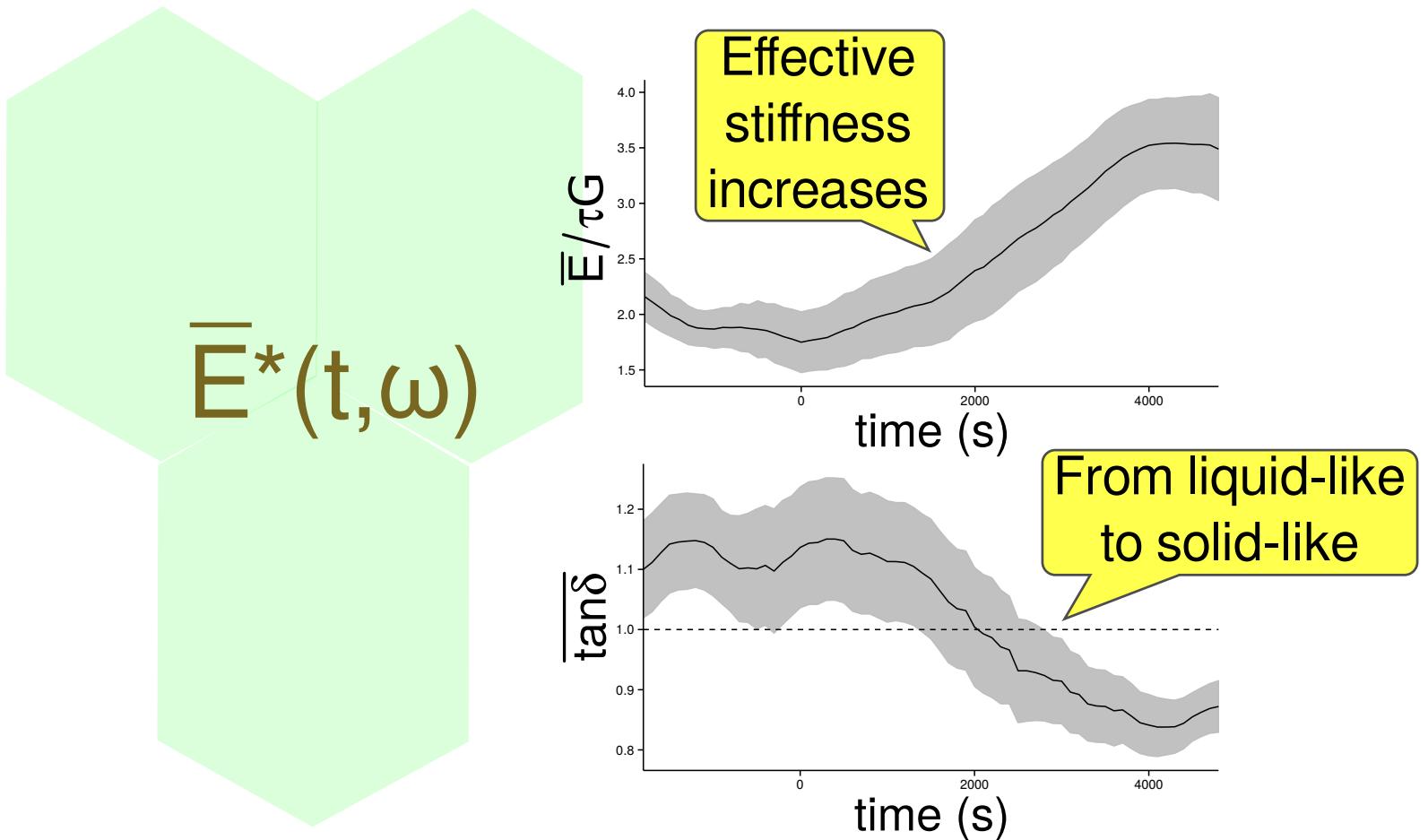
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$$\sigma = E_1^*(t, \omega) \epsilon$$
$$E^*(t, \omega)$$



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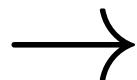
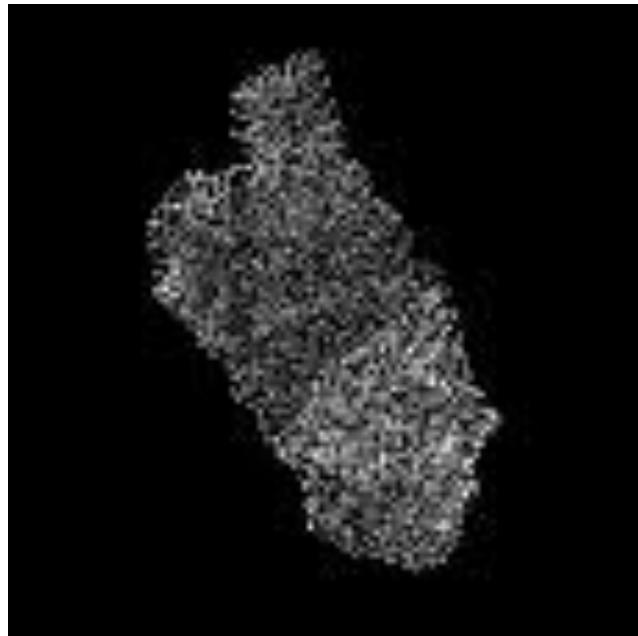
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Myosin pulsations in dorsal closure

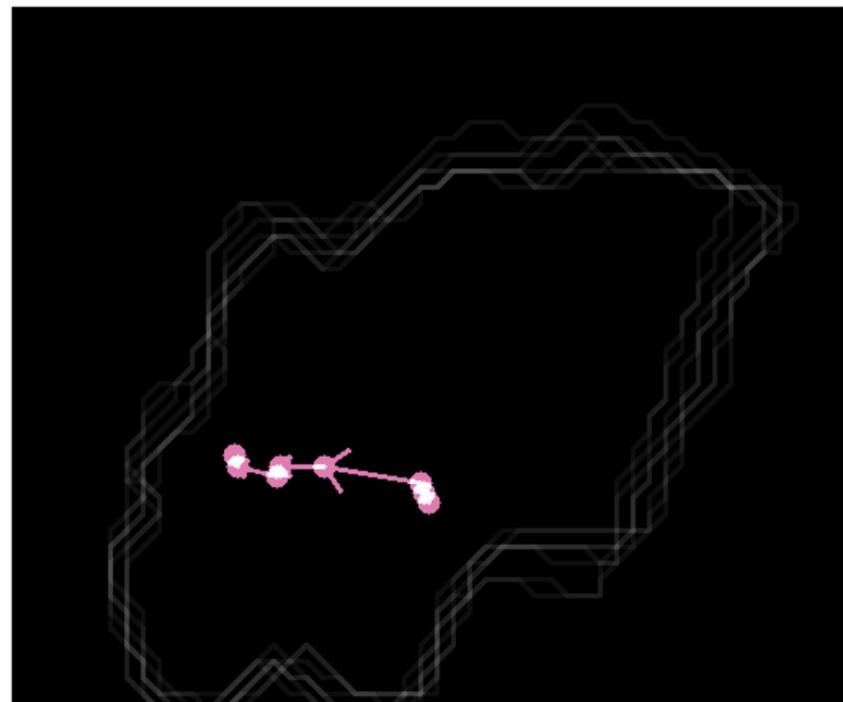
with Guy Blanchard (Cambridge) and Nicole Gorfinkiel (Madrid)
PhD of Nilankur Dutta



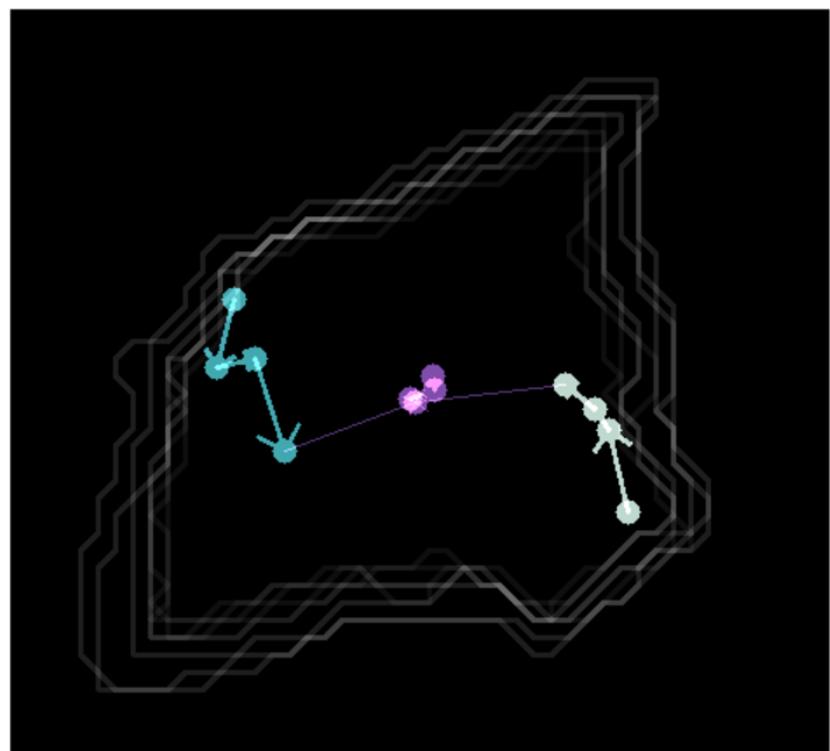
12 embryos, 400 cells, $\sim 10^5$ foci



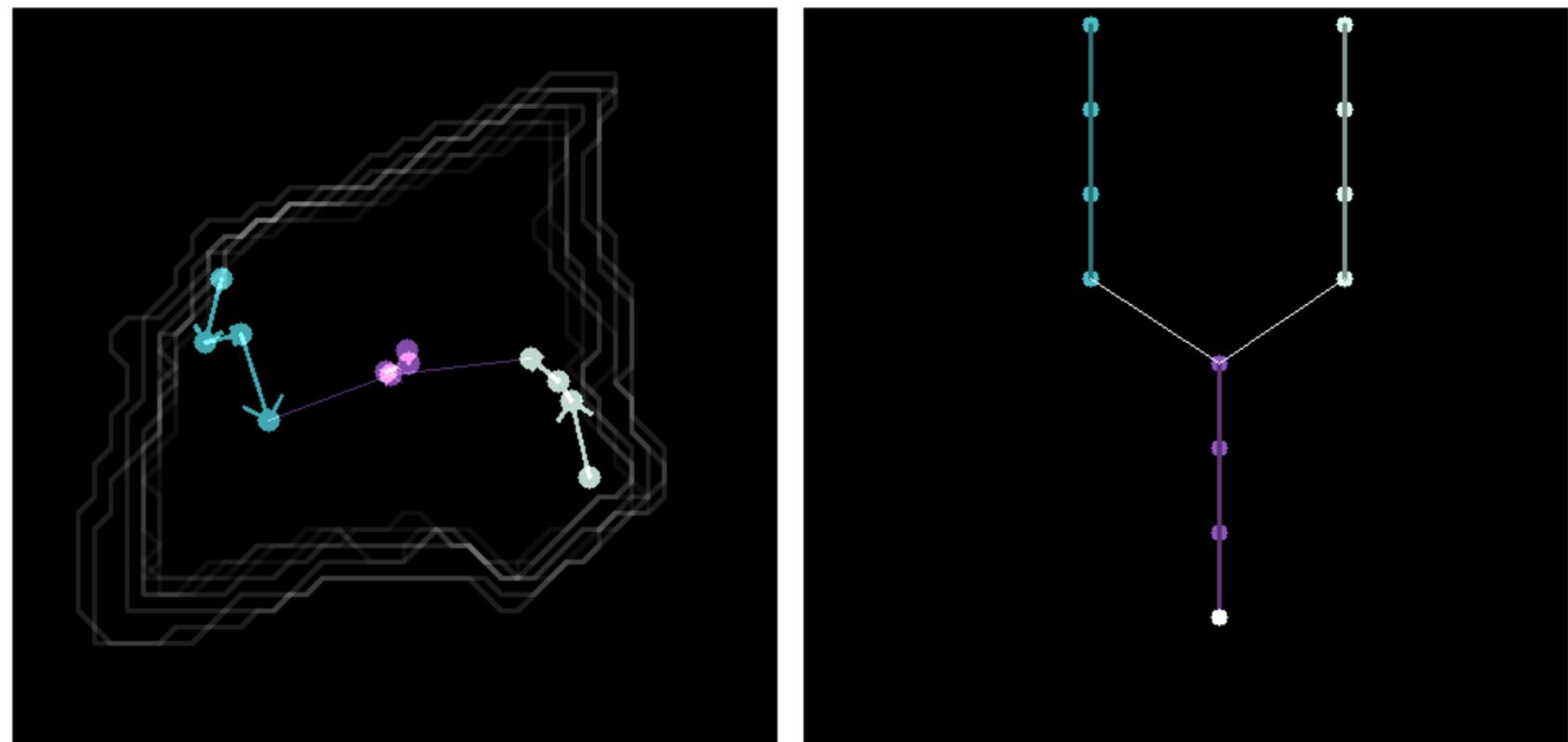
Travelling foci



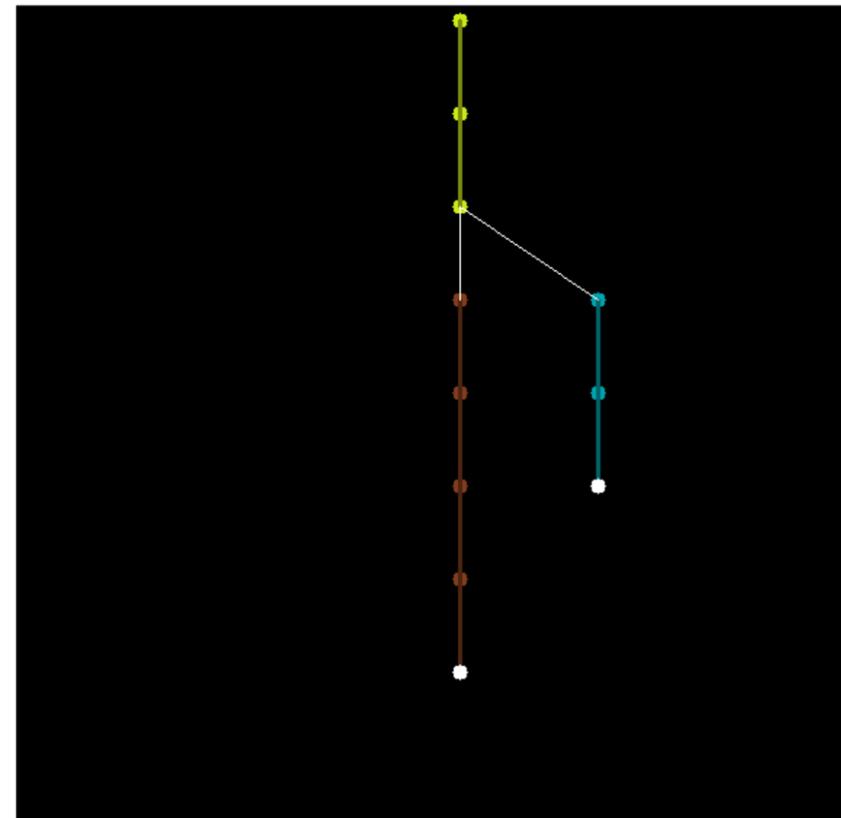
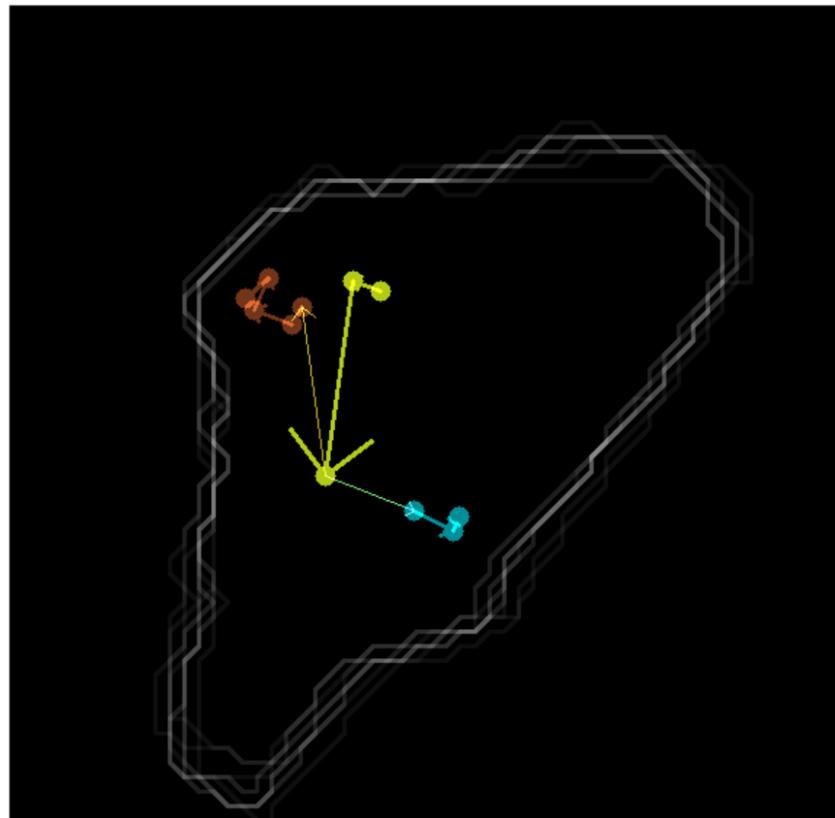
Travelling foci merging



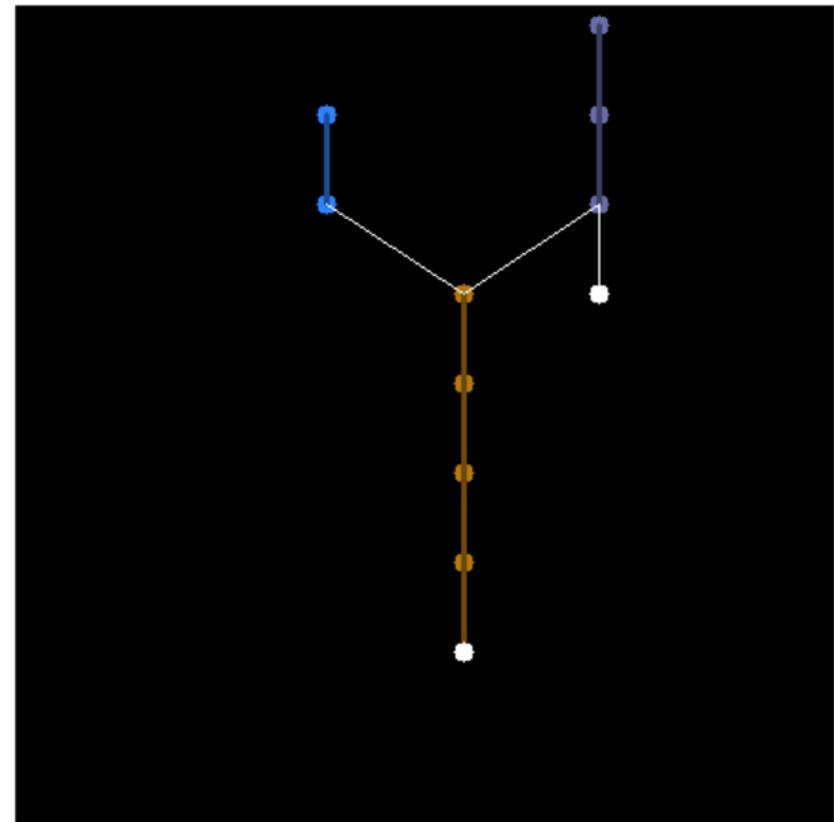
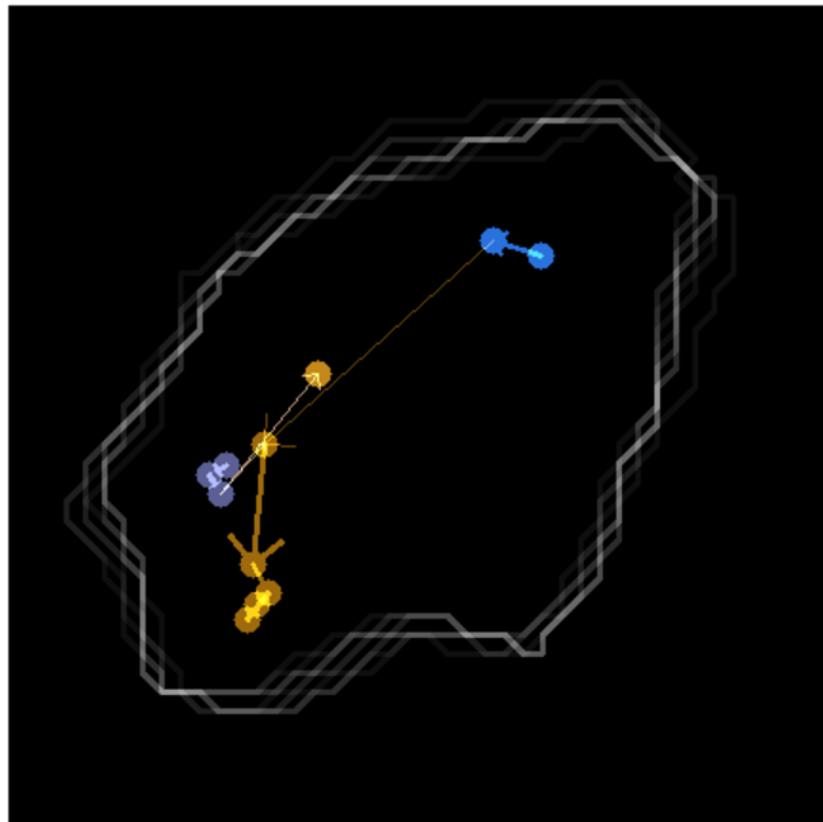
Travelling foci merging and splitting



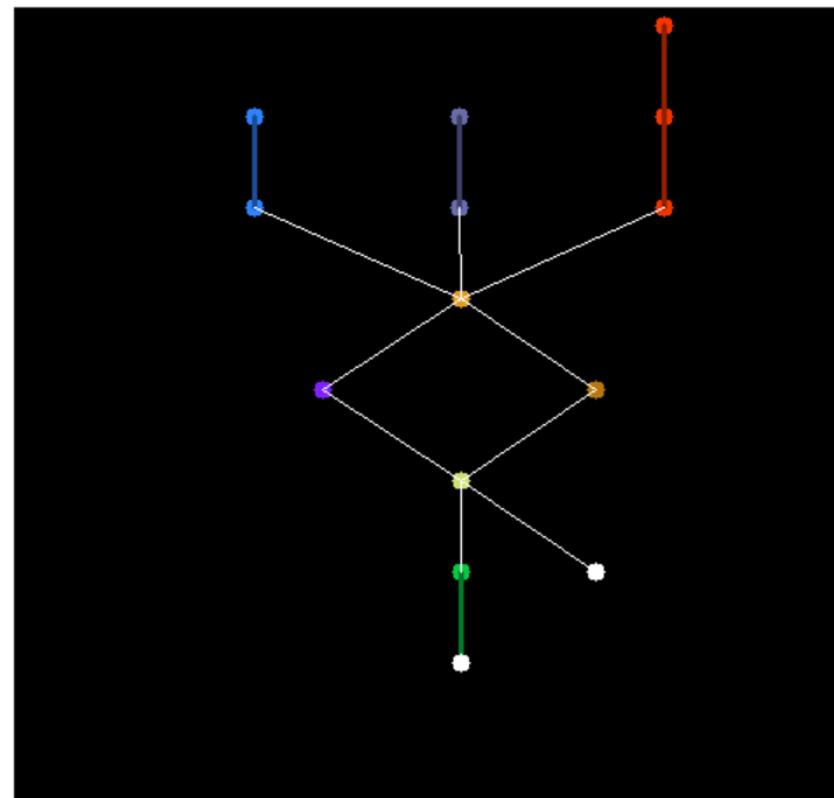
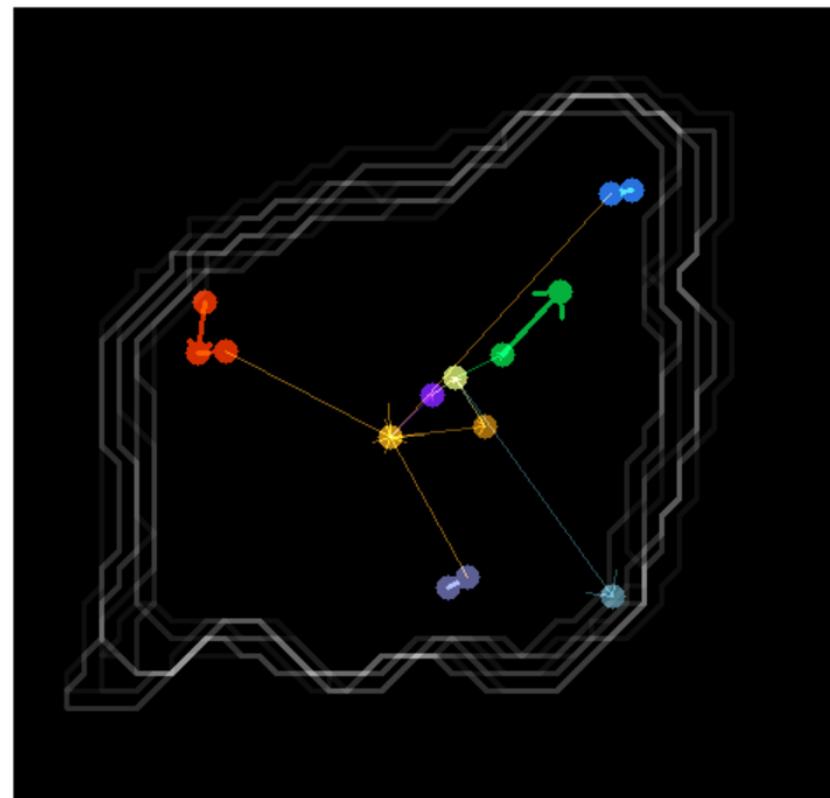
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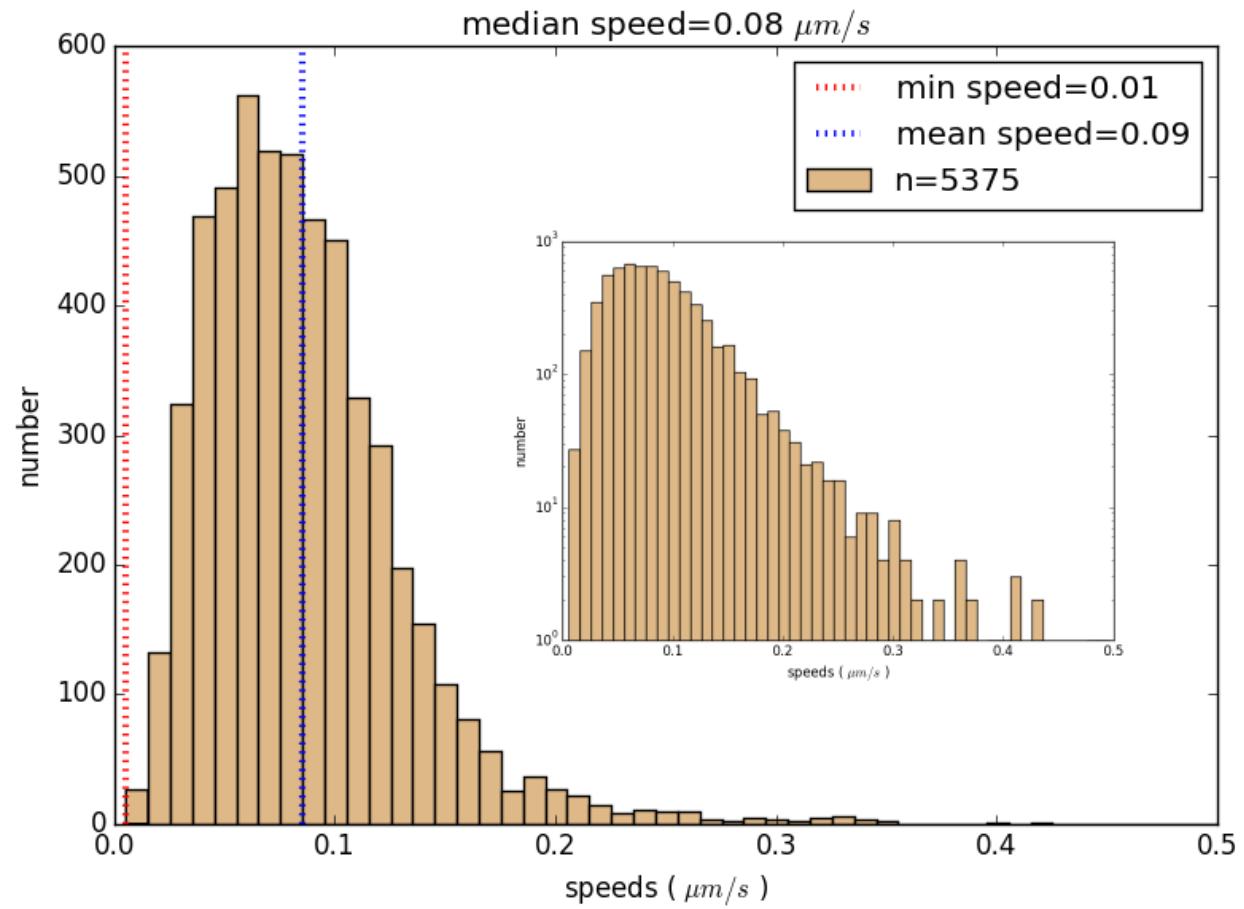
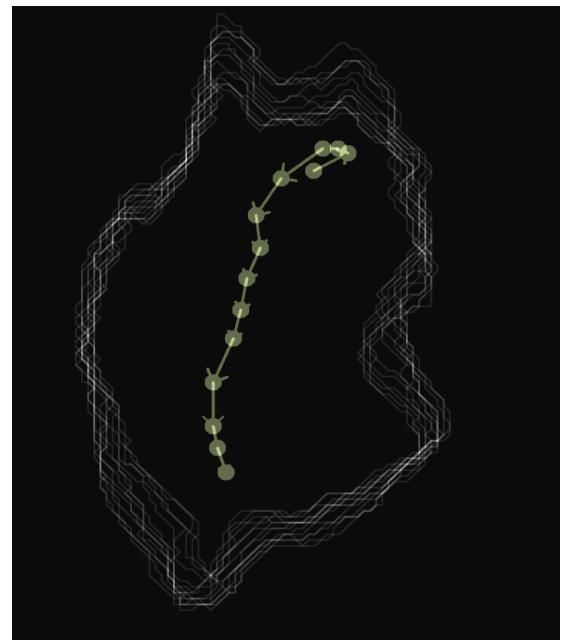
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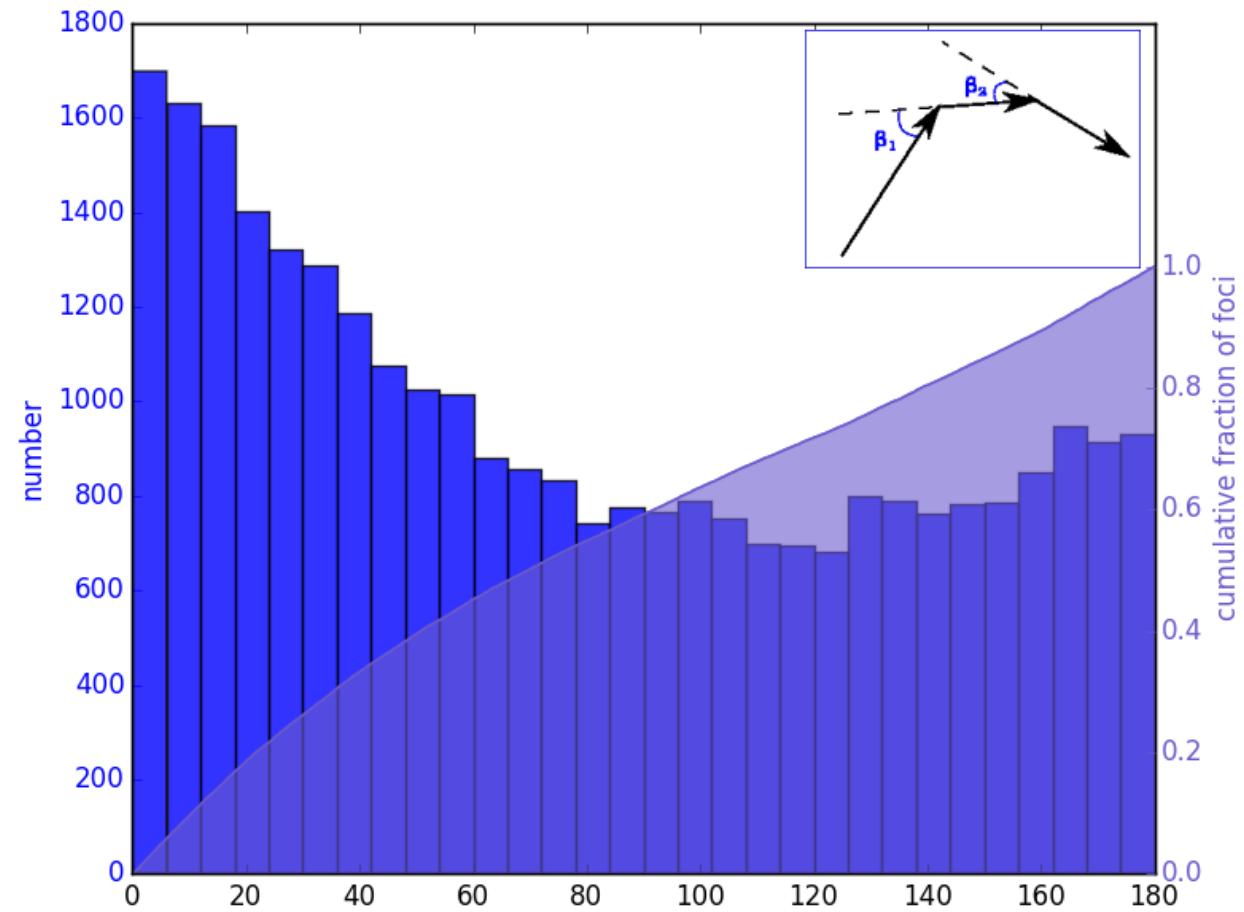
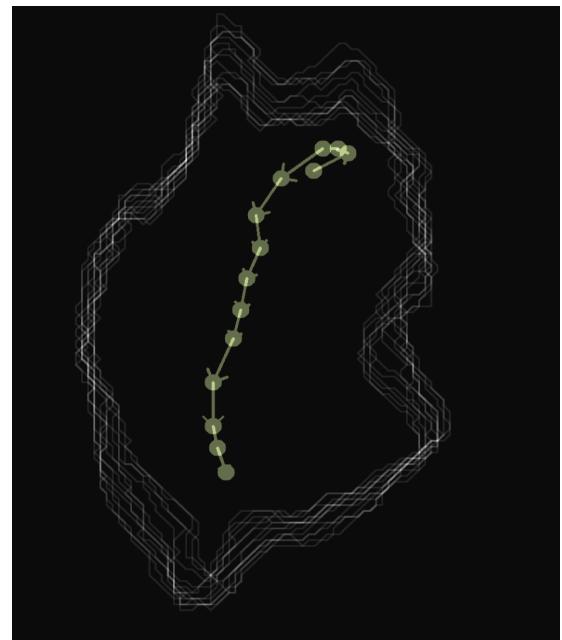
Travelling foci merging and splitting



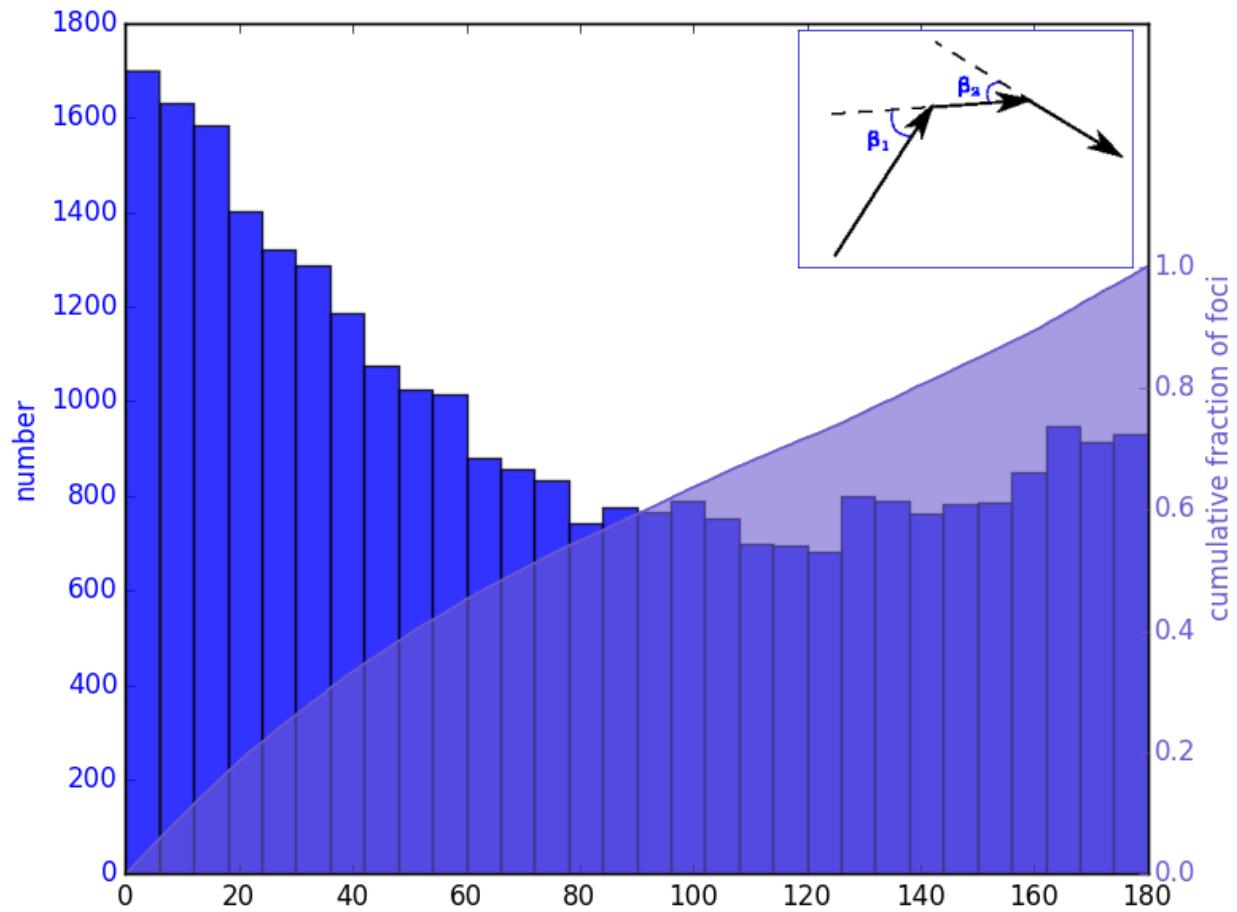
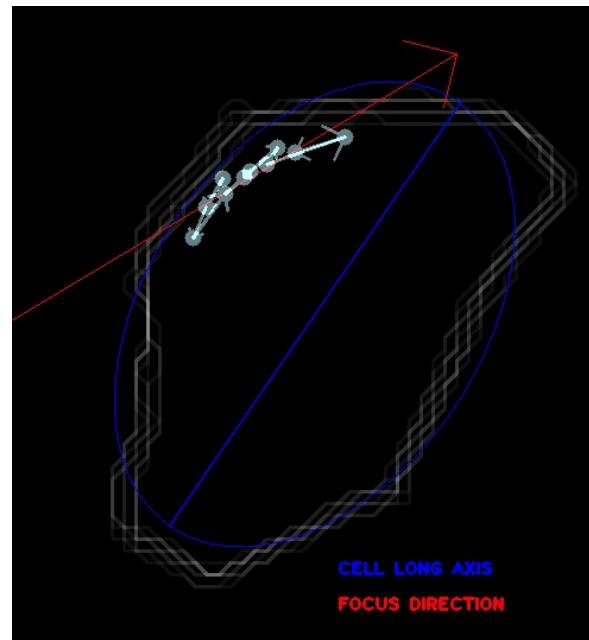
Kinematics of foci



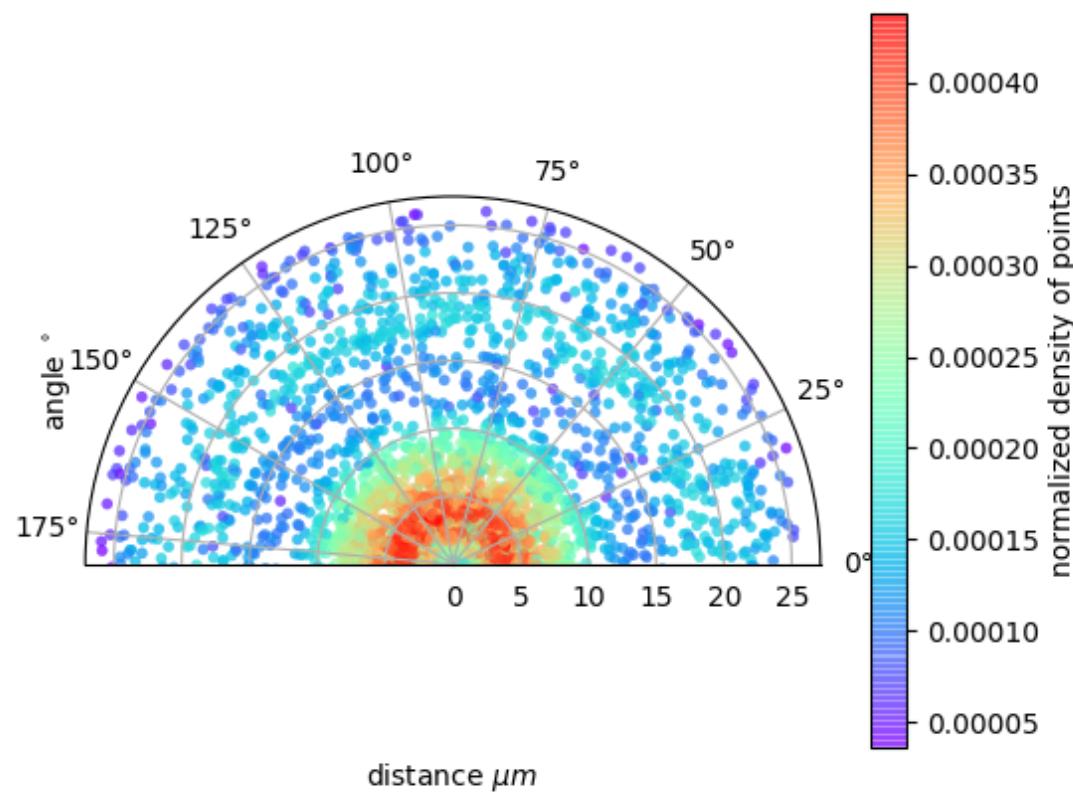
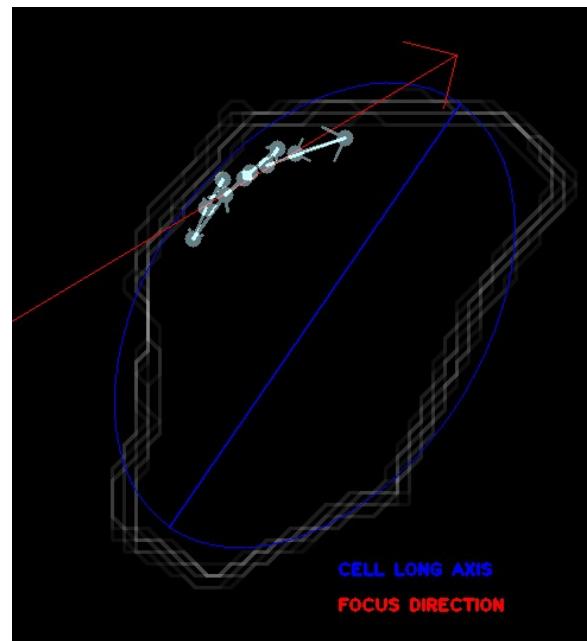
Kinematics of foci



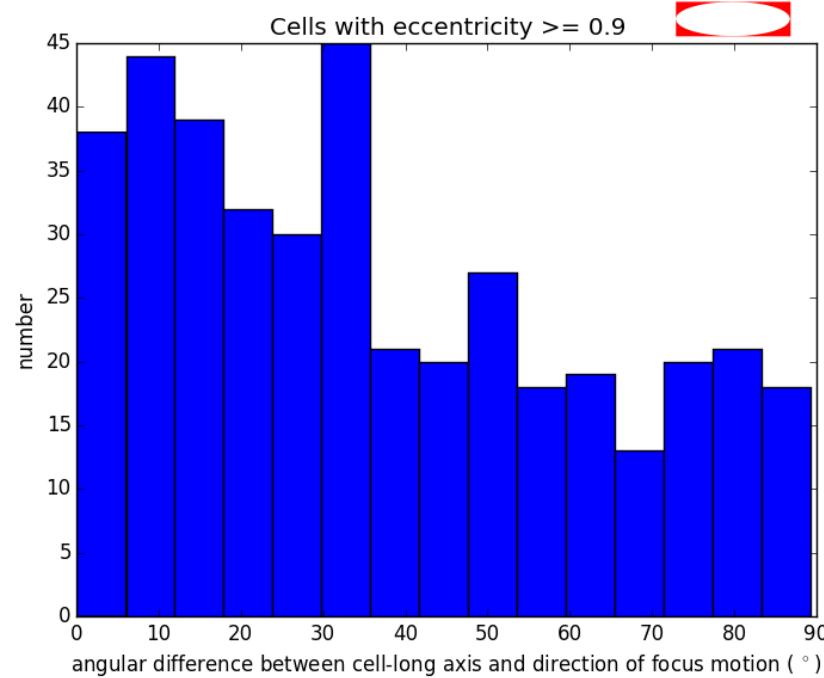
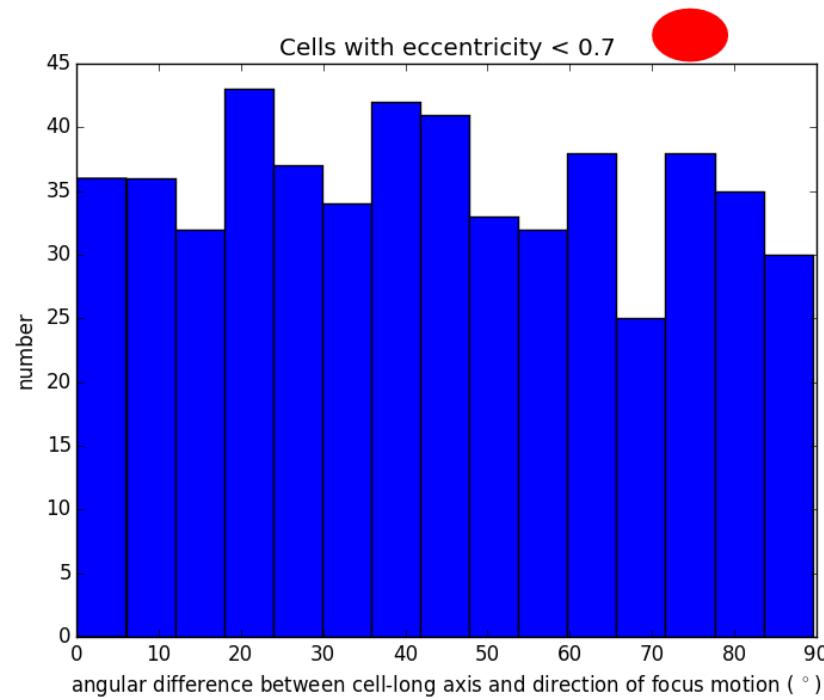
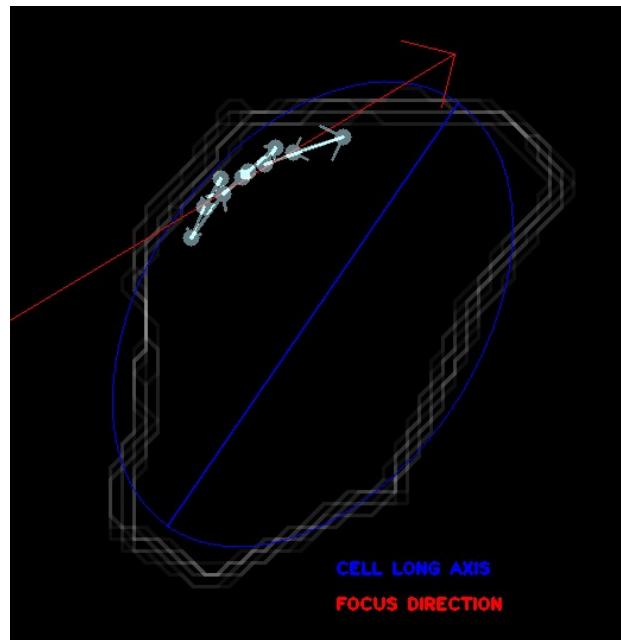
Kinematics of foci



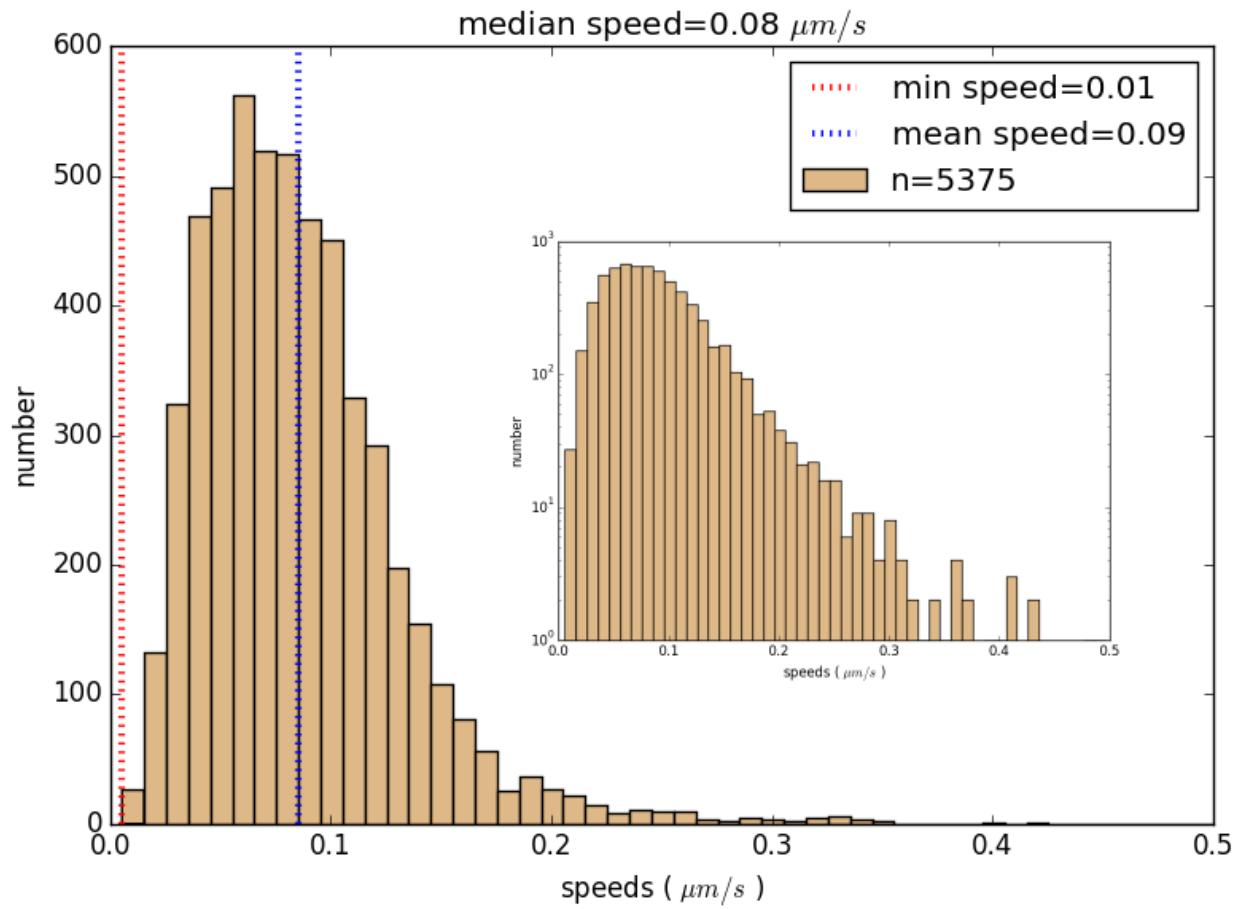
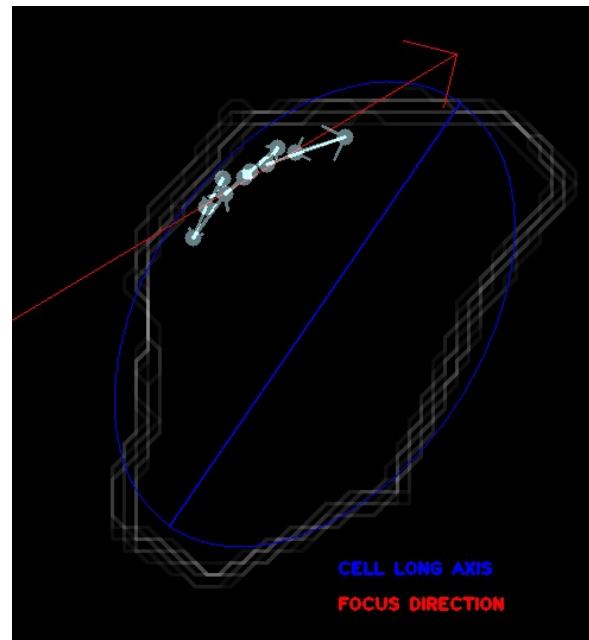
Kinematics of foci



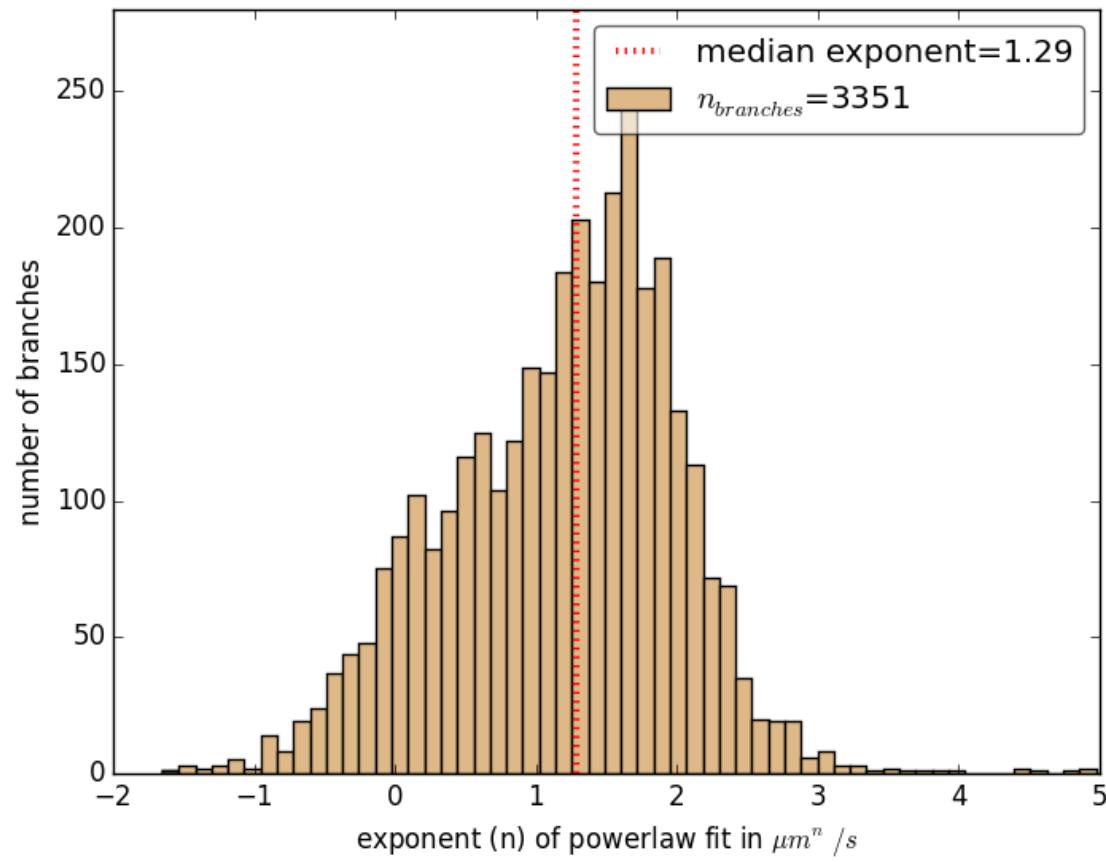
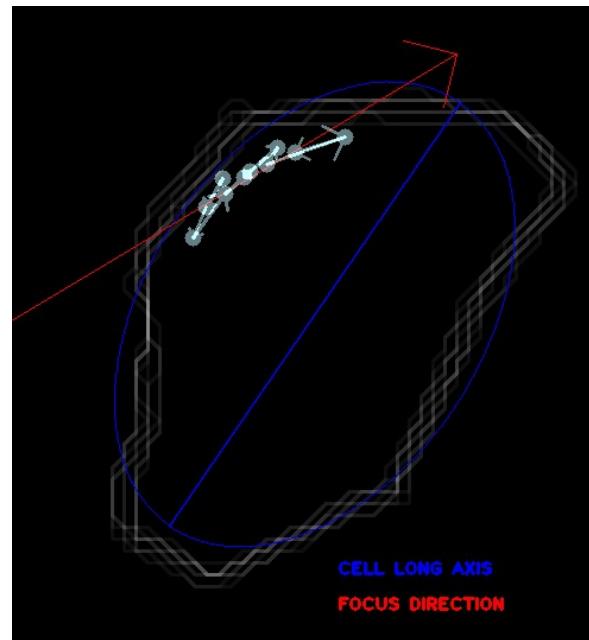
Kinematics of foci



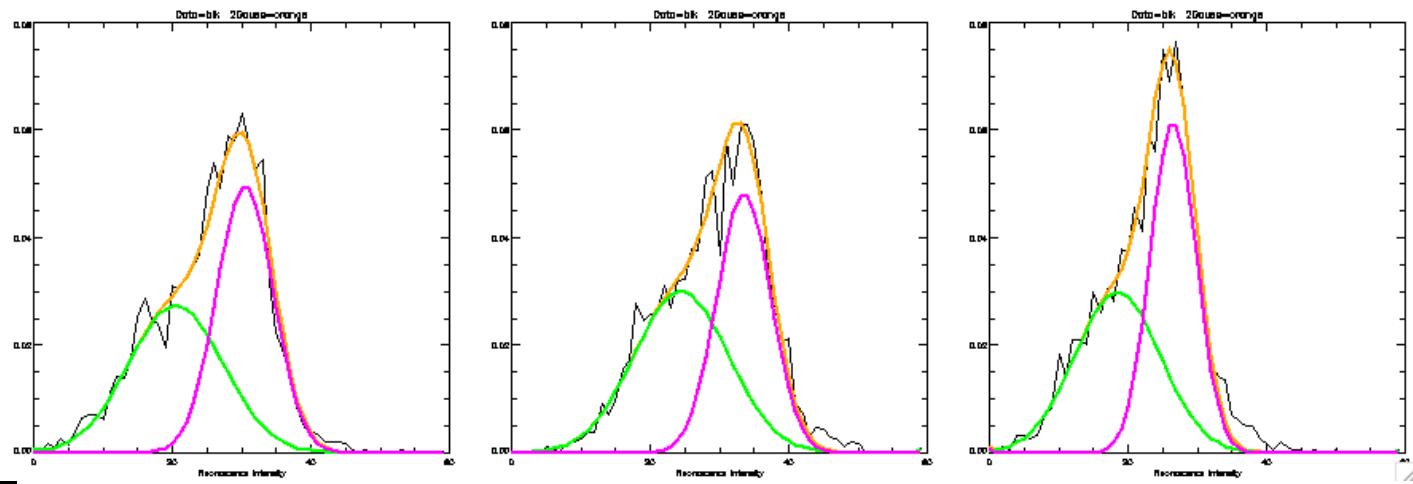
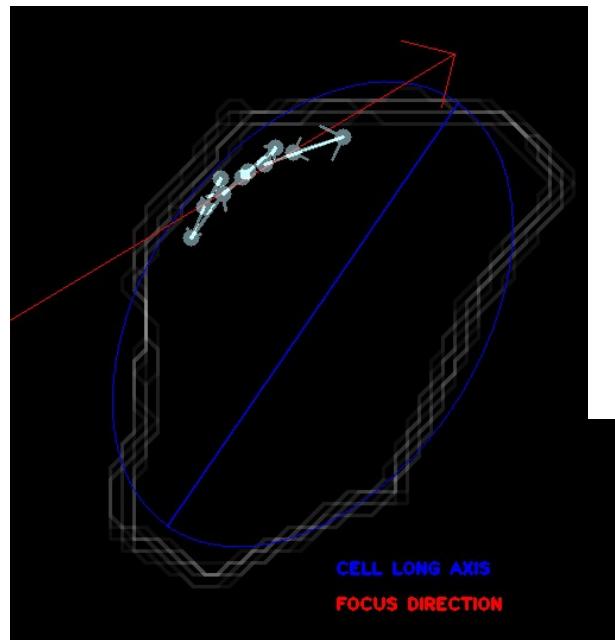
Kinematics of foci



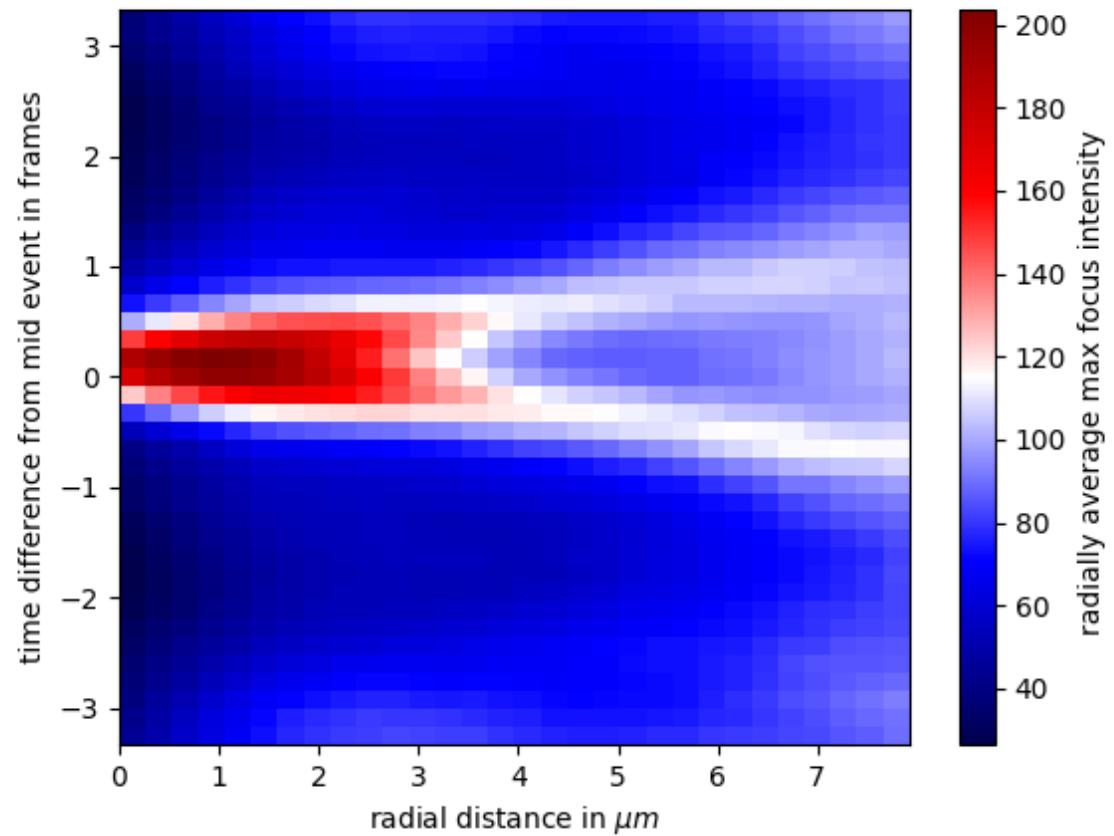
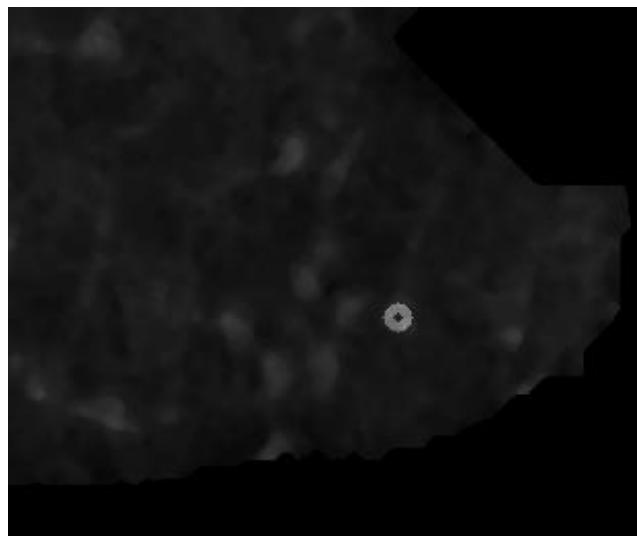
Kinematics of foci



Kinematics of foci

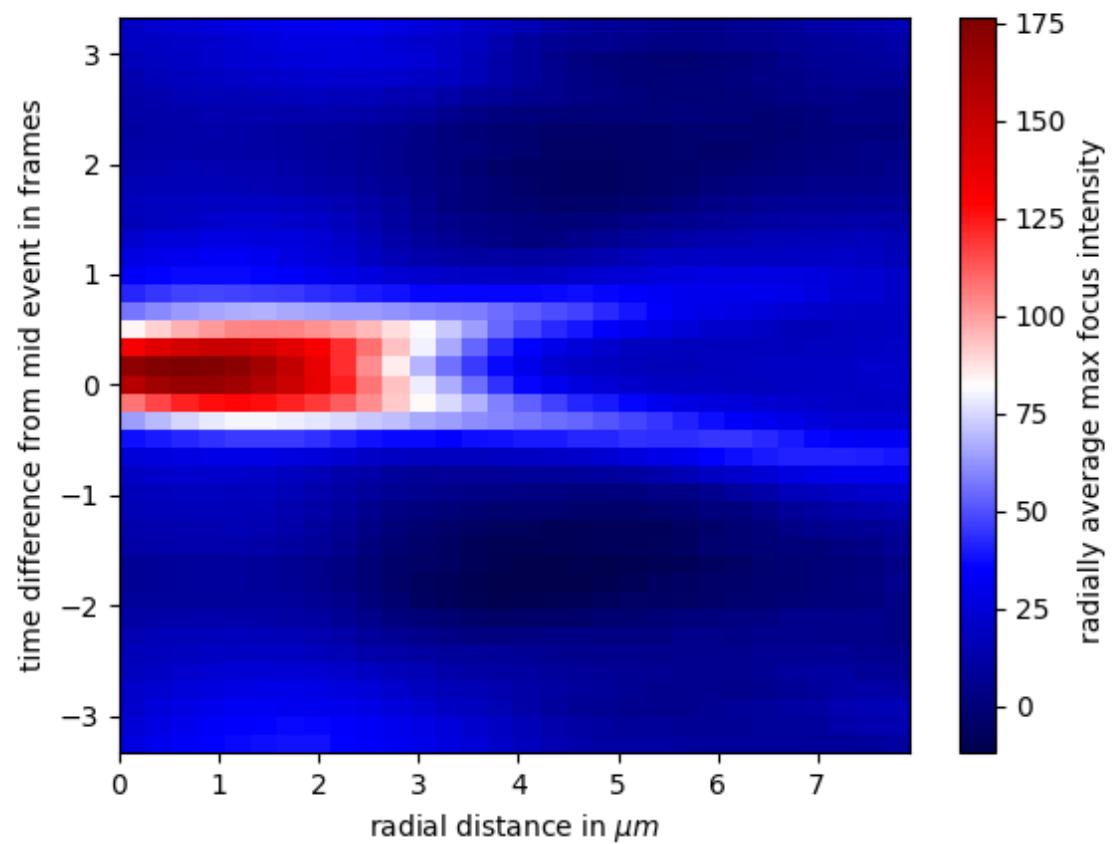
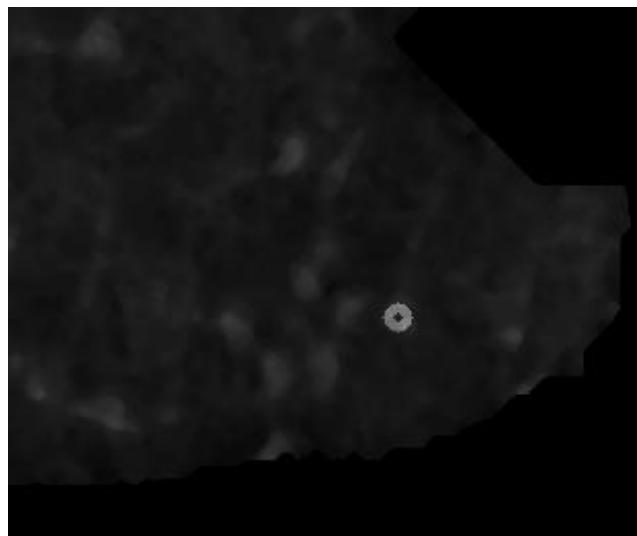


Myosin around foci



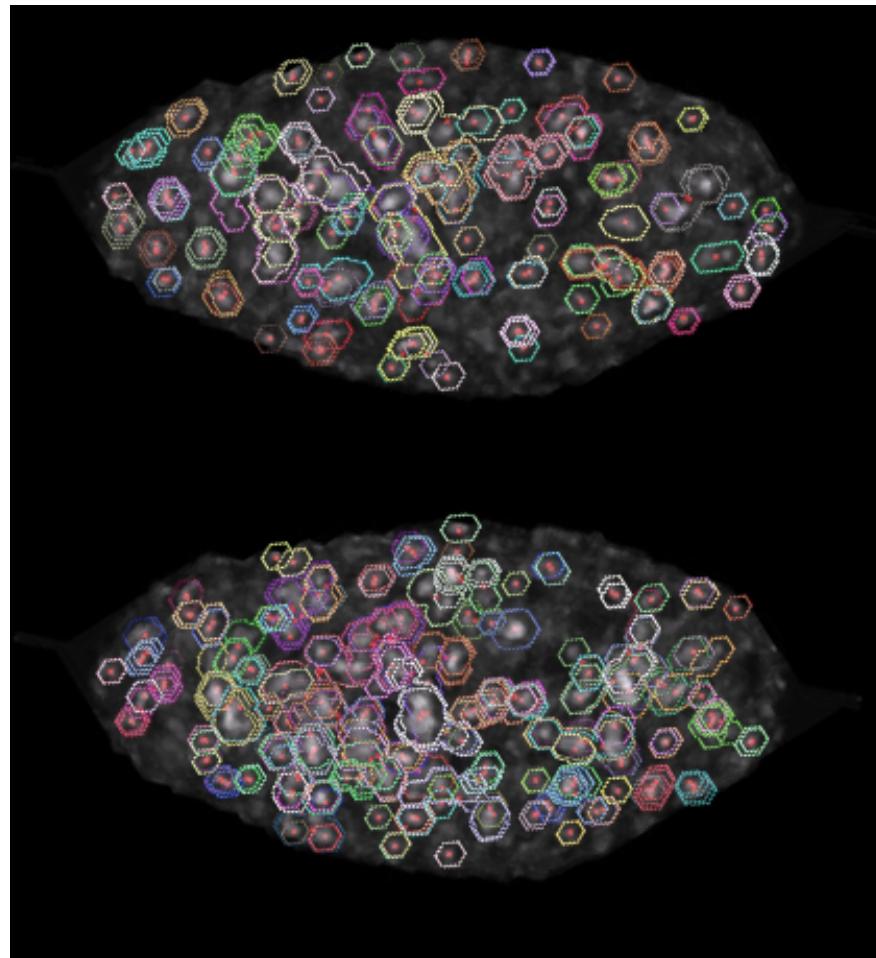
$$I_F(r, \tau) = \left\langle \max_{d(\mathbf{x}, \mathbf{x}_F) = r} I(\mathbf{x}, t_F + \tau) \right\rangle_{F_i \in F}$$

Myosin around foci

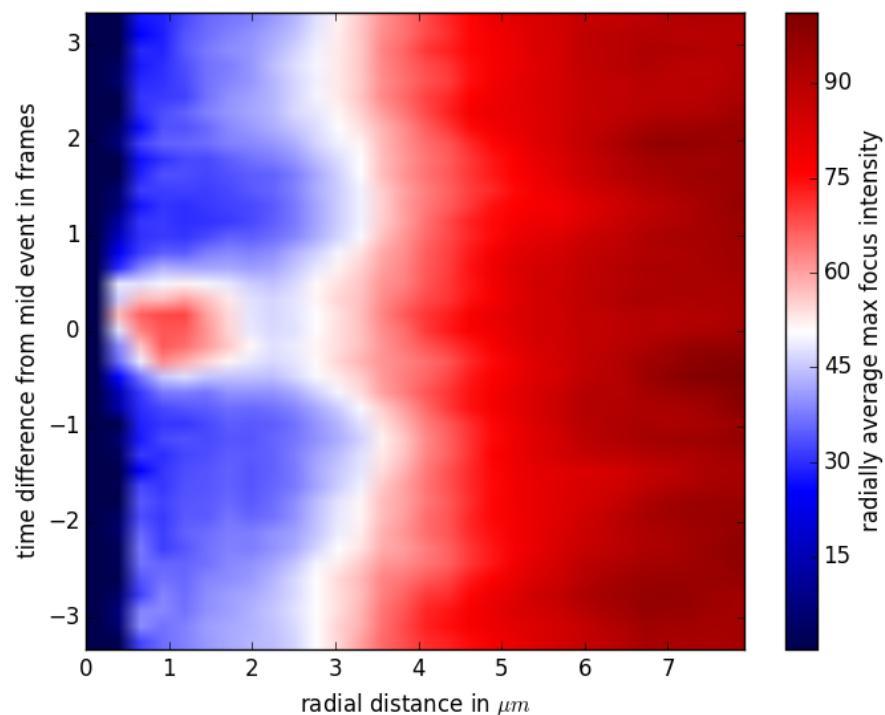


$$I_F(r, \tau) = \left\langle \max_{d(\mathbf{x}, \mathbf{x}_F)=r} I(\mathbf{x}, t_F + \tau) \right\rangle_{F_i \in F} - \left\langle \max_{d(\mathbf{x}, \mathbf{x}_b)=r} I(\mathbf{x}, t_F + \tau) \right\rangle_{\mathbf{x}_b}$$

Foci coverage of the tissue

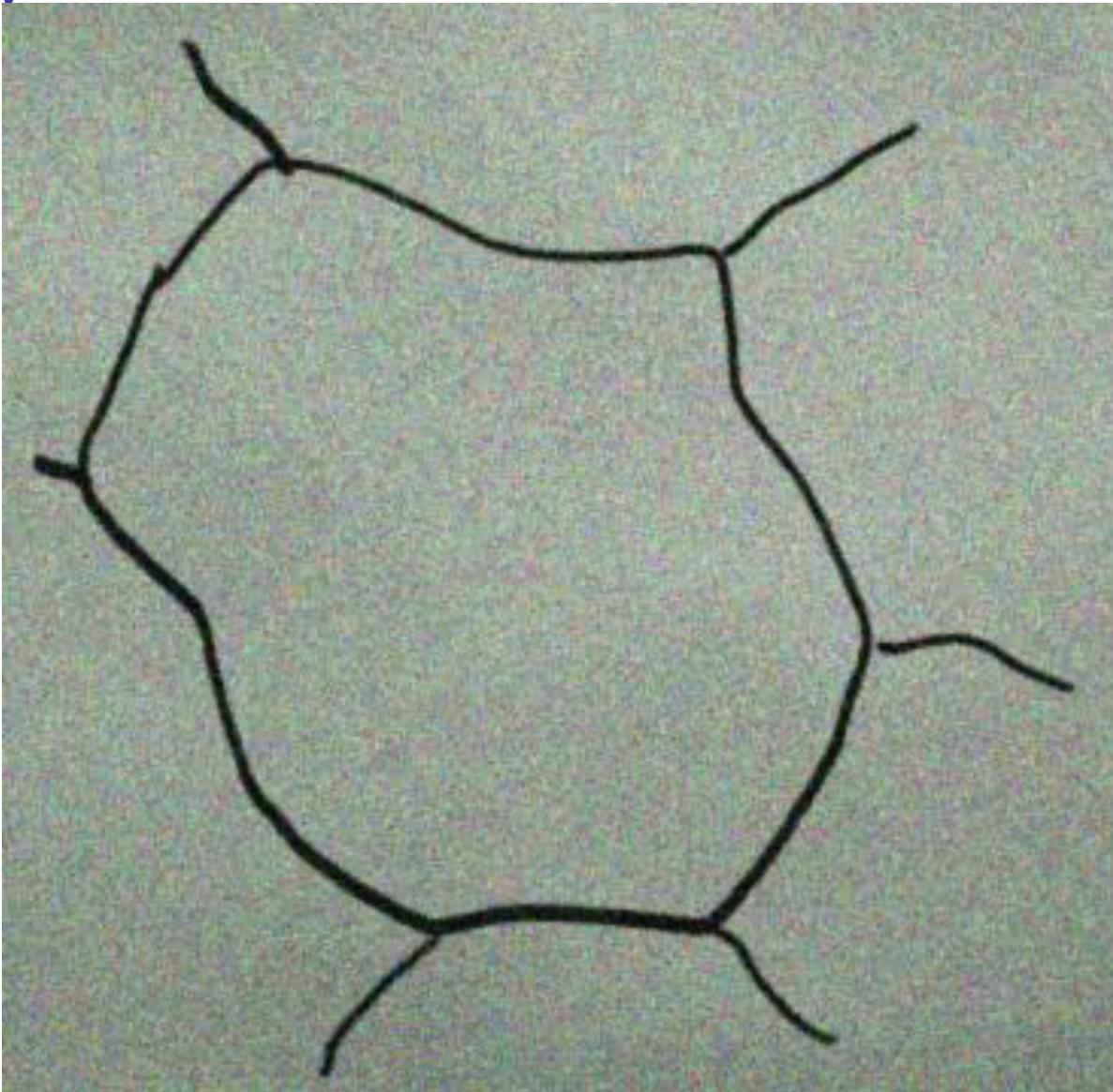


Myosin in other cells

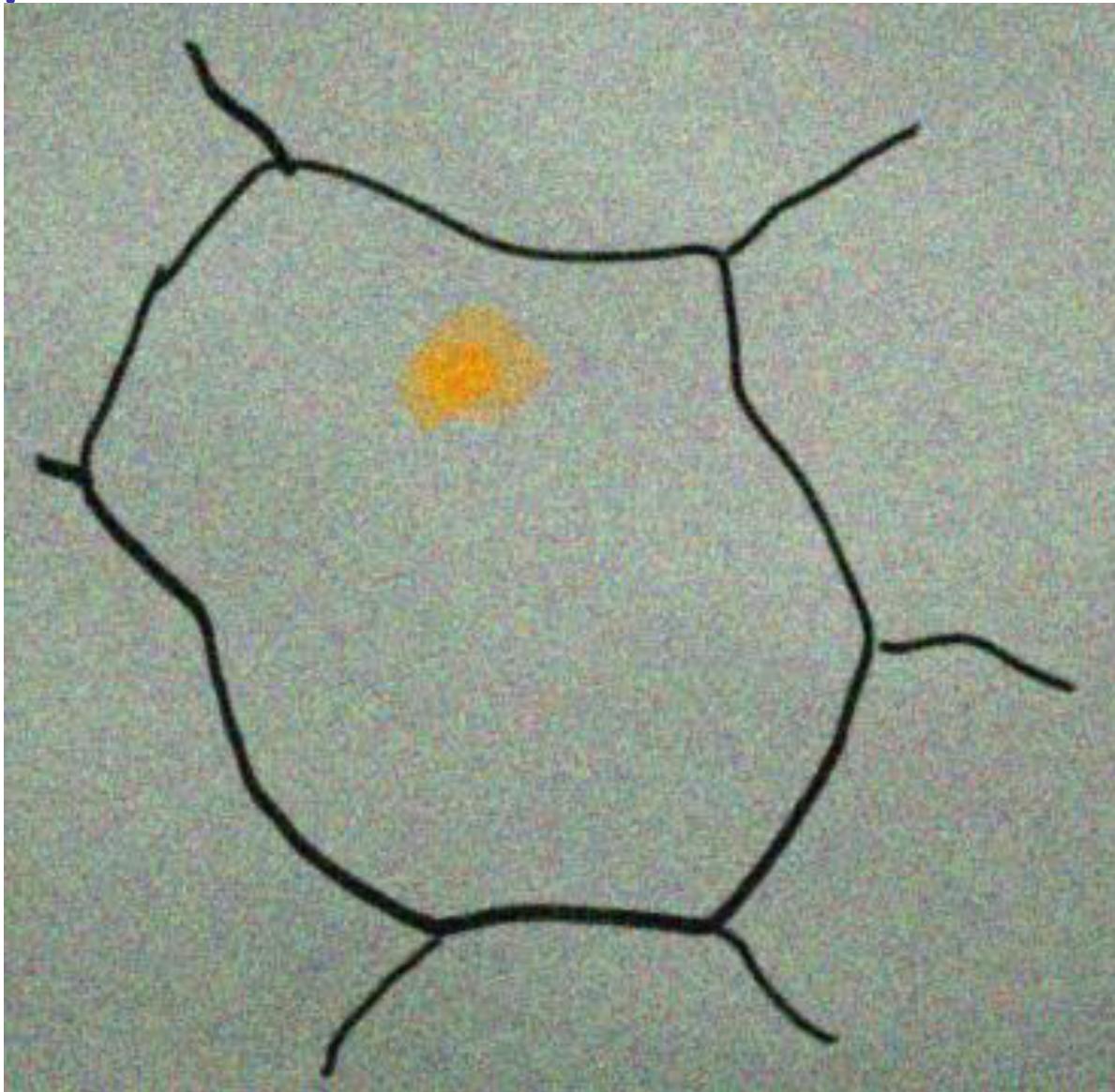


$$I_{\bar{F}}(r, \tau) = \left\langle \max_{\substack{d(\mathbf{x}, \mathbf{x}_F) = r \\ \mathbf{x} \notin \text{Cell}(F)}} I(\mathbf{x}, t_F + \tau) \right\rangle_{F_i \in \mathcal{F}}$$

Proposed mechanism

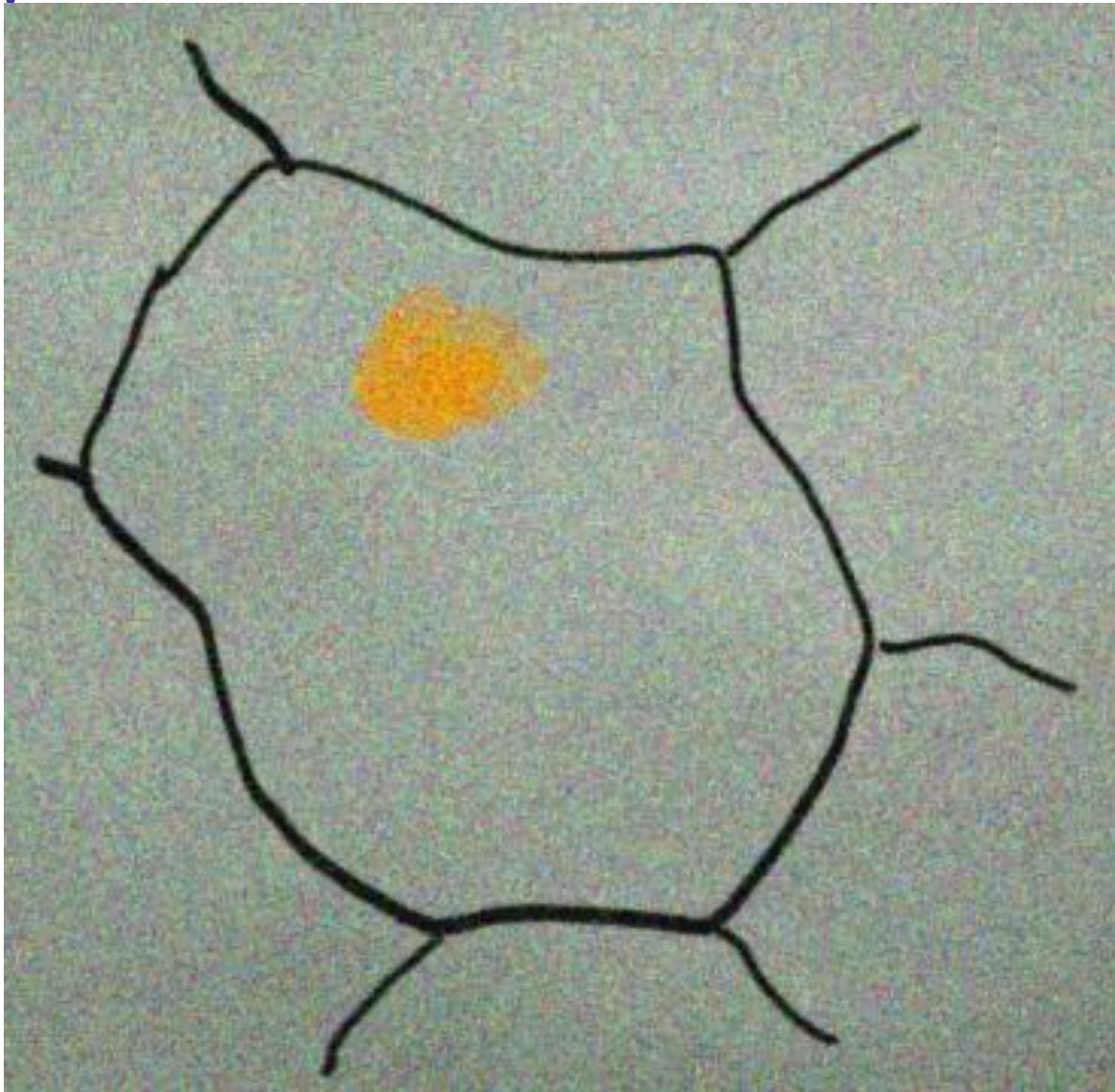


Proposed mechanism



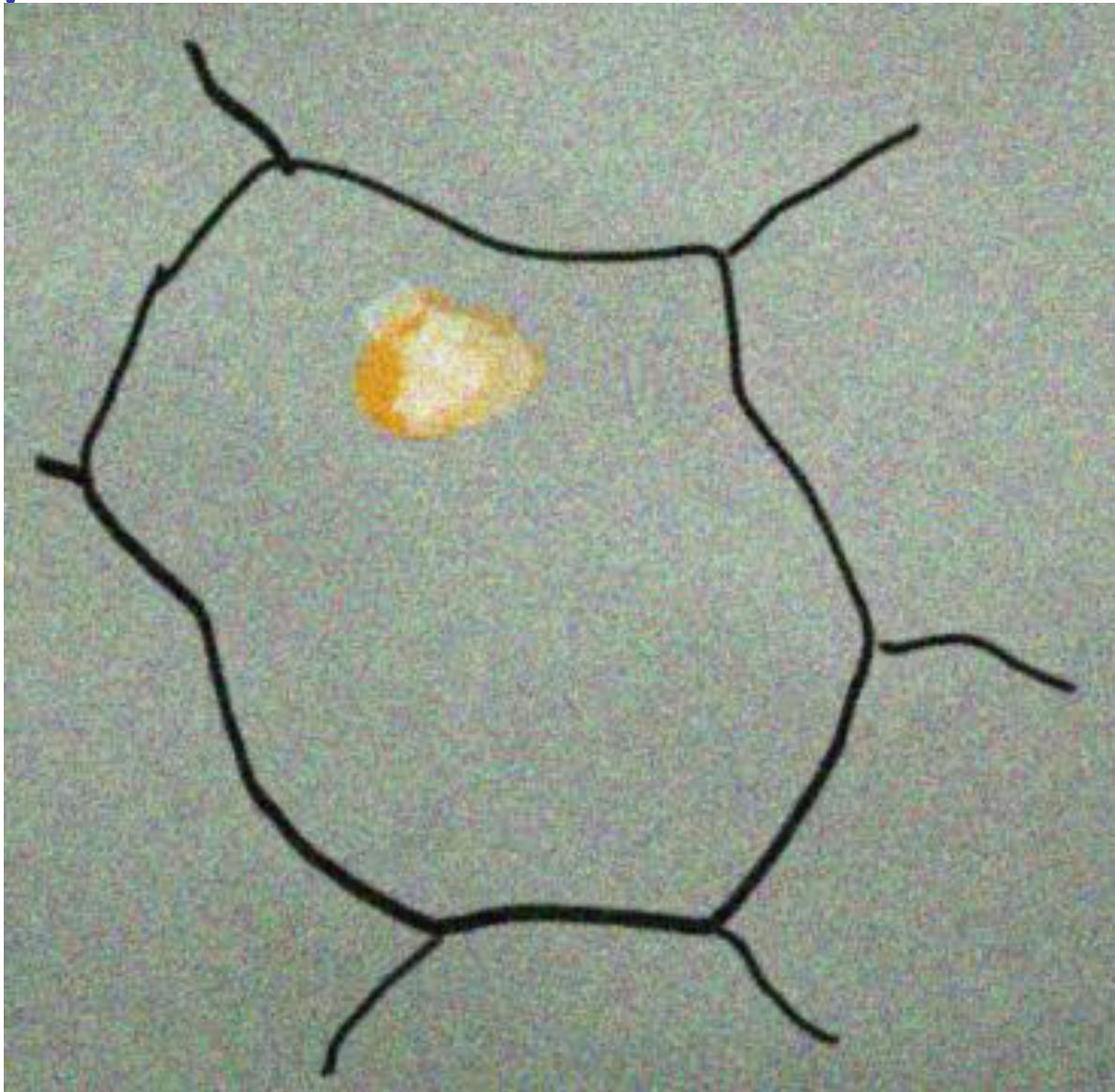
Assembly

Proposed mechanism



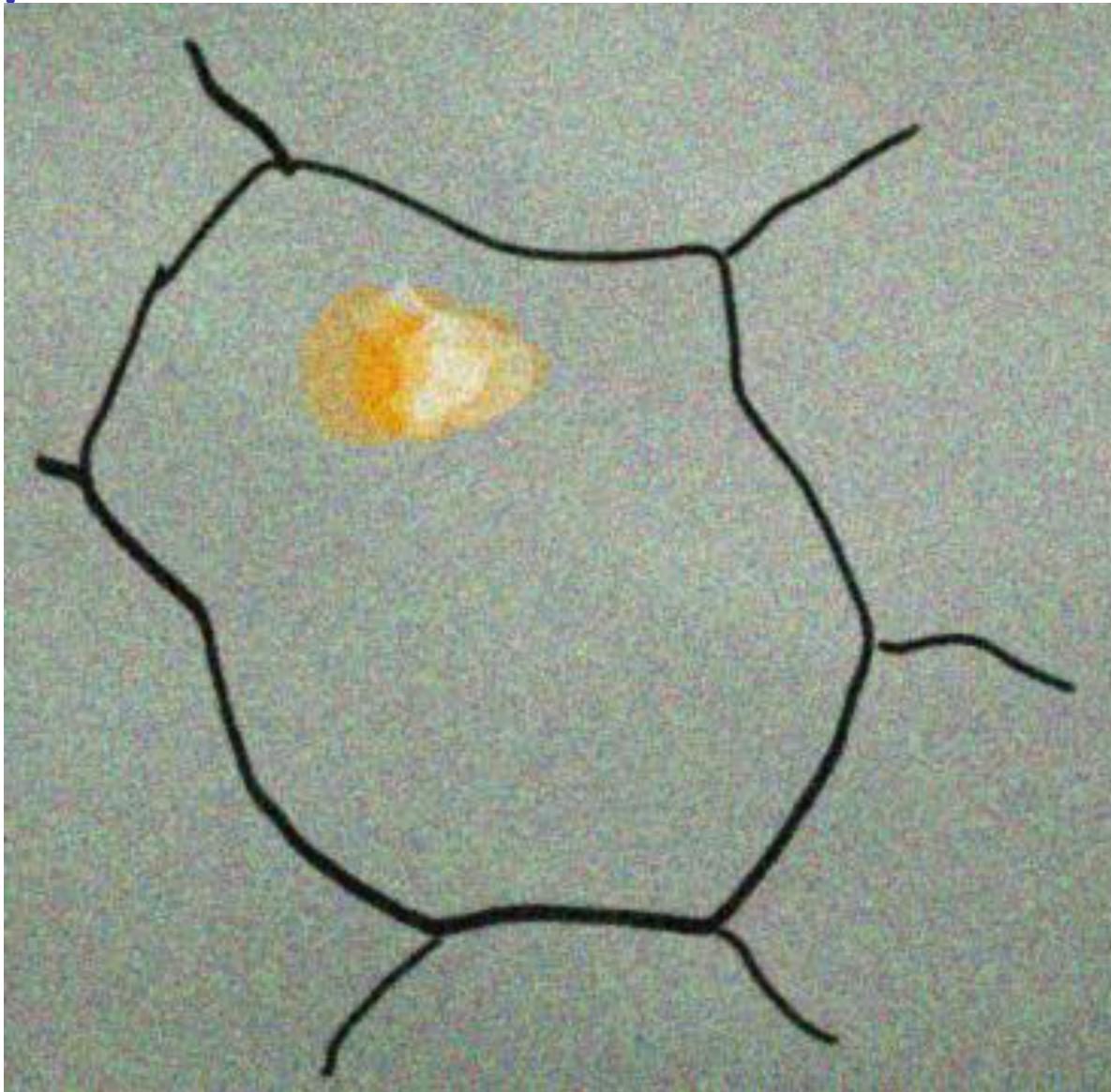
Assembly

Proposed mechanism



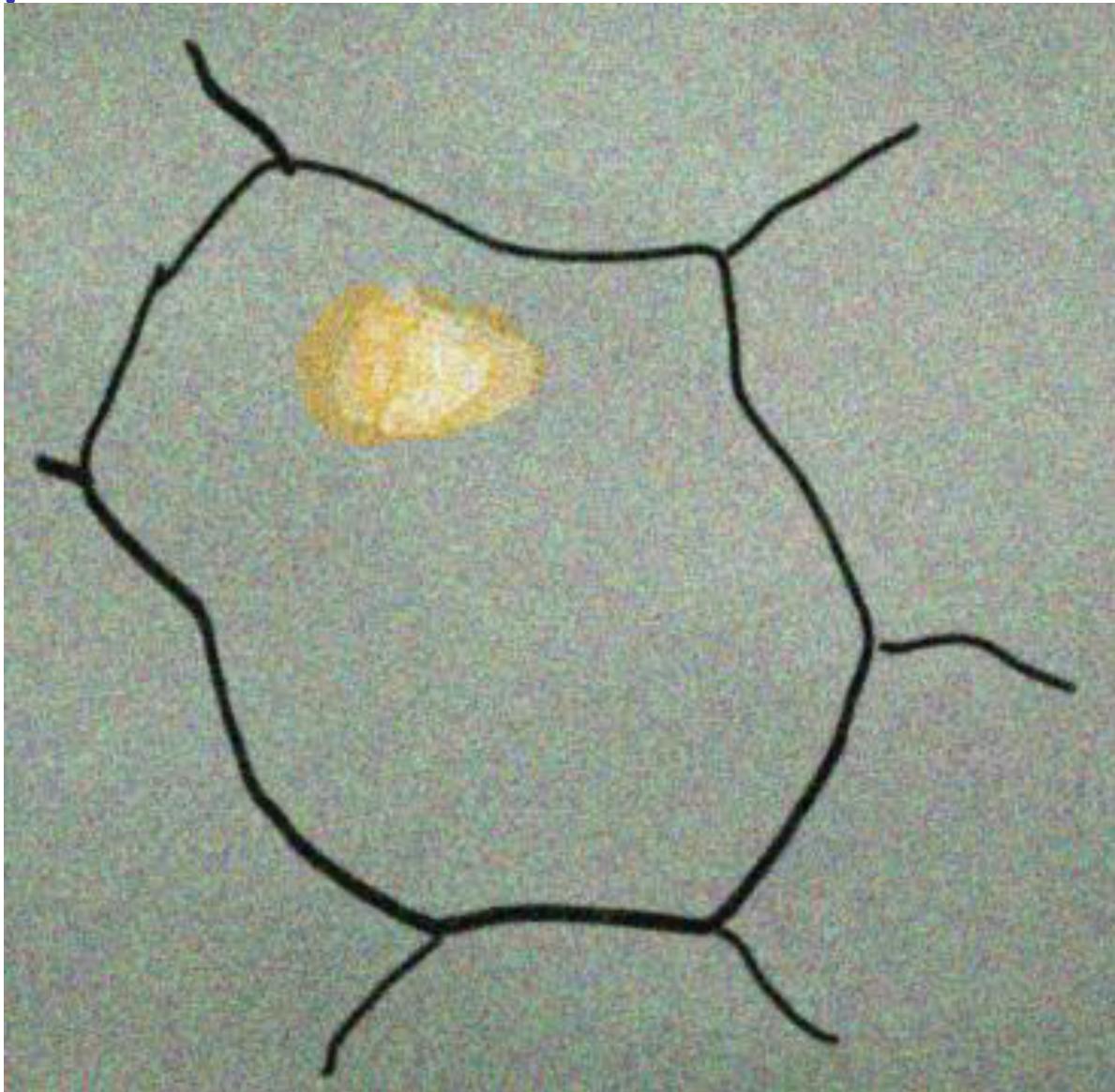
Assembly and appearance of Myosin-refractory regions

Proposed mechanism



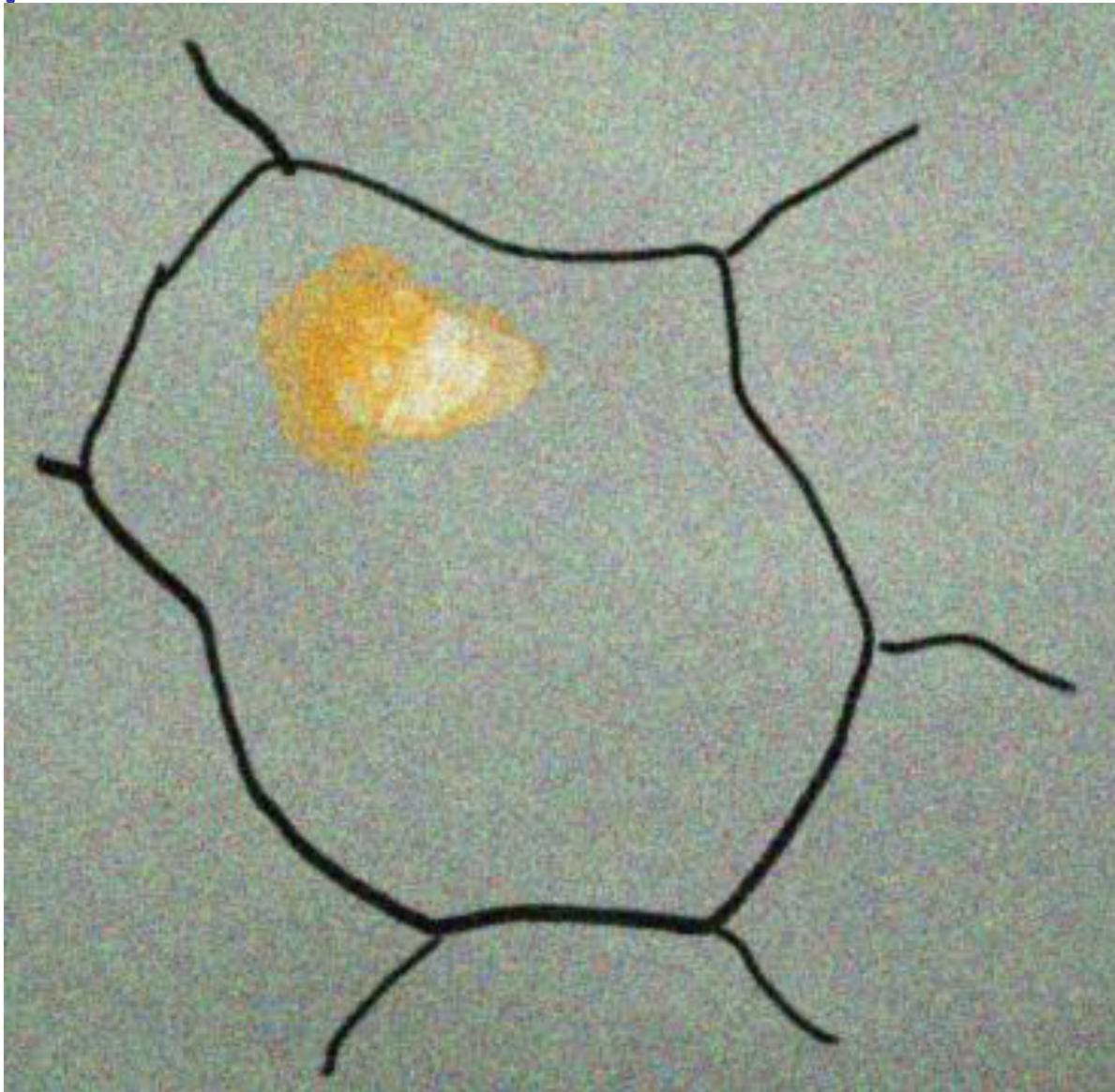
Assembly and appearance of Myosin-refractory regions

Proposed mechanism



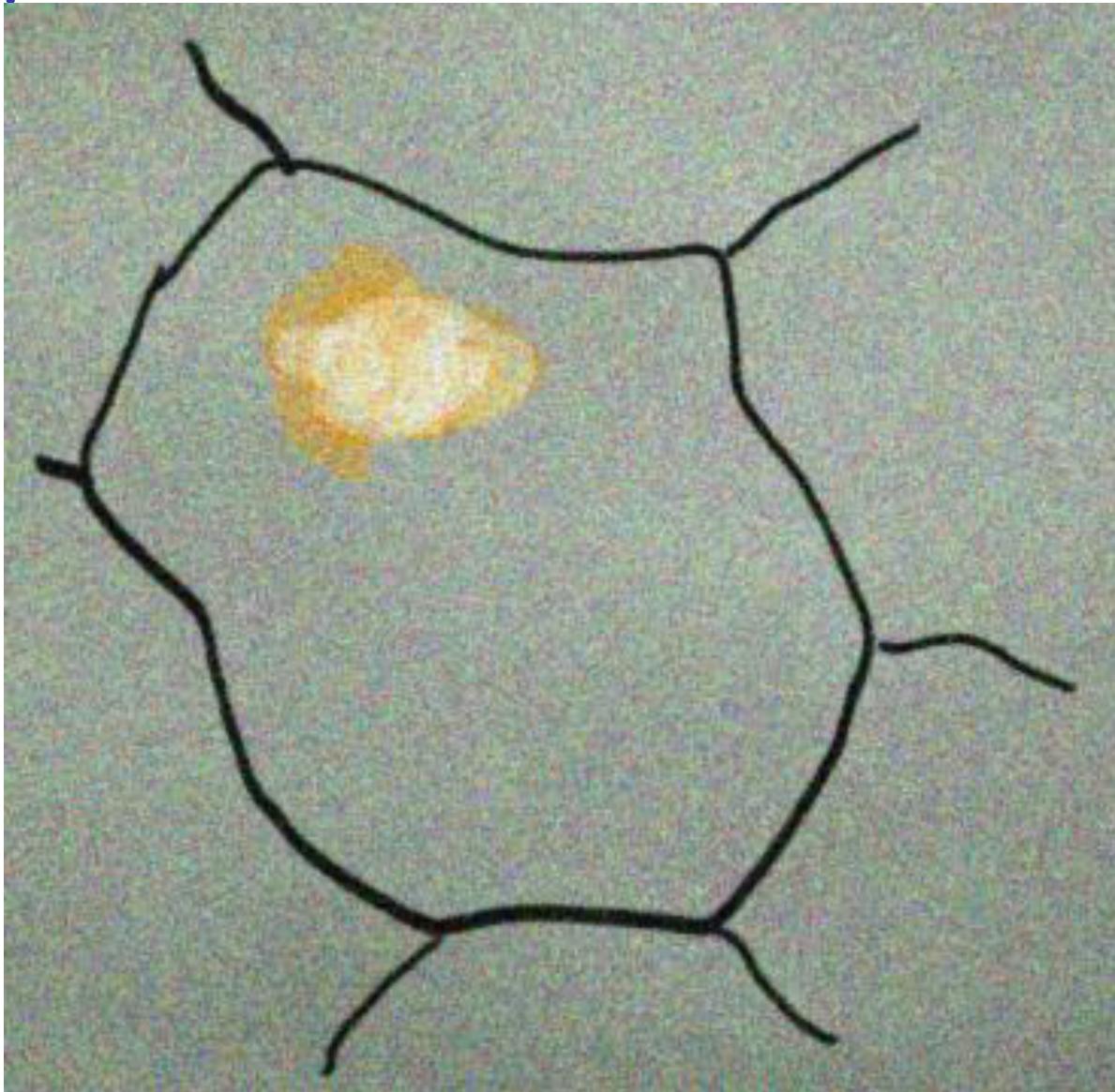
Assembly and appearance of Myosin-refractory regions

Proposed mechanism



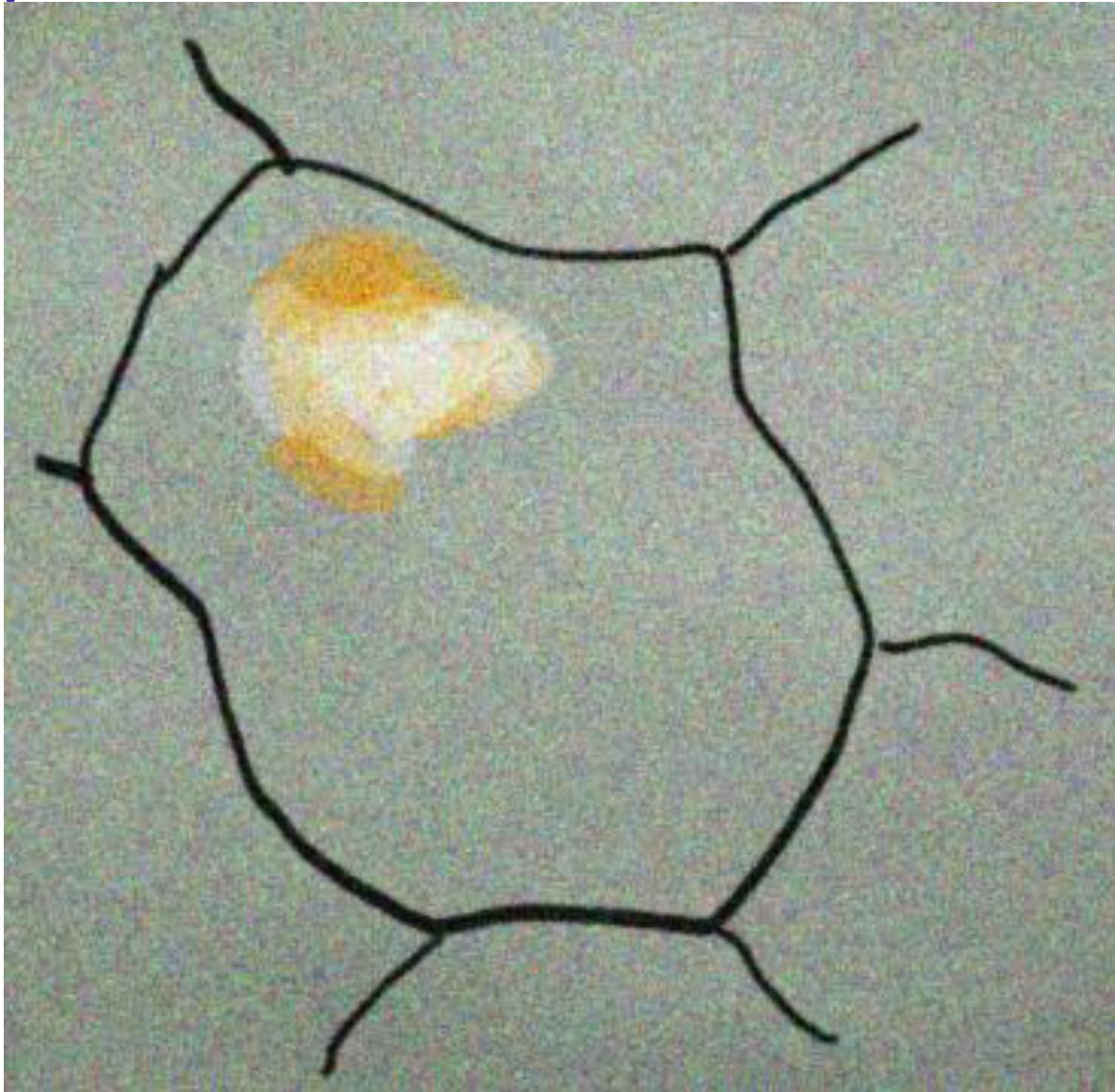
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk

Proposed mechanism



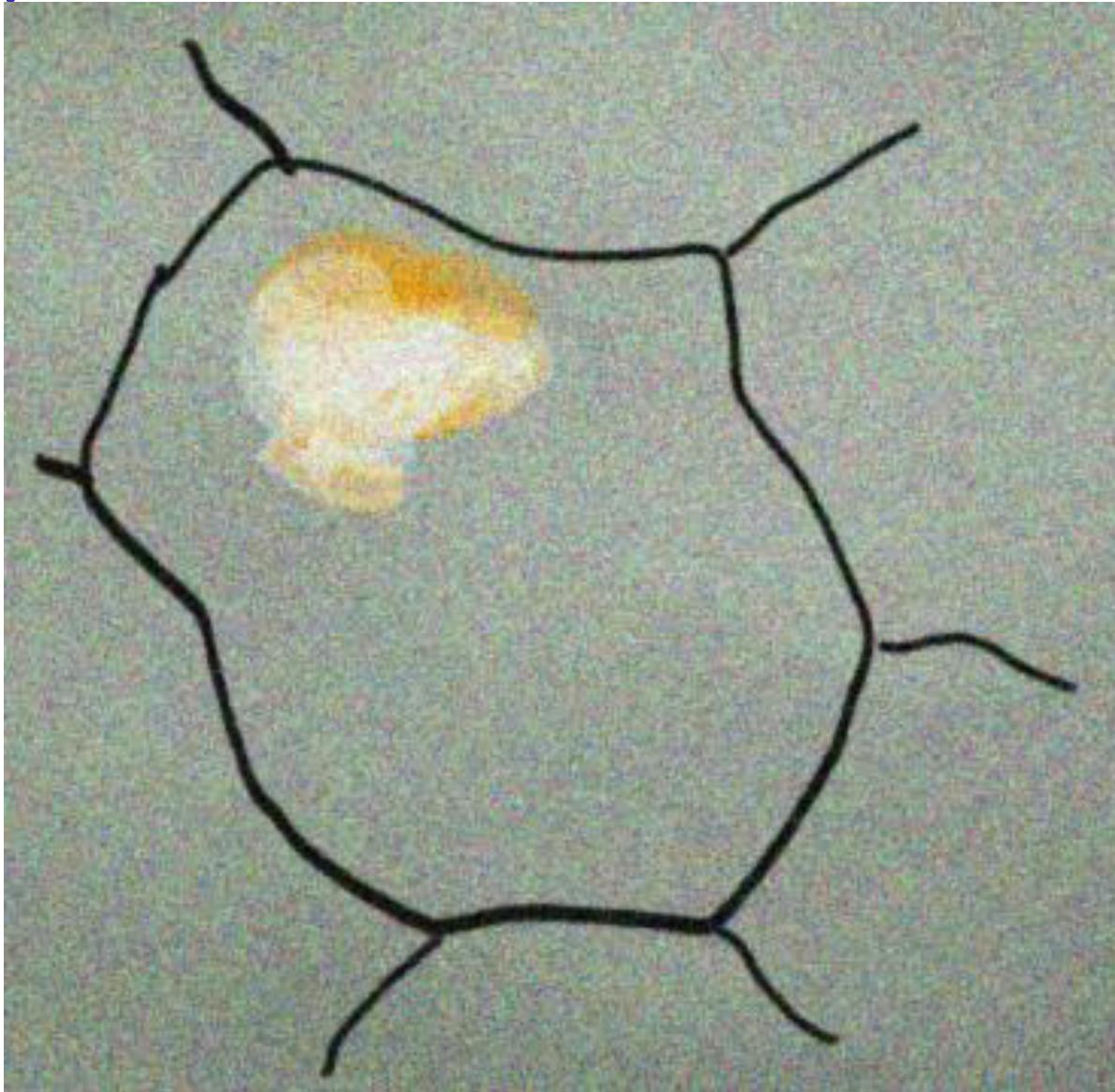
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk

Proposed mechanism



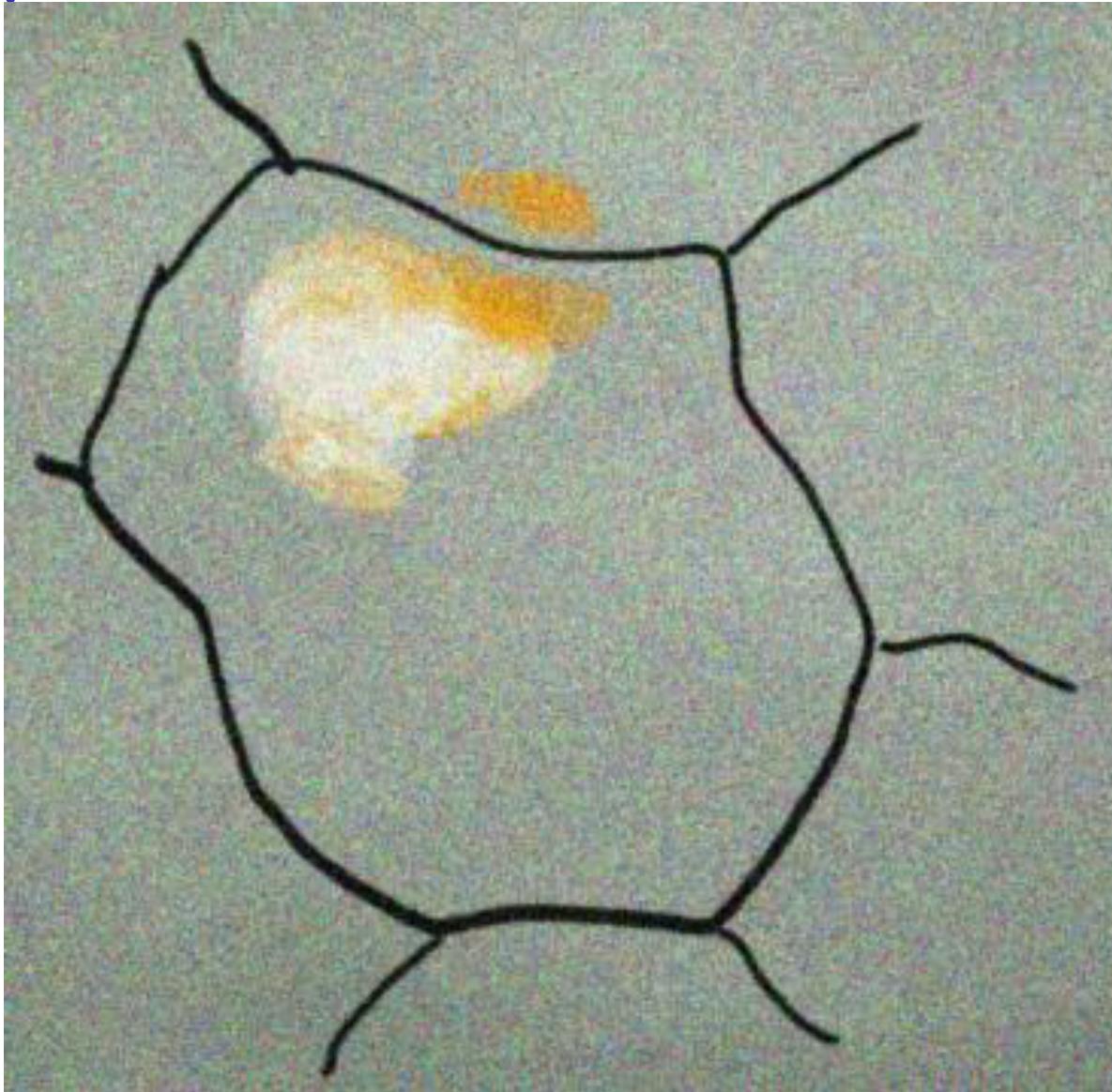
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.

Proposed mechanism



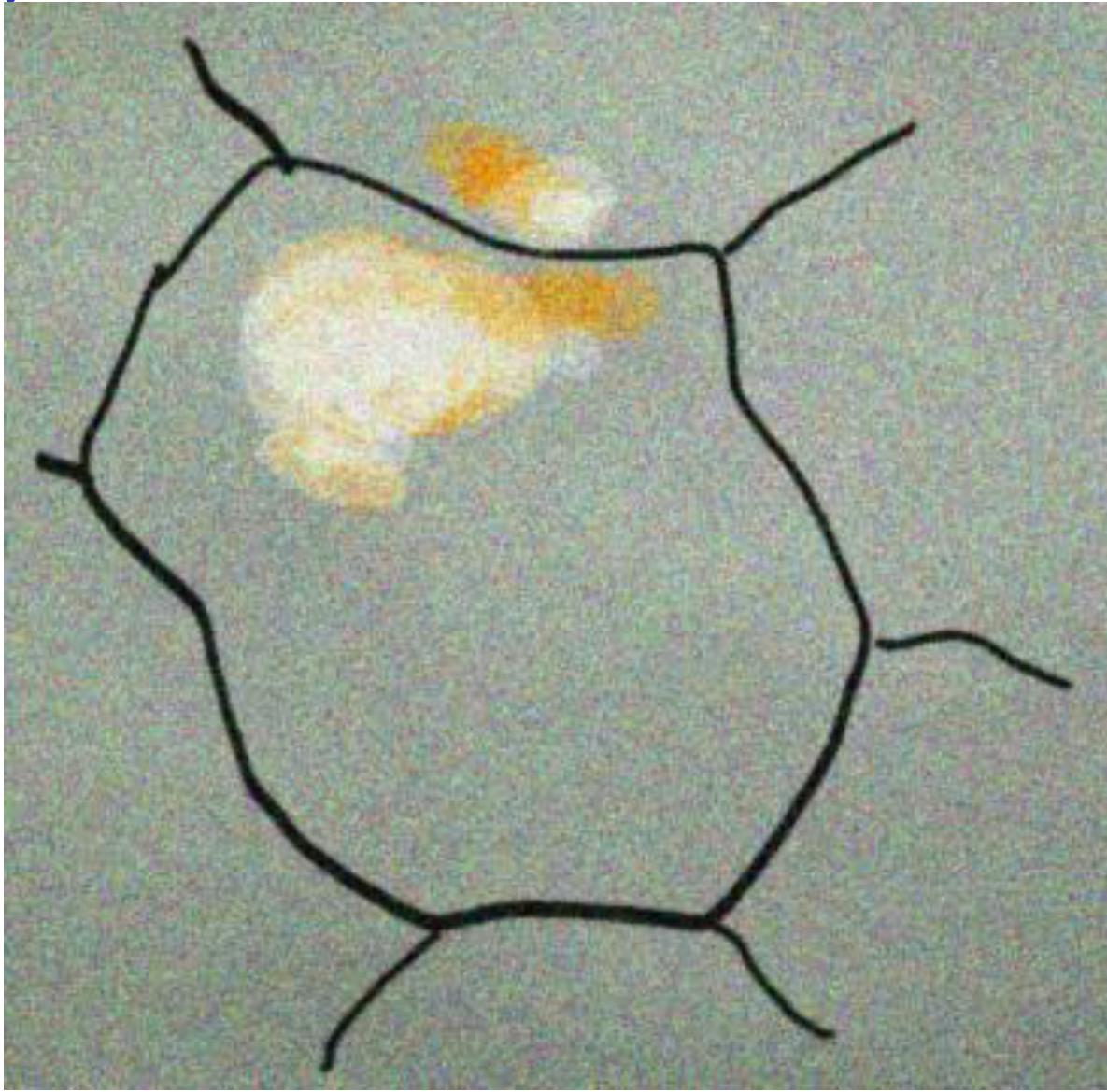
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.

Proposed mechanism



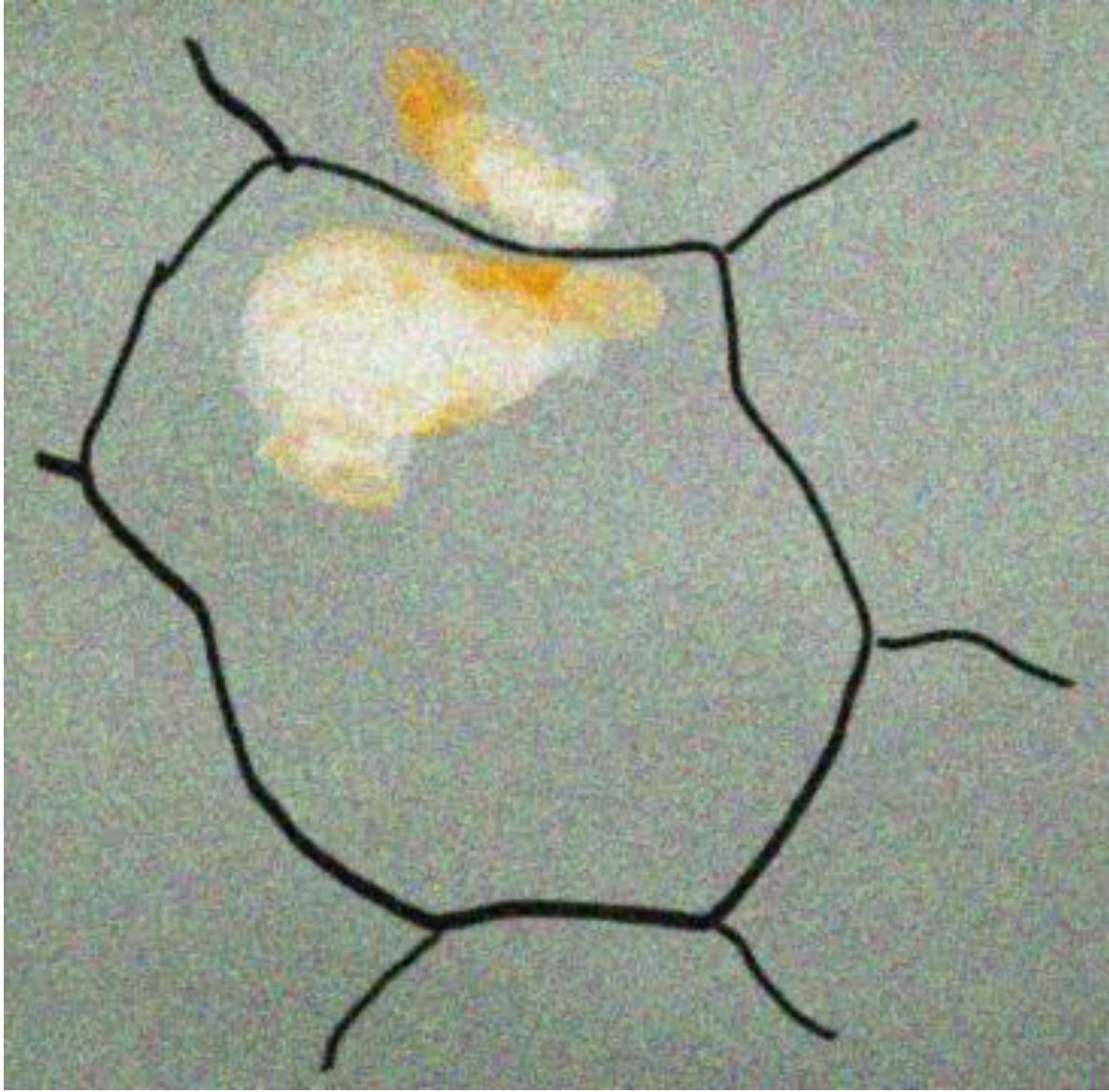
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.
'Infection' of nearby cells.

Proposed mechanism



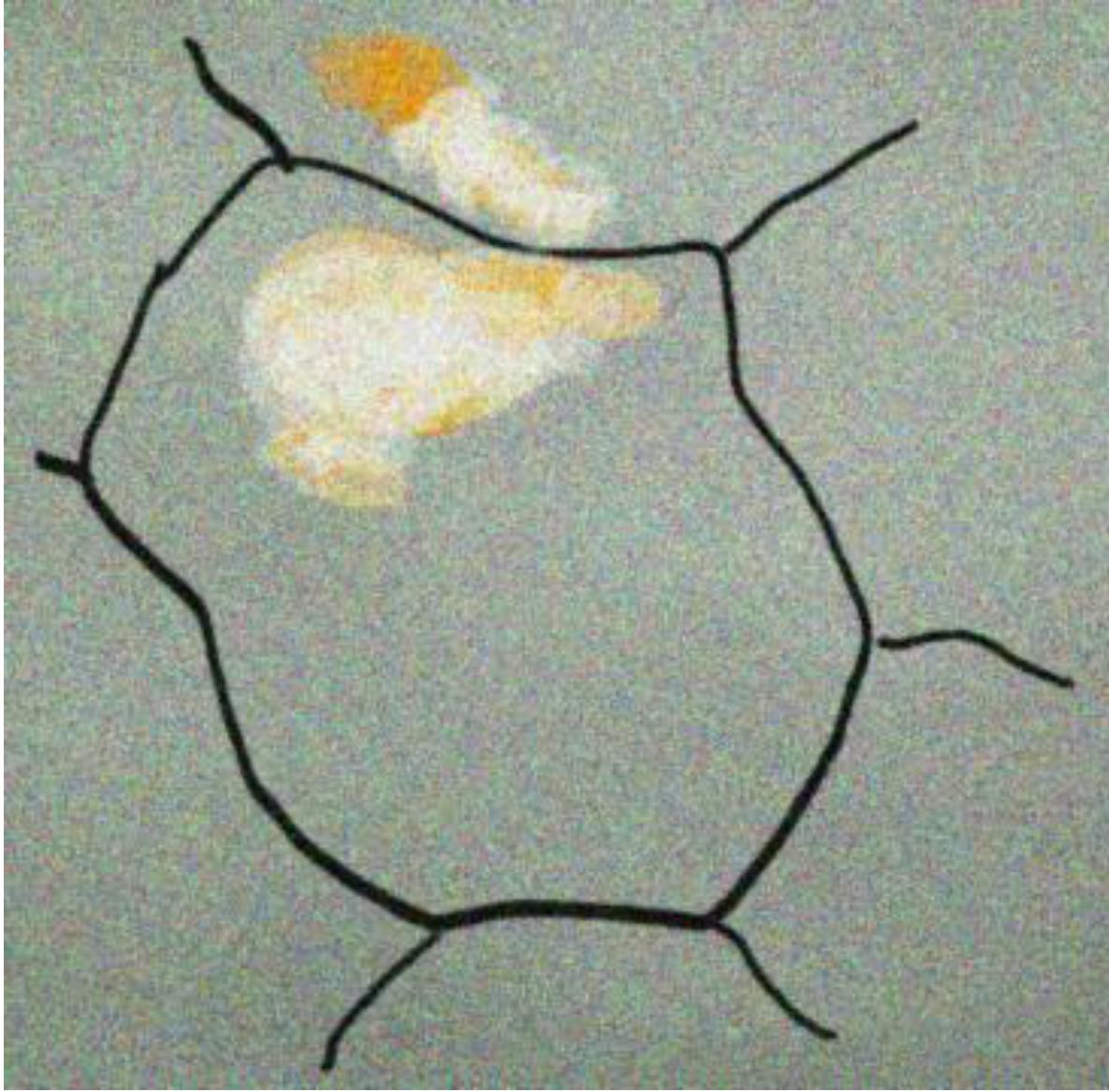
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.
'Infection' of nearby cells.

Proposed mechanism



Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.
'Infection' of nearby cells. Disassembly when 'trapped'

Proposed mechanism



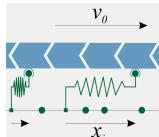
Assembly and appearance of Myosin-refractory regions leading to self-avoiding walk with occasional splitting.
'Infection' of nearby cells. Disassembly when 'trapped'

Co-workers

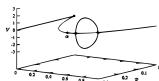
LIPHY:Physics@Grenoble



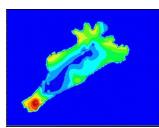
Nilankur Dutta



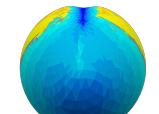
Haythem Chelly



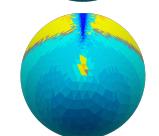
Pierre Recho



Claude Verdier



Catherine Quilliet



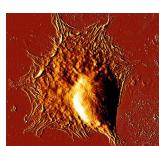
Philippe Marmottant



Alexandr Farutin

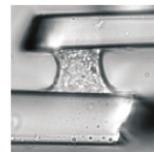


Chaouqi Misbah



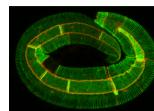
Valérie Laurent

MSC:Physics@Paris



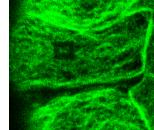
Atef Asnacios

IGDR:DevBiol@Rennes

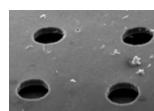


Grégoire Michaux

LTM:Nanomat@Grenoble

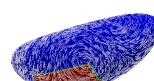


Sara Bouizakarne

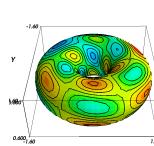


Alice Nicolas

LJK:Maths@Grenoble

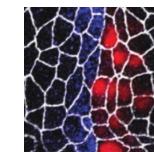


Mahamar Dicko

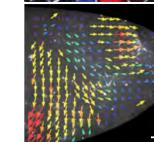


Pierre Saramito

PDN:DevBiol@Cambridge



Bénédicte Sanson

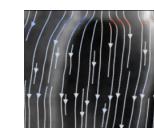


Claire Lye



Guy Blanchard

DAMTP:Maths@Cambridge



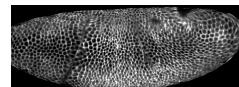
Lukas Lang



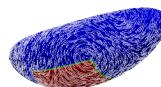
Nicole Gorfinkiel



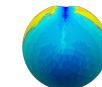
The apical drive of Myosin for convergence-extension (and folding)



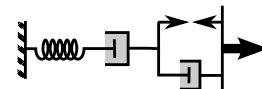
Guy Blanchard
Claire Lye
Bénédicte Sanson
PDN, Univ. Cambridge



Mahamar Dicko
Pierre Saramito
LJK, CNRS–Univ. Grenoble Alpes



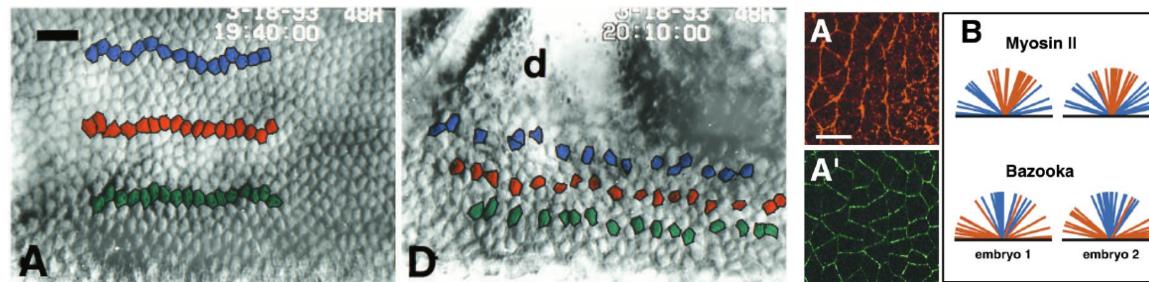
Julien Fierling
Alexandre Torzynski
Catherine Quilliet
Philippe Marmottant



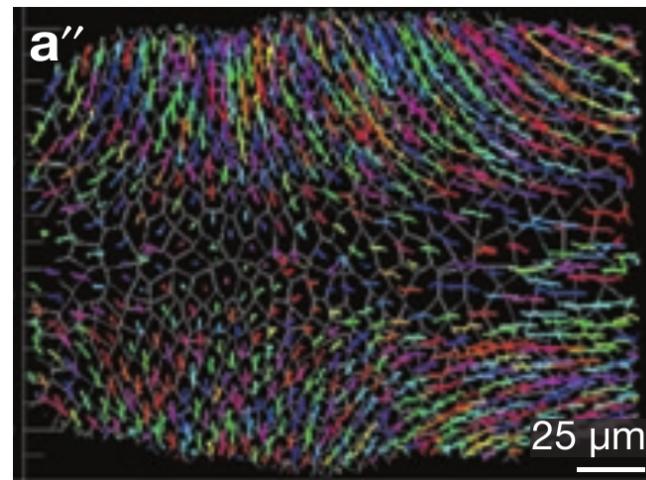
Jocelyn Étienne

LIPHY, CNRS–Univ. Grenoble Alpes

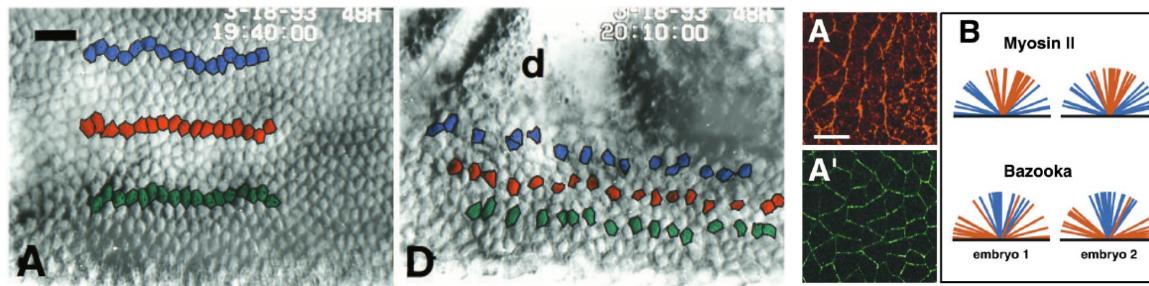
Convergence–extension during germband axis extension



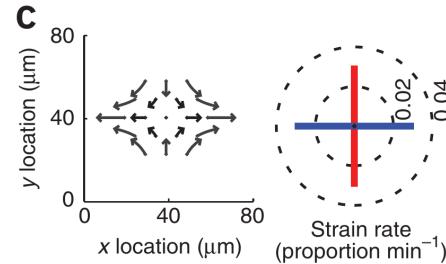
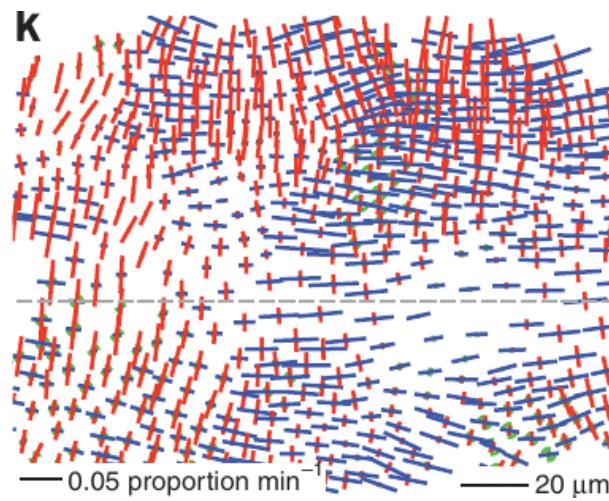
Irvine and Wieschaus, Devel. 1994, Zallen et al., Dev. Cell 2004



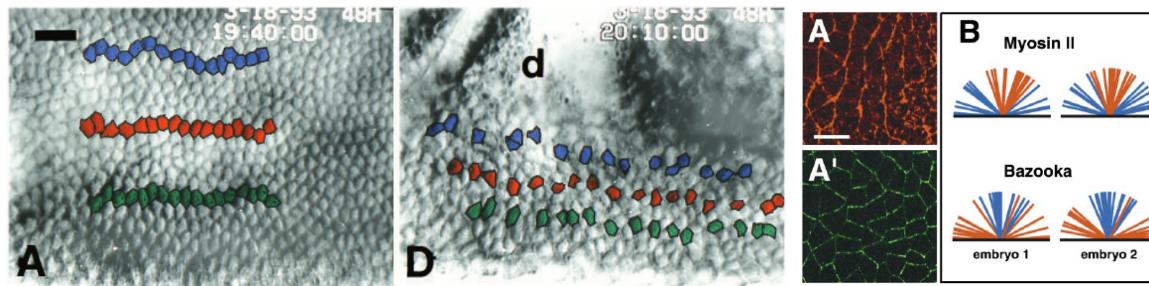
Convergence–extension during germband axis extension



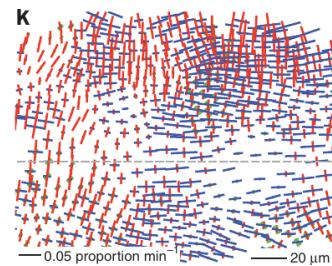
Irvine and Wieschaus, Devel. 1994, Zallen et al., Dev. Cell 2004



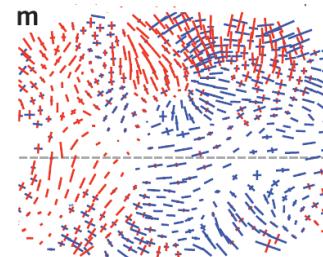
Convergence–extension during germband axis extension



Irvine and Wieschaus, Devel. 1994, Zallen et al., Dev. Cell 2004

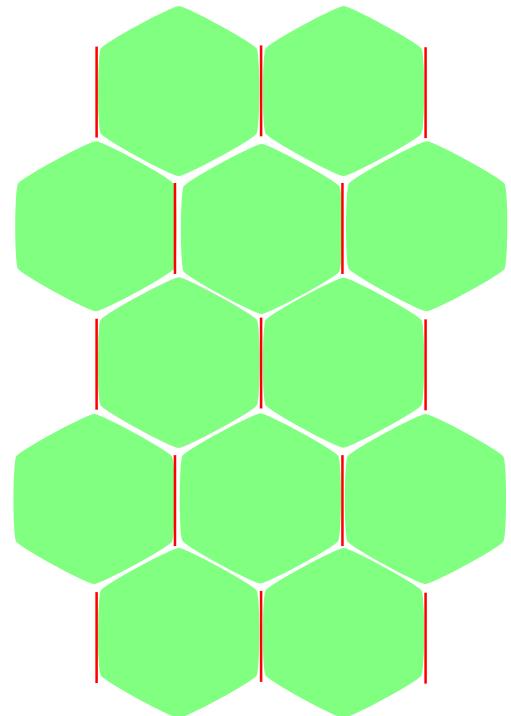


tissue strain rate

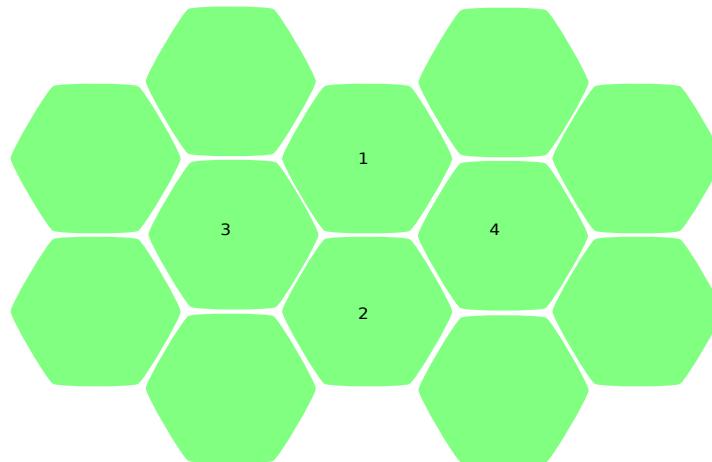
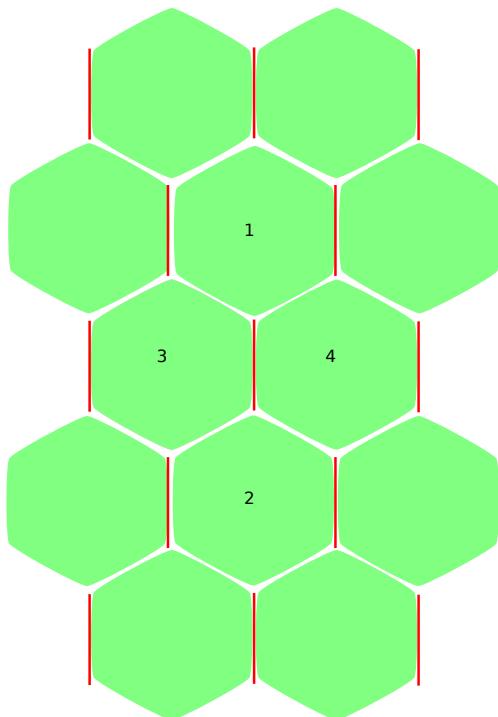


cell strain rate

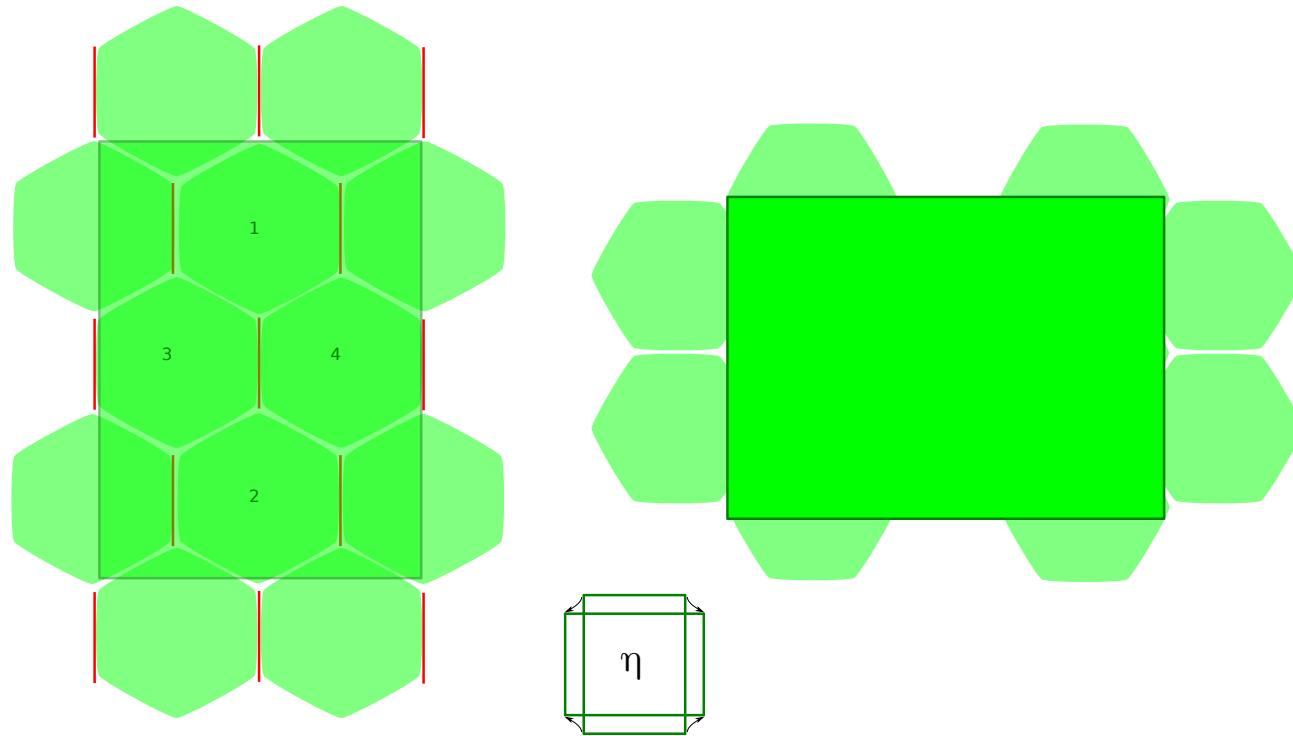
Planar-polarised myosin and convergence–extension



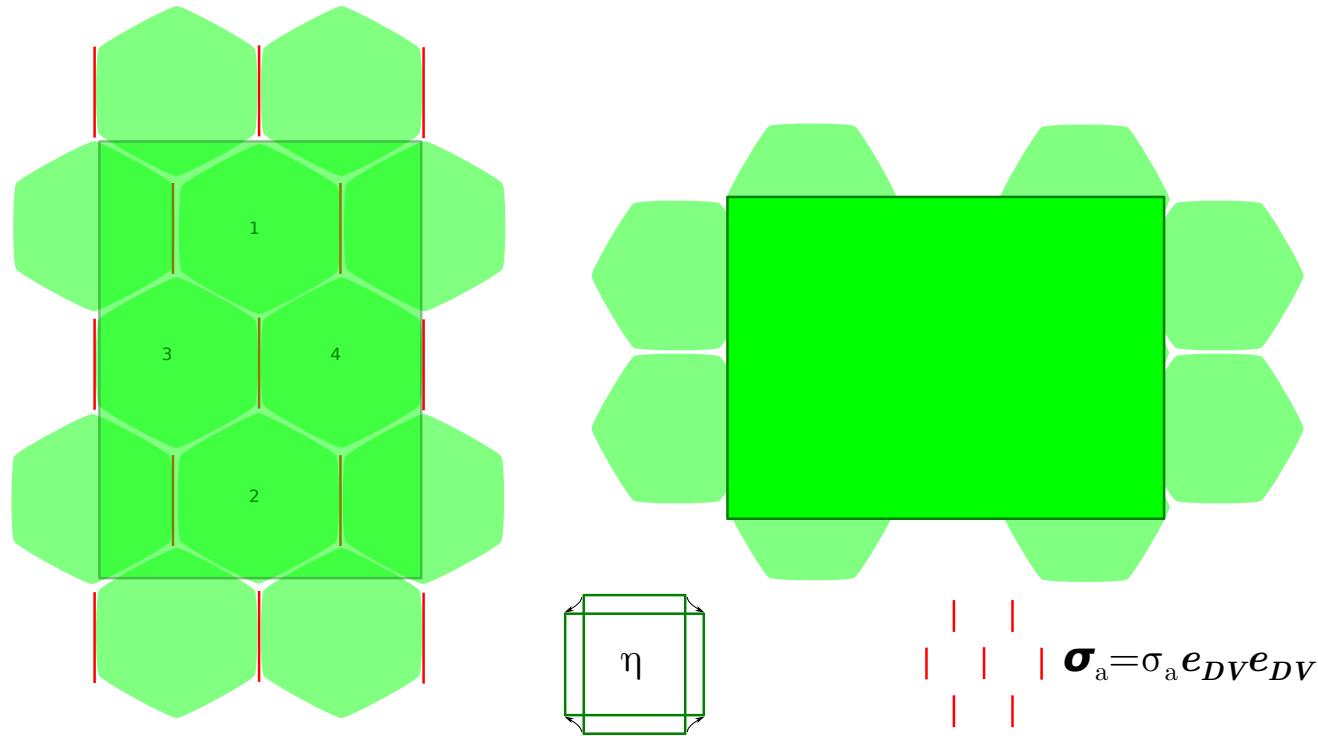
Planar-polarised myosin and convergence–extension



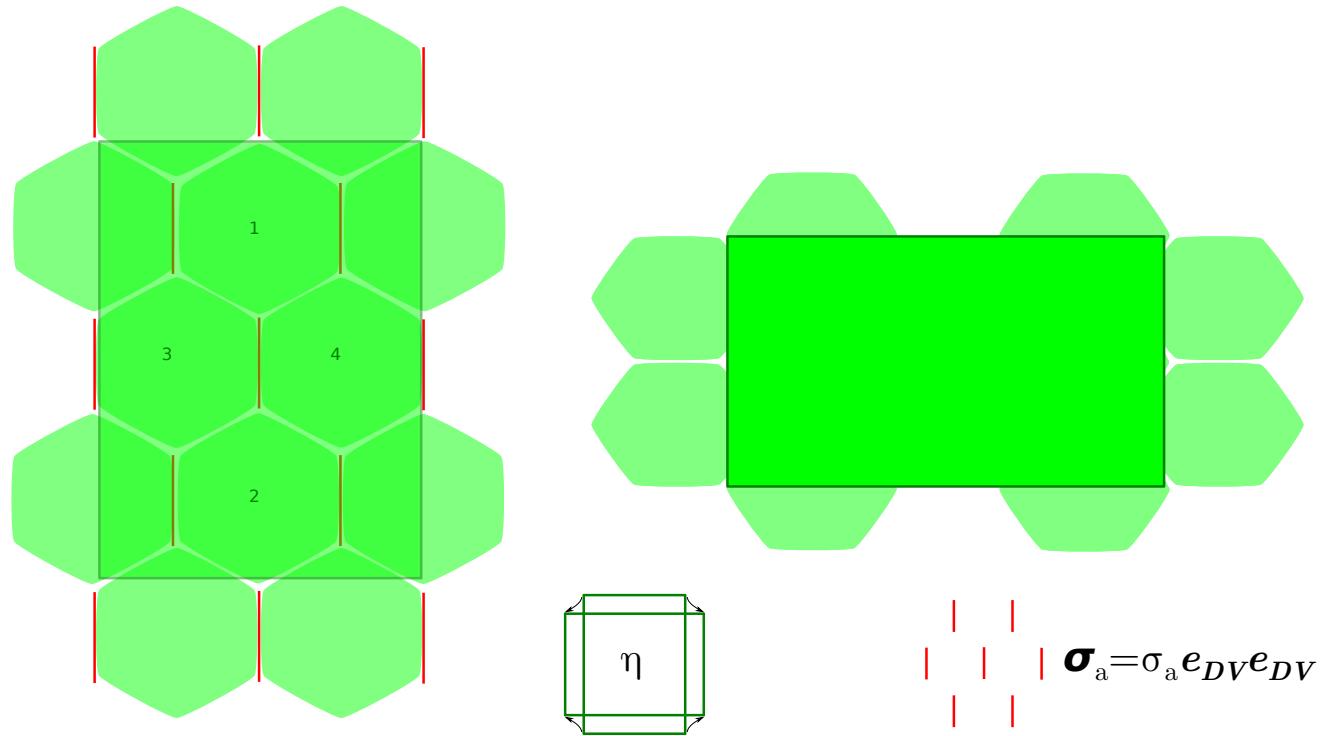
Planar-polarised myosin and convergence–extension



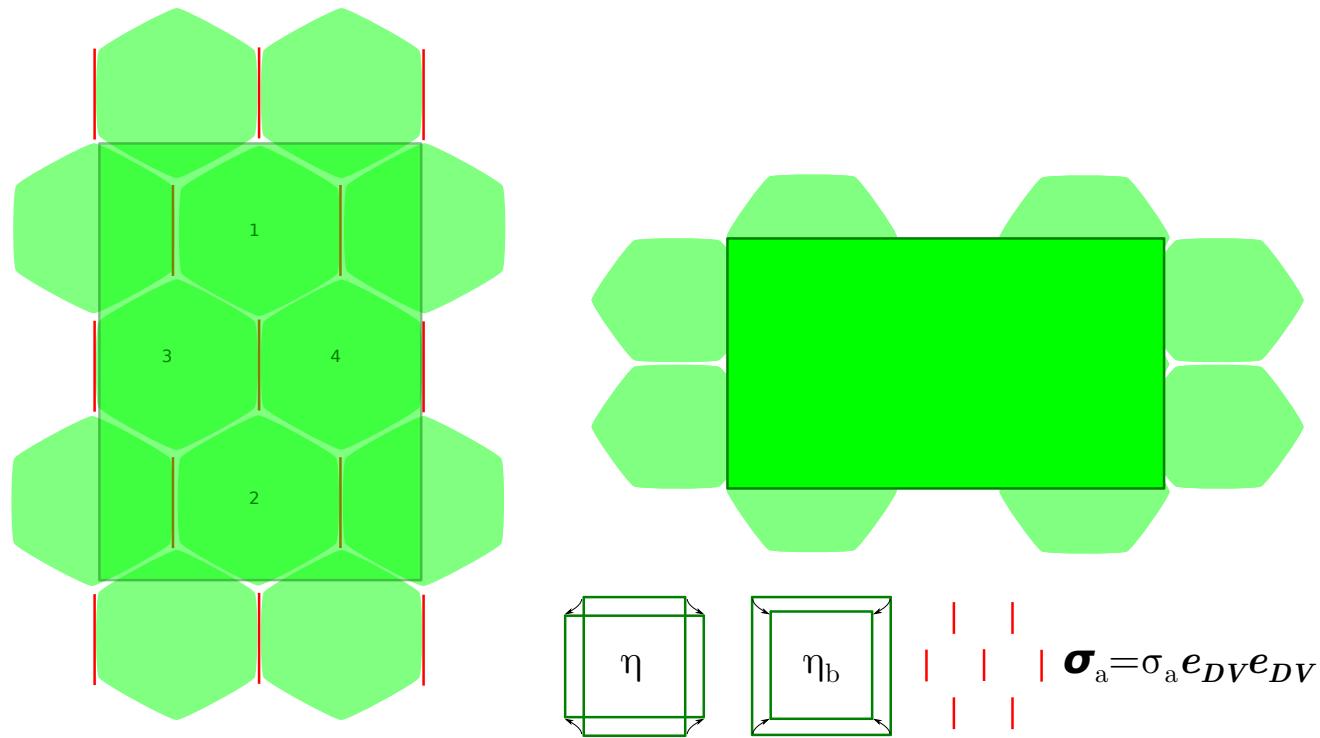
Planar-polarised myosin and convergence–extension



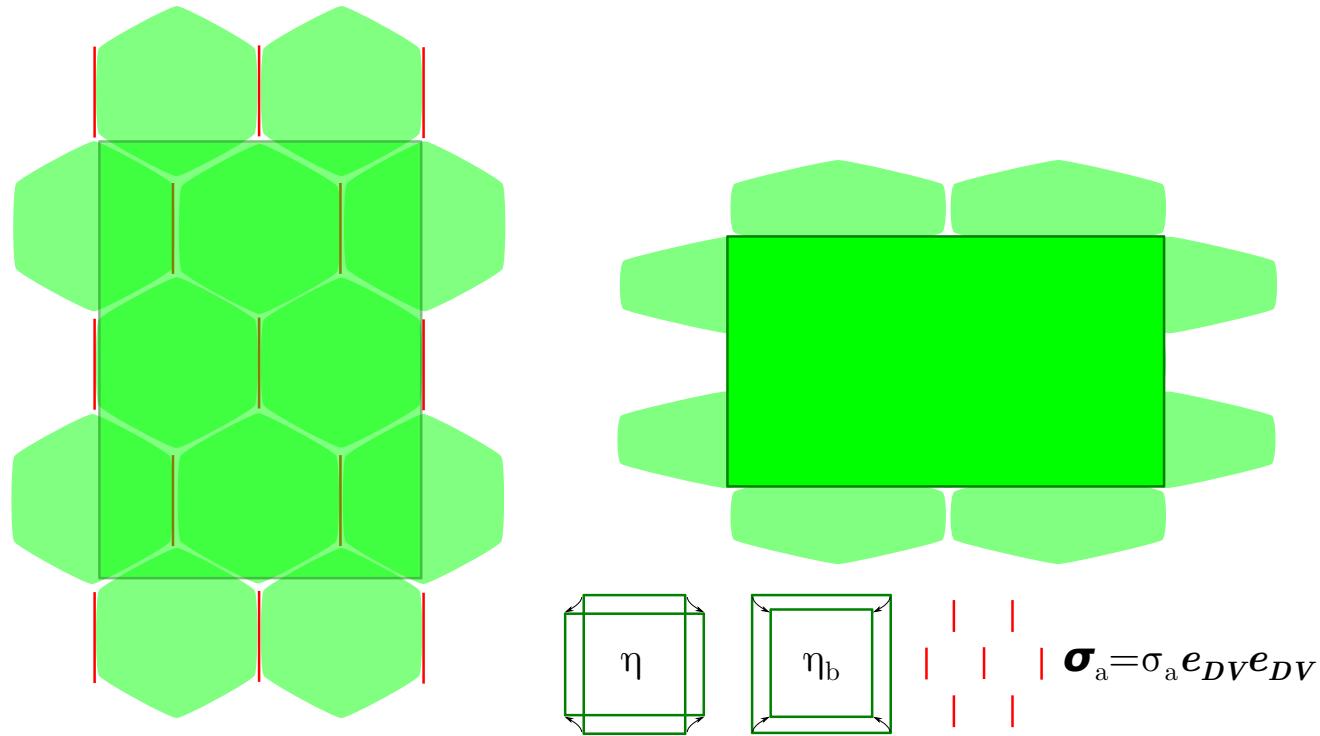
Planar-polarised myosin and convergence–extension



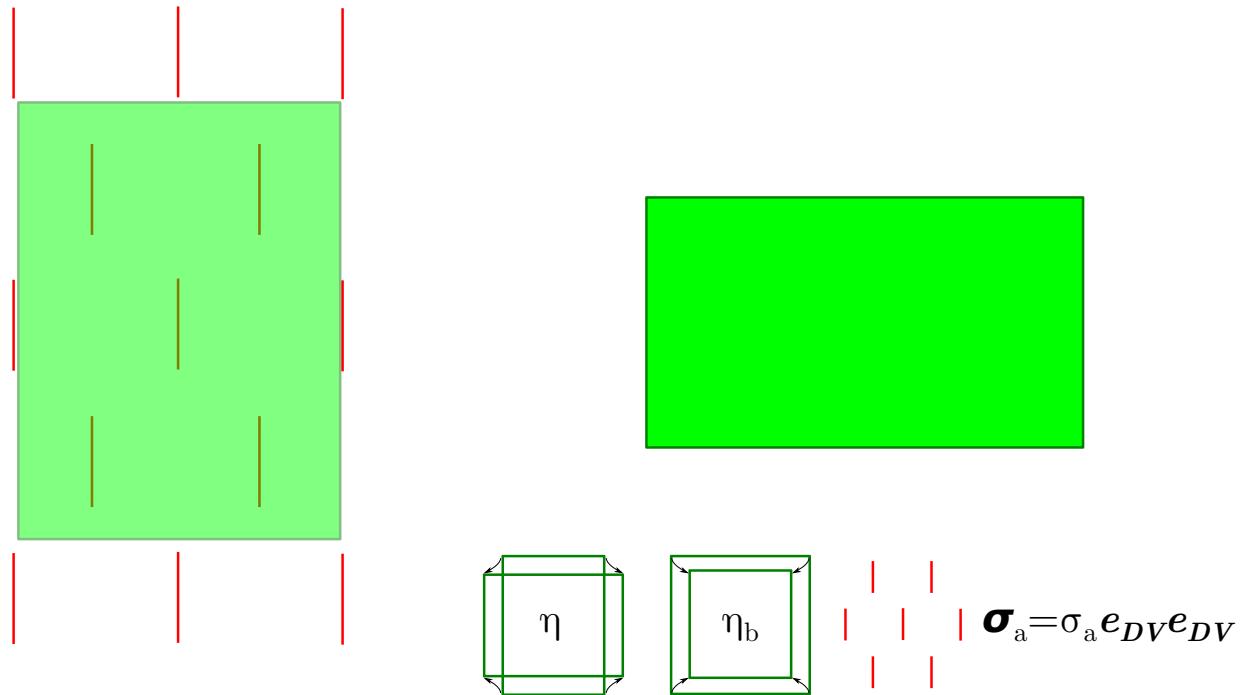
Planar-polarised myosin and convergence–extension



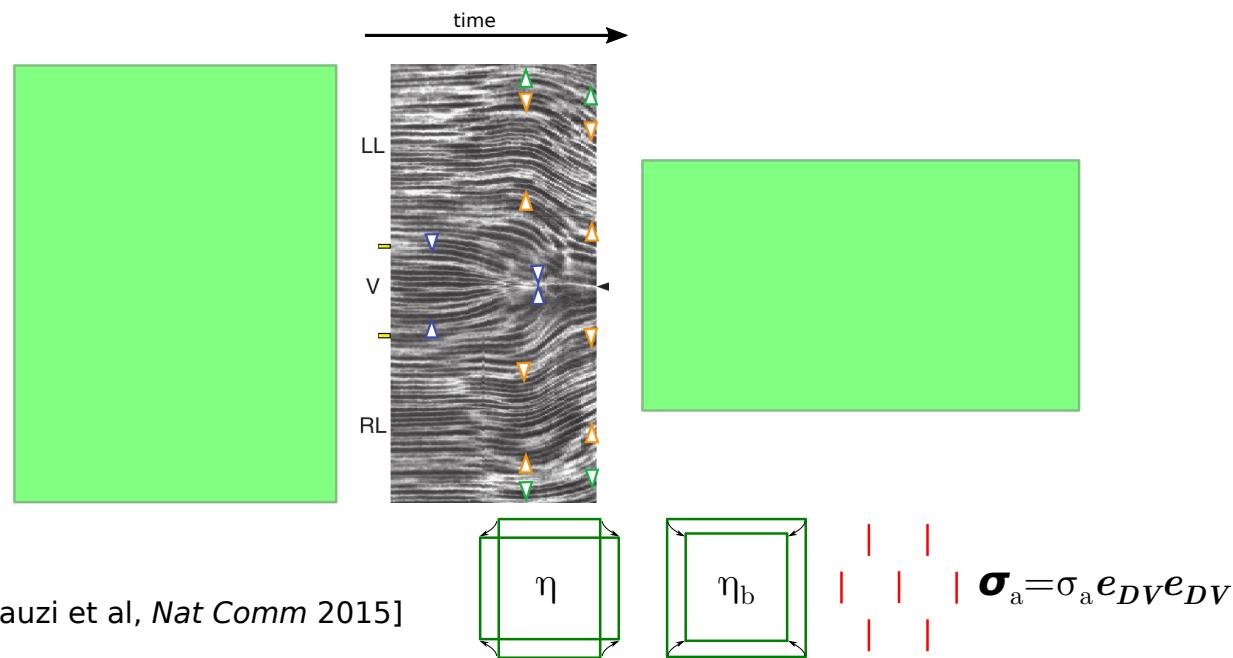
Planar-polarised myosin and convergence–extension



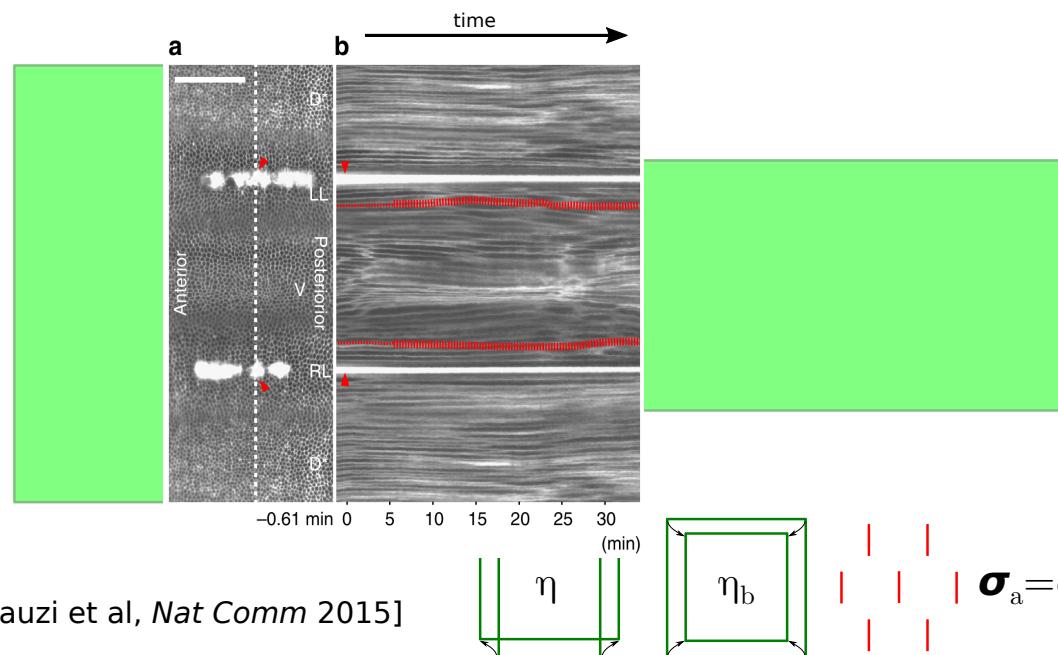
Tissue stress-strain relation



Tissue stress-strain relation...is not enough!

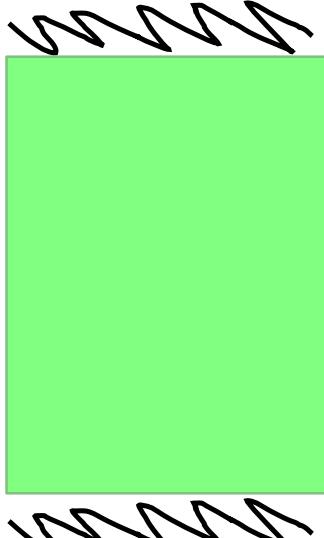


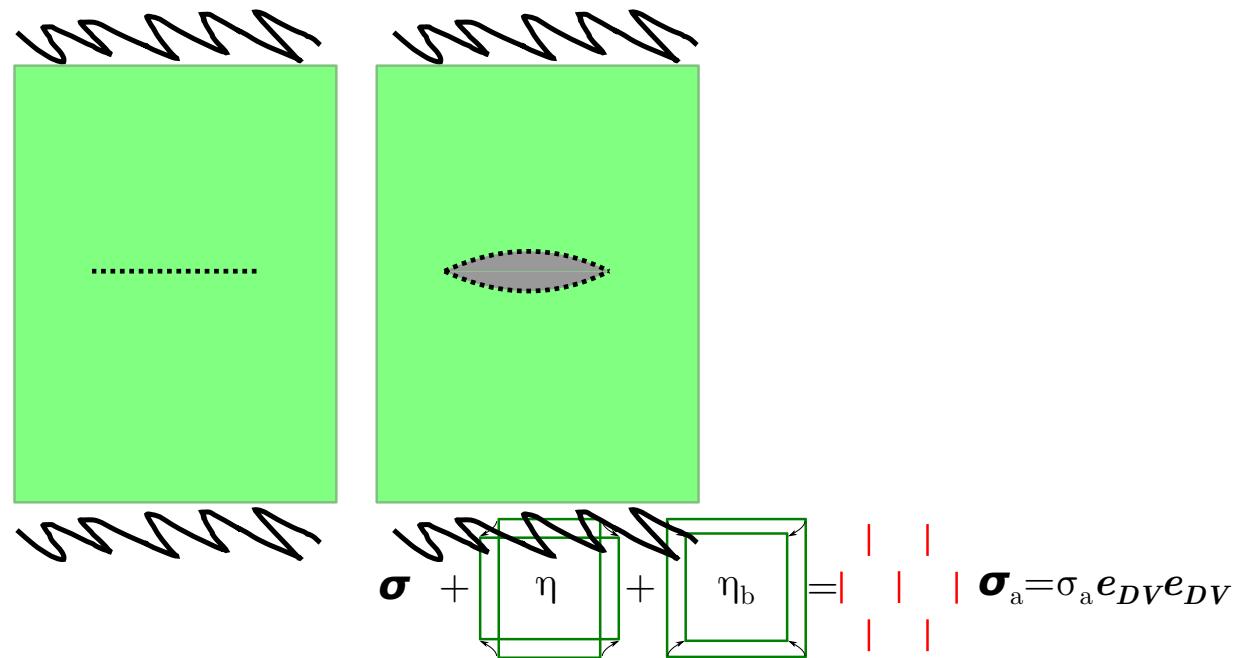
Tissue stress-strain relation...is not enough!

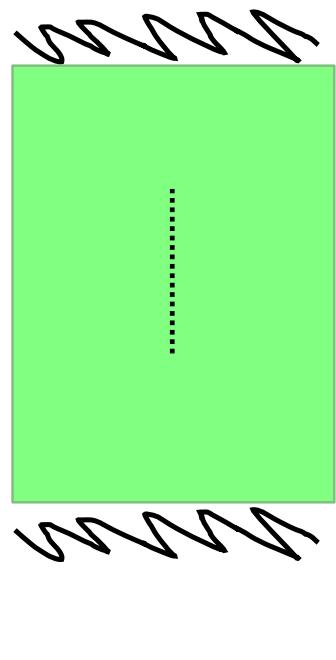


[Rauzi et al, *Nat Comm* 2015]

Mechanical balance

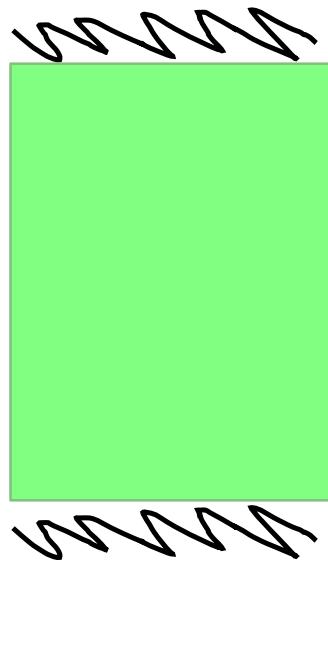

$$\sigma + \eta + \eta_b = \sigma_a = \sigma_a e_{DV} e_{DV}$$





$$\sigma + \eta + \eta_b = | \quad | \quad | \quad \sigma_a = \sigma_a e_{DV} e_{DV}$$

Mechanical balance

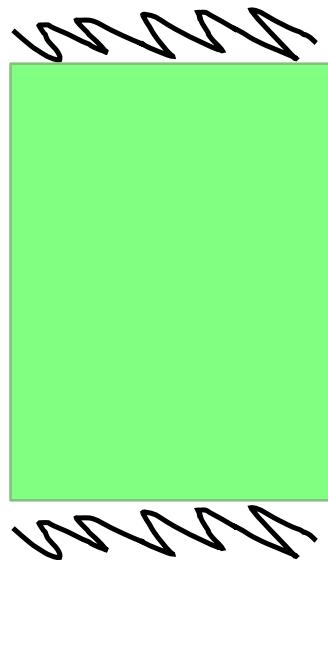


Mechanical balance

$$\nabla \cdot \sigma = 0$$

$$\sigma + \boxed{\eta} + \boxed{\eta_b} = \boxed{\sigma_a = \sigma_a e_{DV} e_{DV}}$$

Mechanical balance



Mechanical balance

$$\nabla \cdot \sigma = F_{\text{friction}}$$

$$\sigma + \boxed{\eta} + \boxed{\eta_b} = \boxed{\sigma_a = \sigma_a e_{DV} e_{DV}}$$

Model of epithelium

Mechanical balance

$$\nabla \cdot \sigma = F_{\text{friction}}$$

Constitutive relation (material property):

$$\sigma - 2\eta \dot{\epsilon}(v) - \eta_b (\nabla \cdot v) I = \sigma_a$$

stress
tensor

dissipation due
to pure shear

dissipation due
to area changes

myosin
pre-stress

$$\sigma + \boxed{\eta} + \boxed{\eta_b} = \boxed{\sigma_a = \sigma_a e_{DV} e_{DV}}$$

Model of epithelium

Mechanical balance

$$\nabla \cdot \boldsymbol{\sigma} = F_{\text{friction}}$$

Constitutive relation (material property):

$$\tau_\alpha \overset{\nabla}{\boldsymbol{\sigma}} + \boldsymbol{\sigma} - 2\eta \dot{\boldsymbol{\varepsilon}}(\boldsymbol{v}) - \eta_b (\nabla \cdot \boldsymbol{v}) \mathbf{I} = \boldsymbol{\sigma}_a$$

viscoelastic
behaviour

stress
tensor

dissipation due
to pure shear

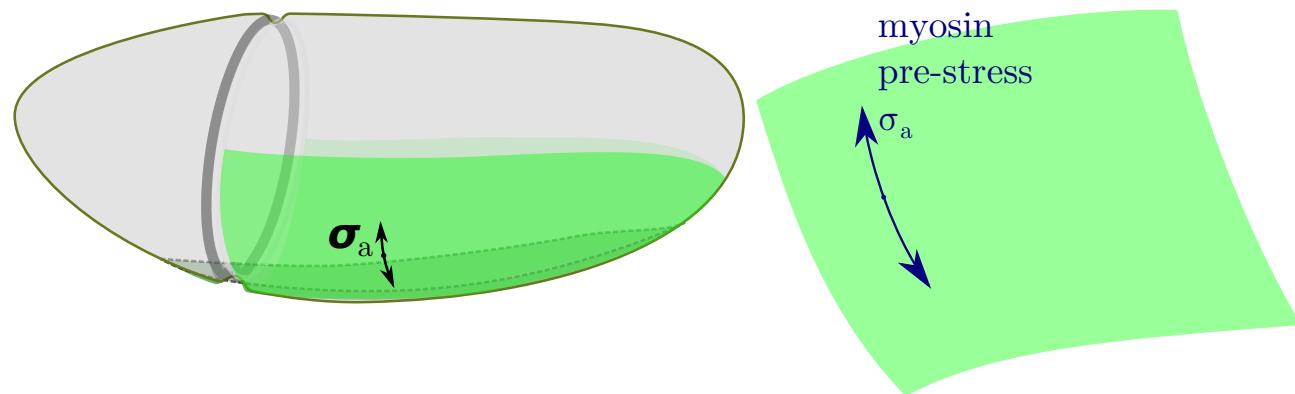
dissipation due
to area changes

myosin
pre-stress

$$\boldsymbol{\sigma} + \boxed{\eta} + \boxed{\eta_b} = \boxed{\boldsymbol{\sigma}_a = \sigma_a e_{DV} e_{DV}}$$

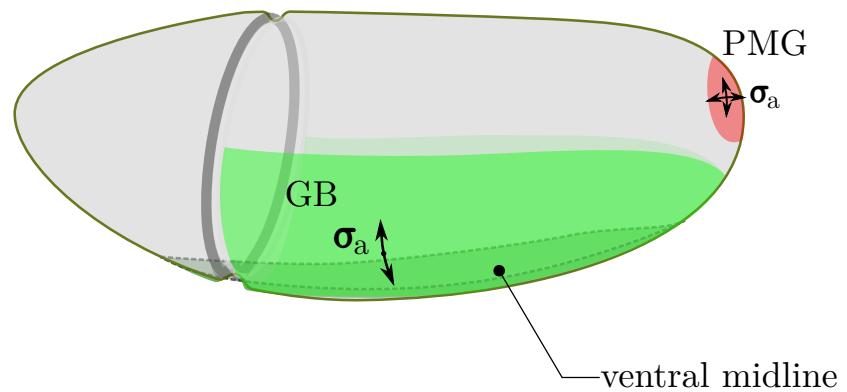
The diagram illustrates the decomposition of the stress tensor $\boldsymbol{\sigma}$ into its components. It shows a large stress tensor $\boldsymbol{\sigma}$ being broken down into two smaller tensors, η and η_b , represented by green-outlined boxes. These two tensors are then added together using a plus sign. The resulting sum is equated to a third tensor, $\boldsymbol{\sigma}_a$, which is defined as the product of a scalar σ_a and two unit tensors e_{DV} and e_{DV} . This visual representation emphasizes the additive nature of the viscoelastic and dissipative contributions to the total stress.

Germband extension modelling



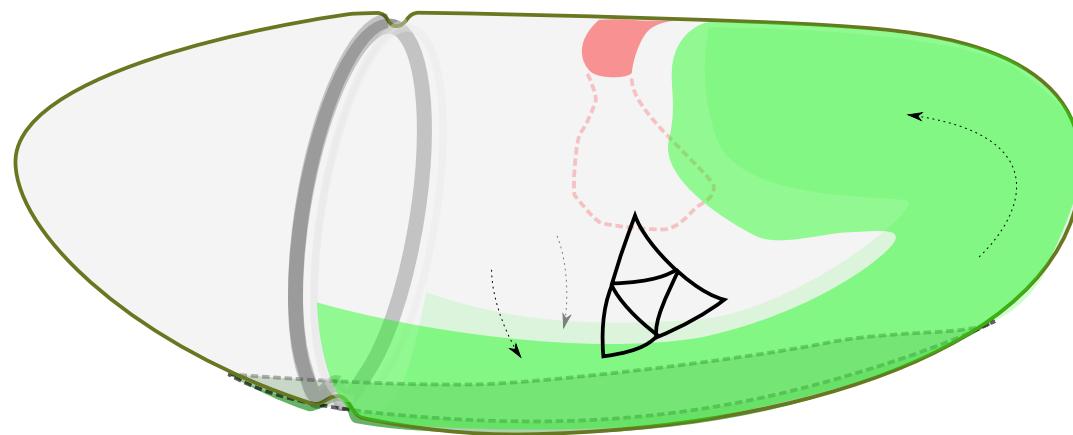
[Dicko et al. PLoS CR 2017]

Mimicking PMG invagination

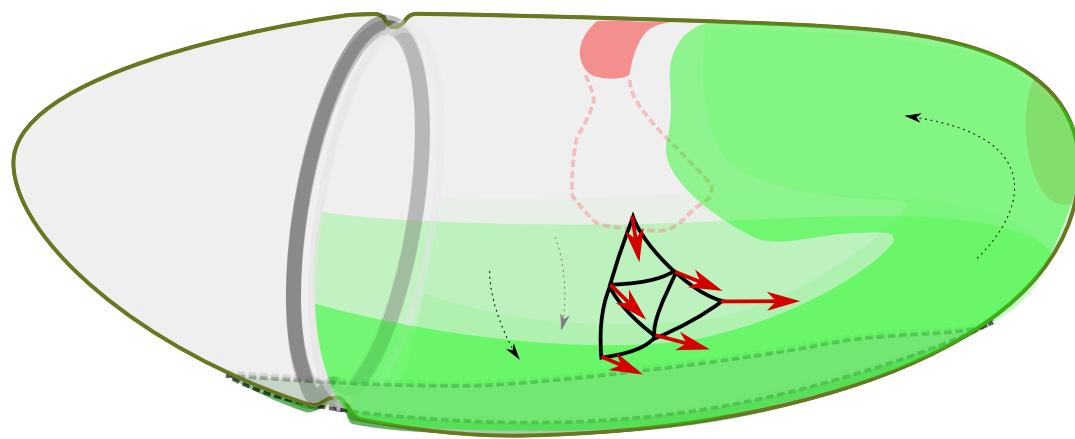


[Rutler et al. 2000; Collinet et al. 2015]

Numerical method

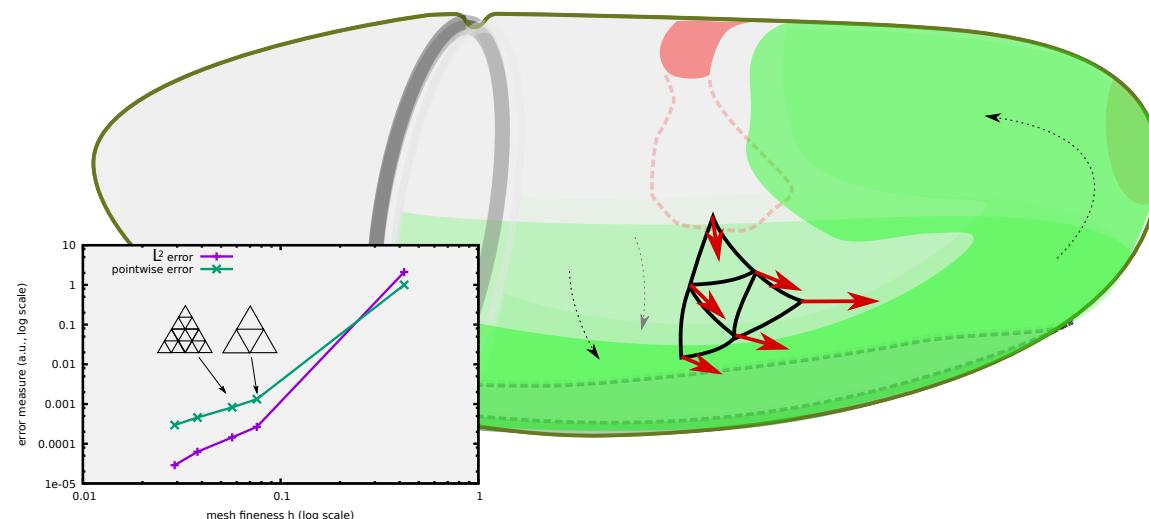


Numerical method



Solve as a constrained minimisation problem, $\min_{\{\mathbf{v} \cdot \mathbf{n} = 0\}} E(\mathbf{v})$

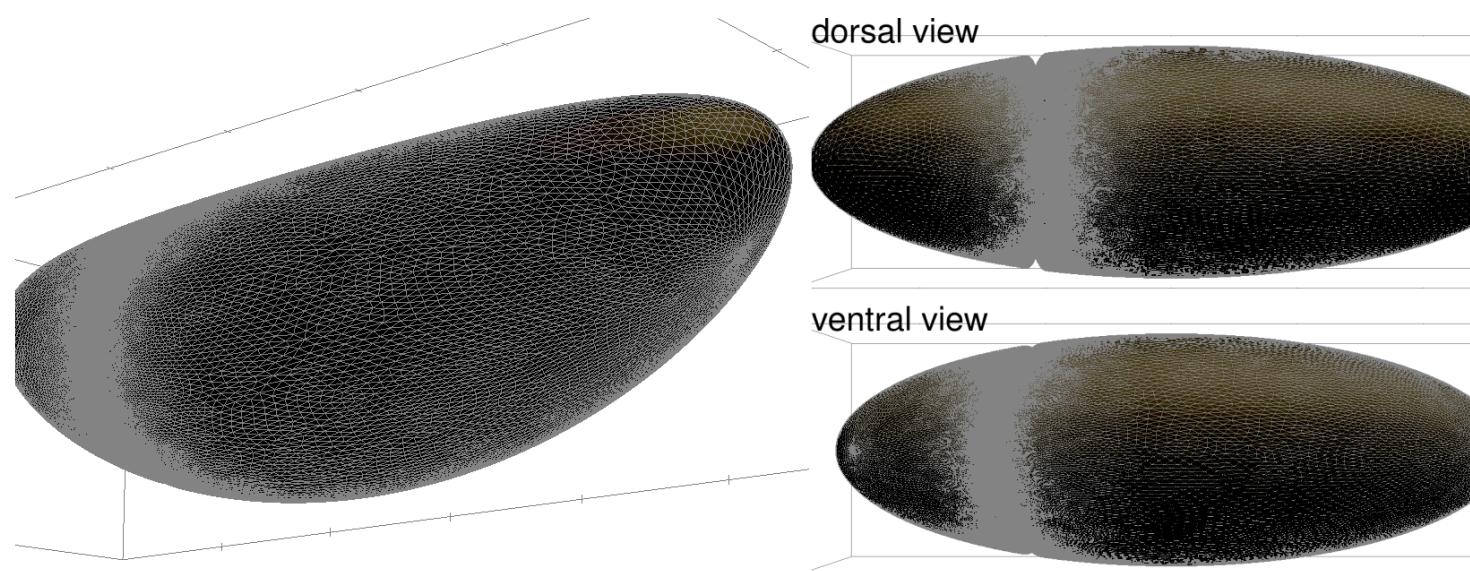
Numerical method : accuracy



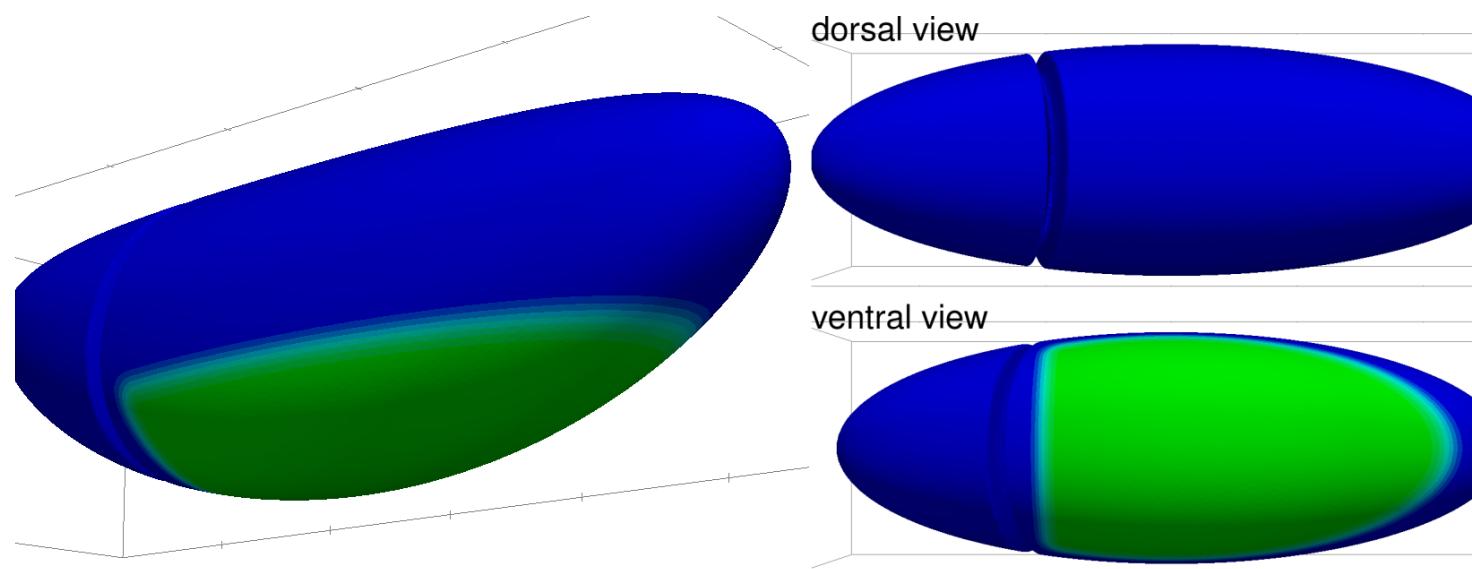
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CEFM - 1st year students - CM 101 [DRAFT] - 11 Dec 2017

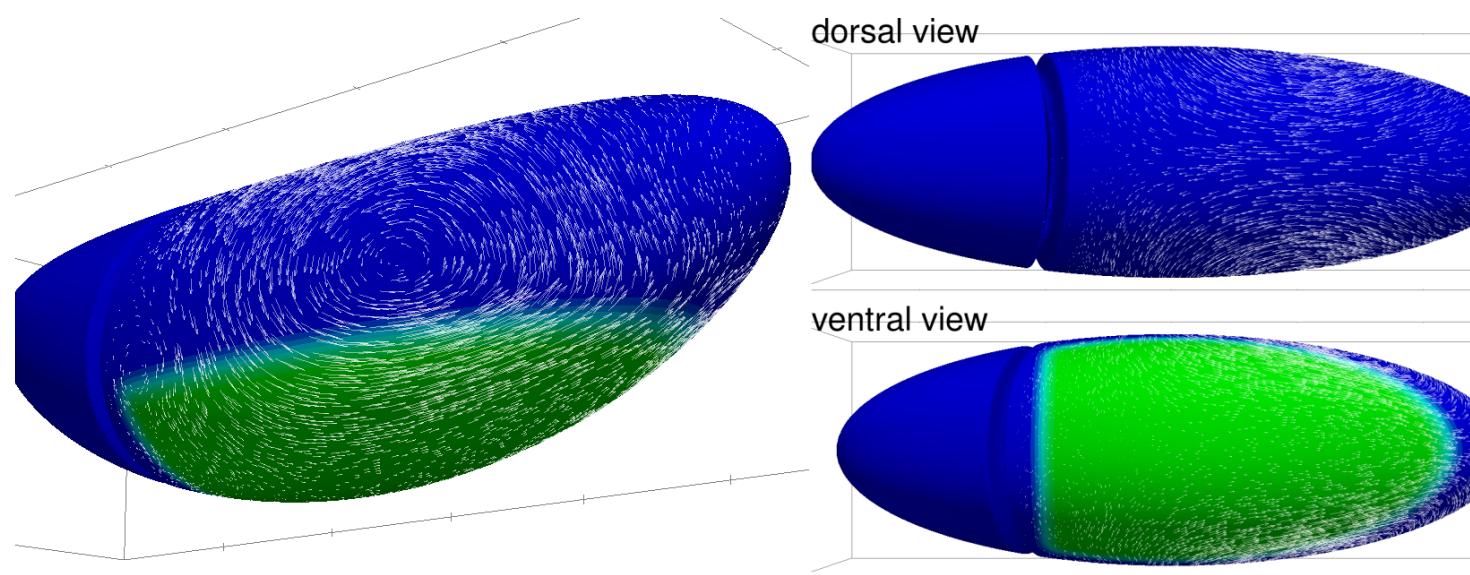
Simulation: Mesh



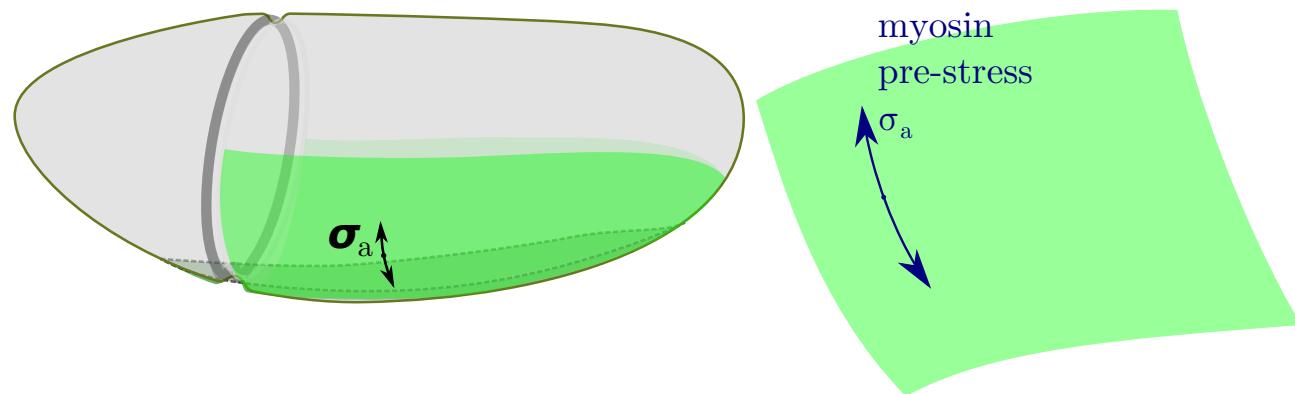
Simulation: Planar-polarised myosin



**Simulation:
Planar-polarised myosin can explain germband extension**

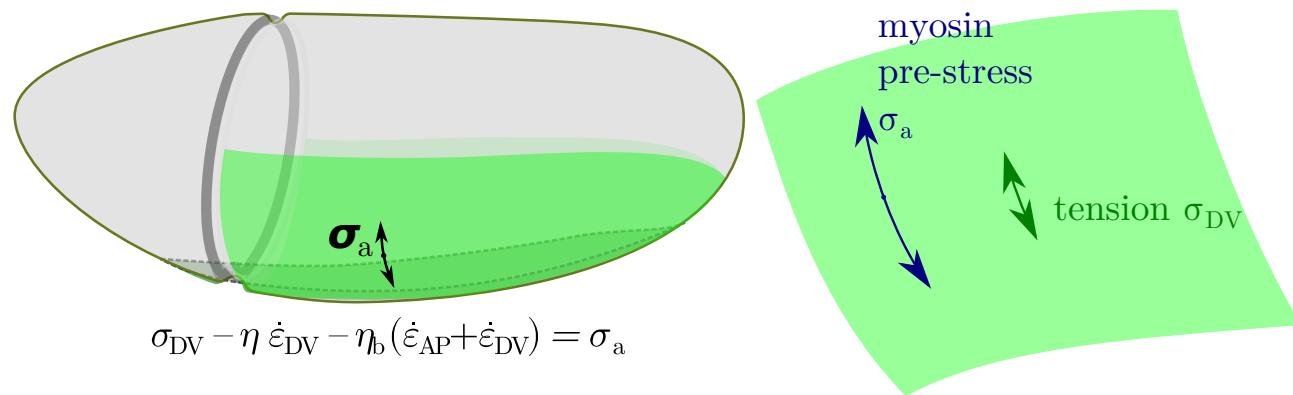


Germband extension modelling



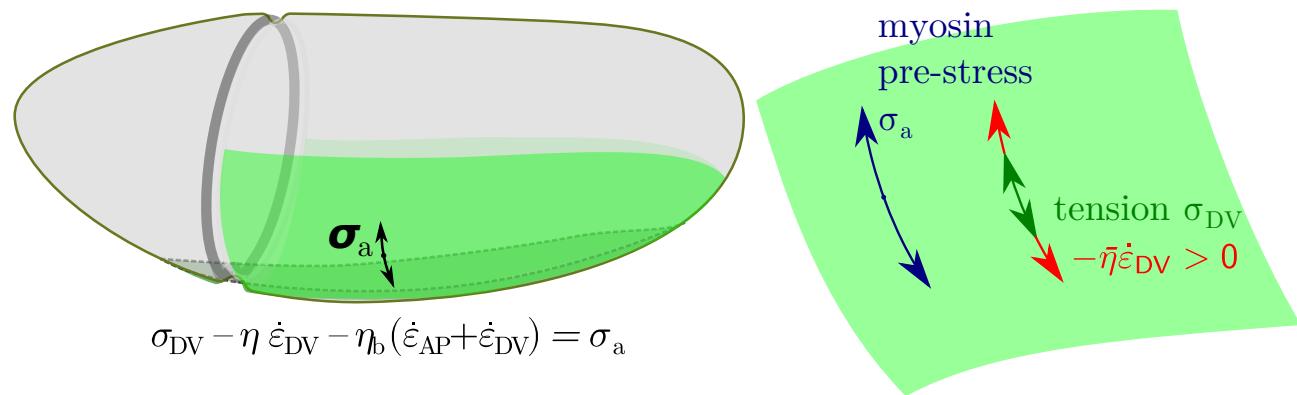
[Dicko et al. PLoS CR 2017]

Germband extension modelling



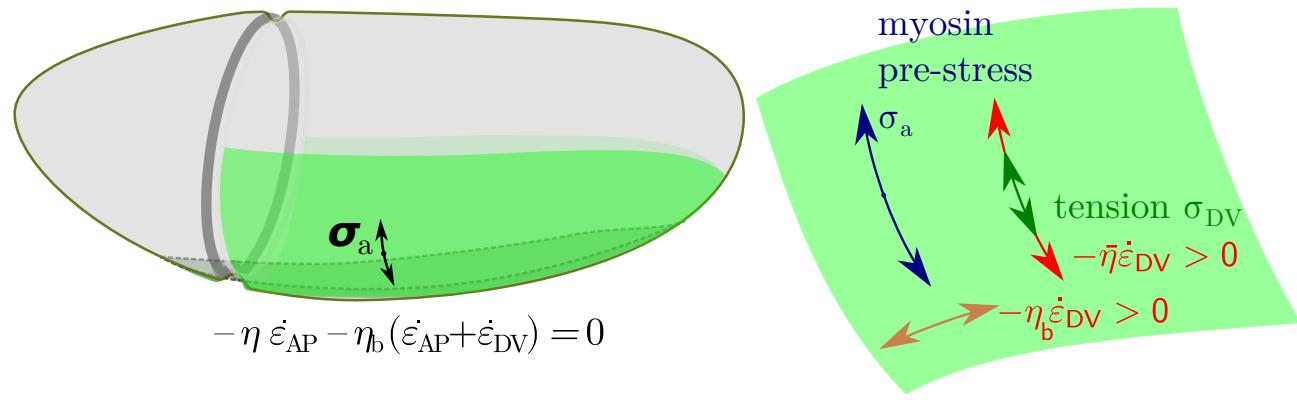
[Dicks et al. PLoS CR 2017]

Germband extension modelling



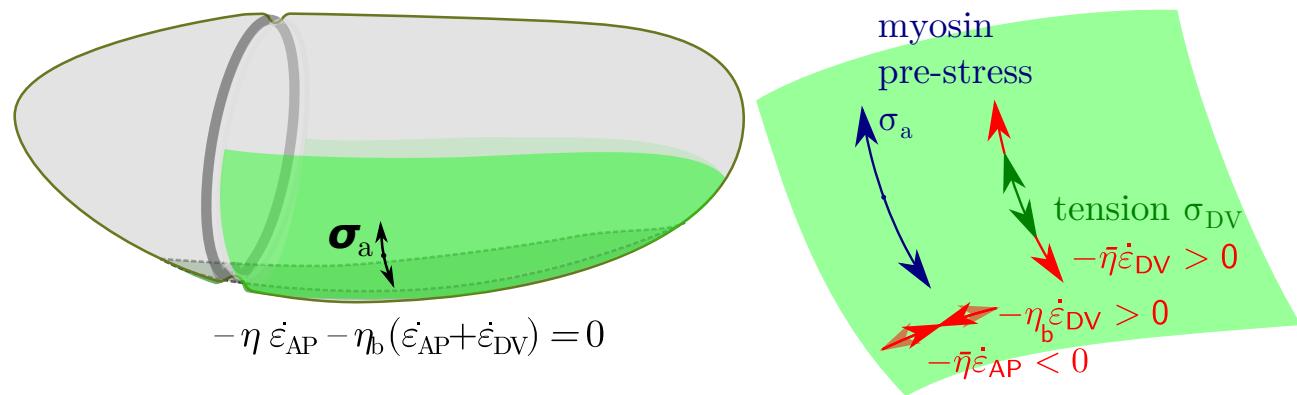
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Germband extension modelling



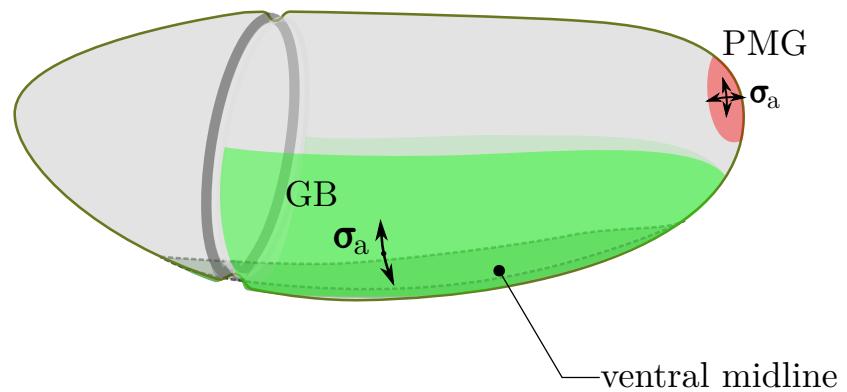
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Germband extension modelling



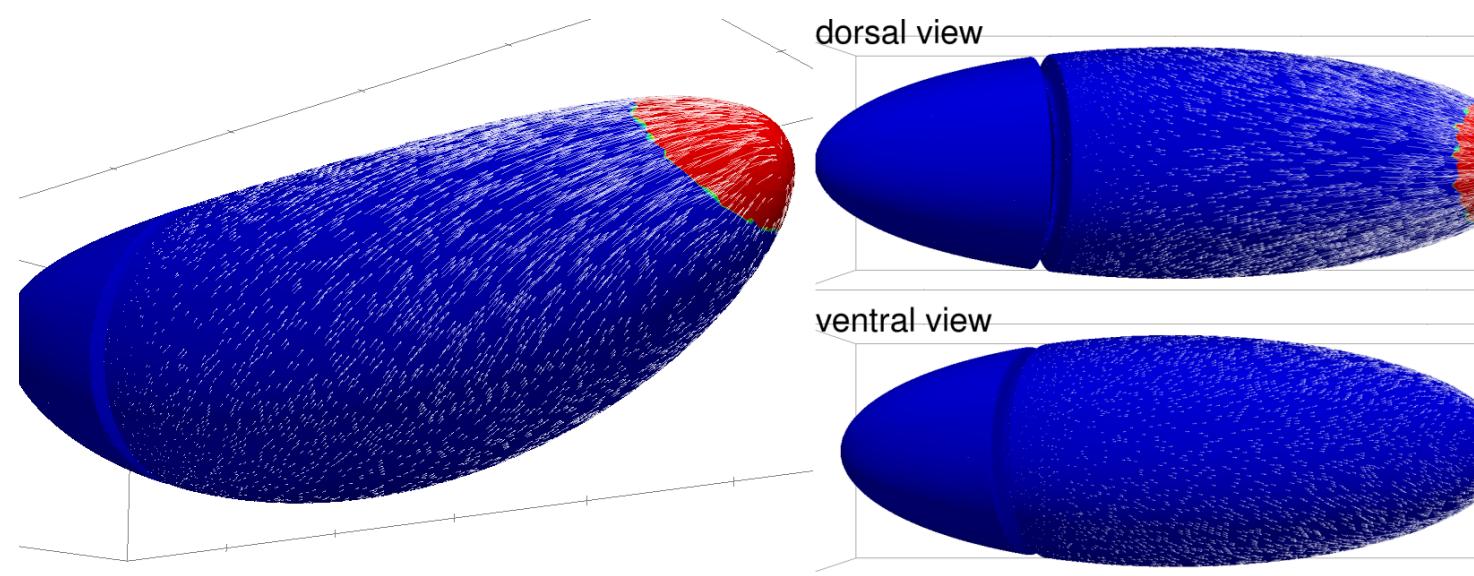
[Dicko et al. PLoS CR 2017]

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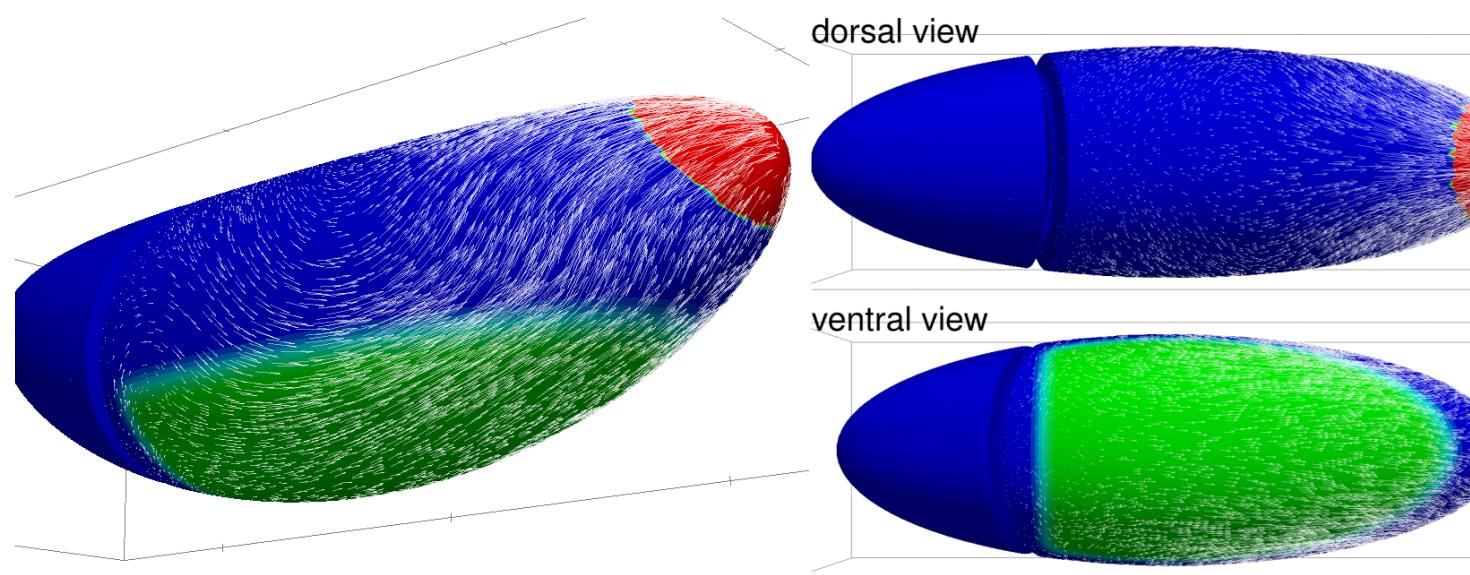


[Rutler et al. 2000; Collinet et al. 2015]

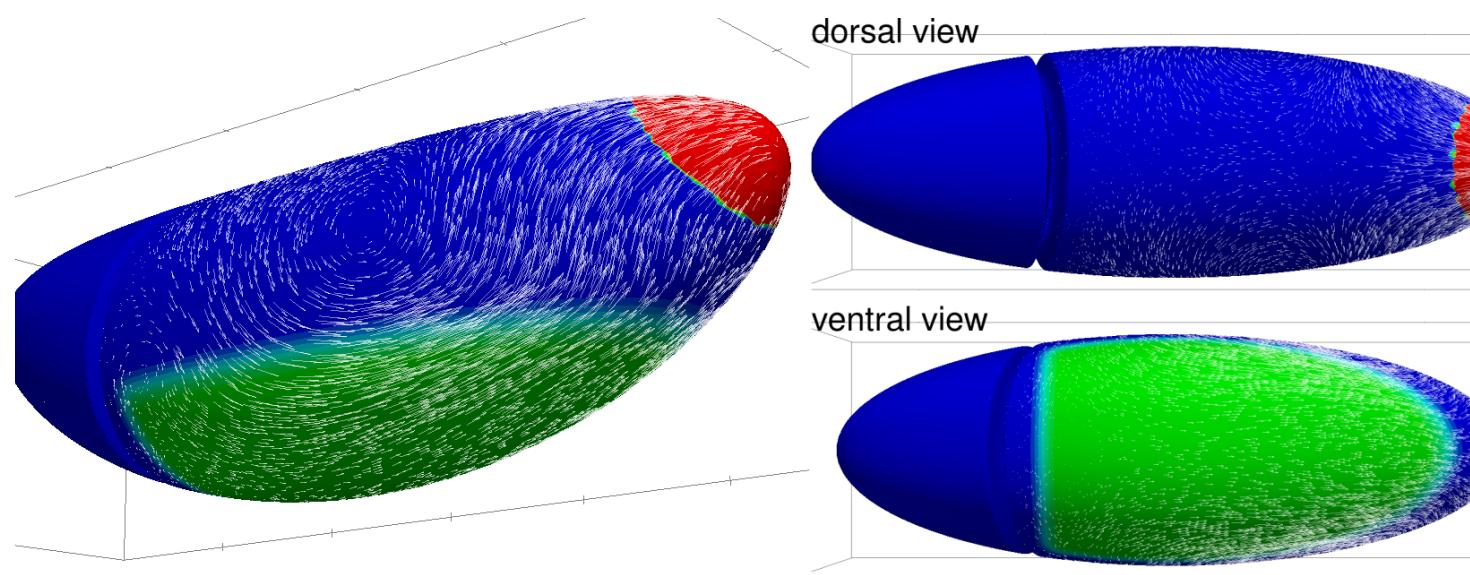
Germband extends under the action of PMG pull



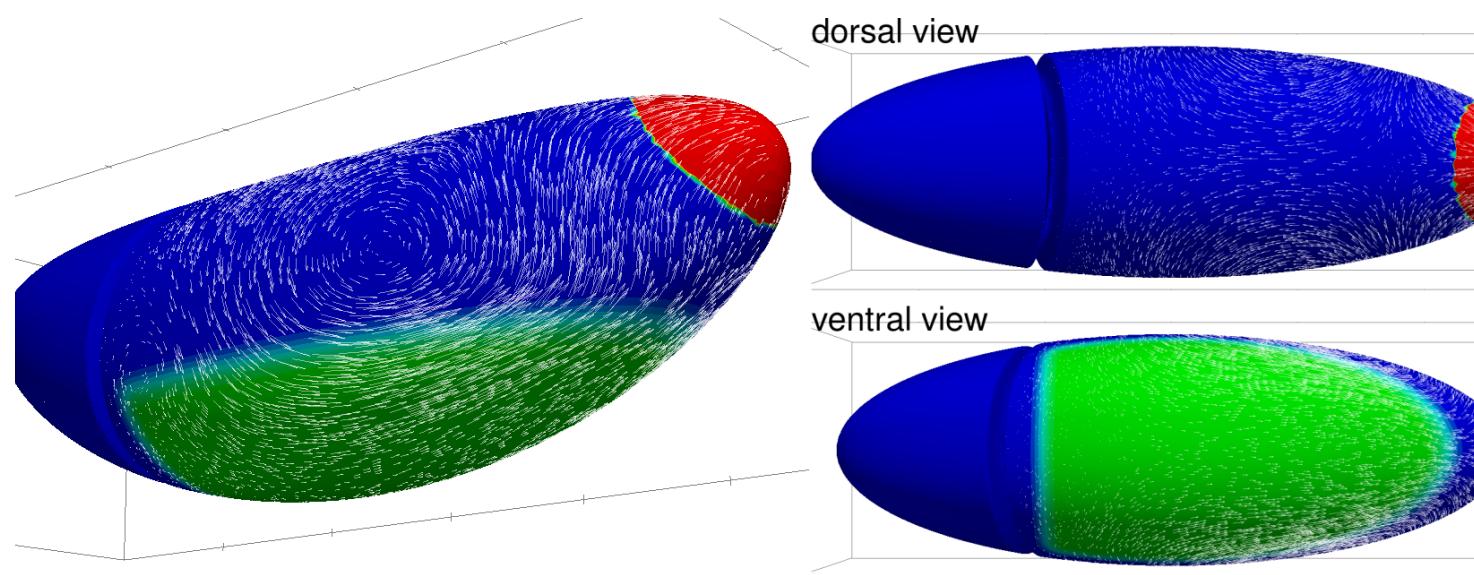
**Germband extends under the action of PMG pull
and/or planar-polarised myosin**



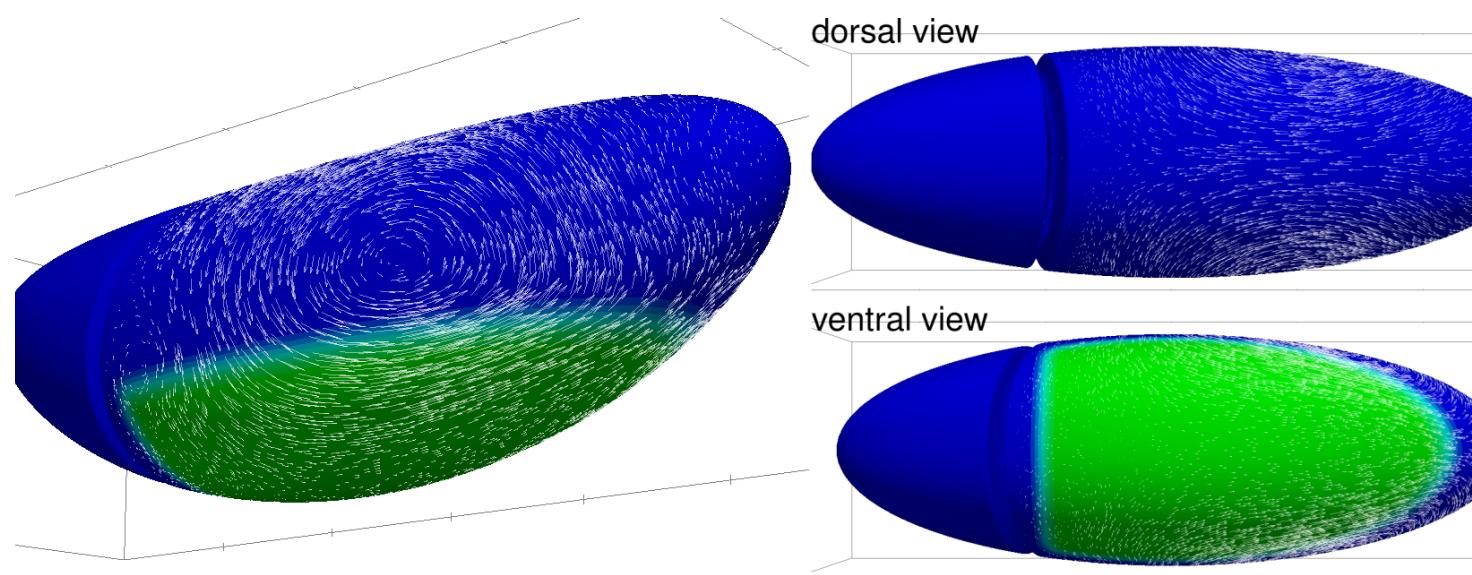
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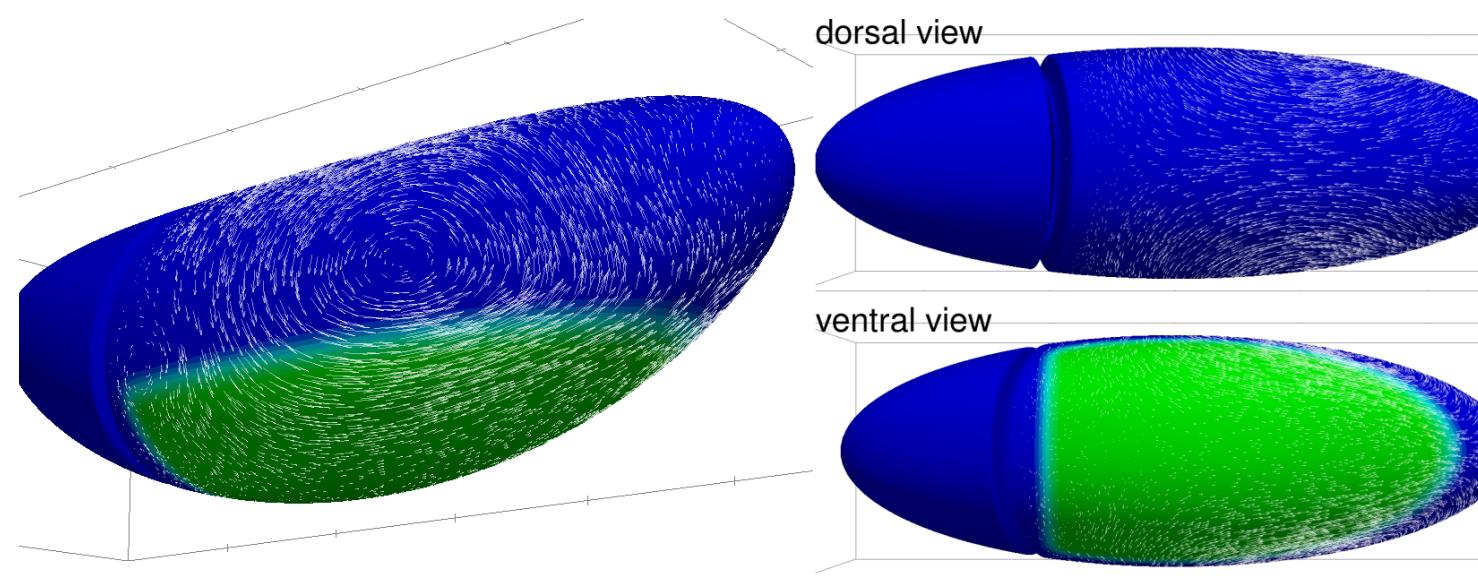
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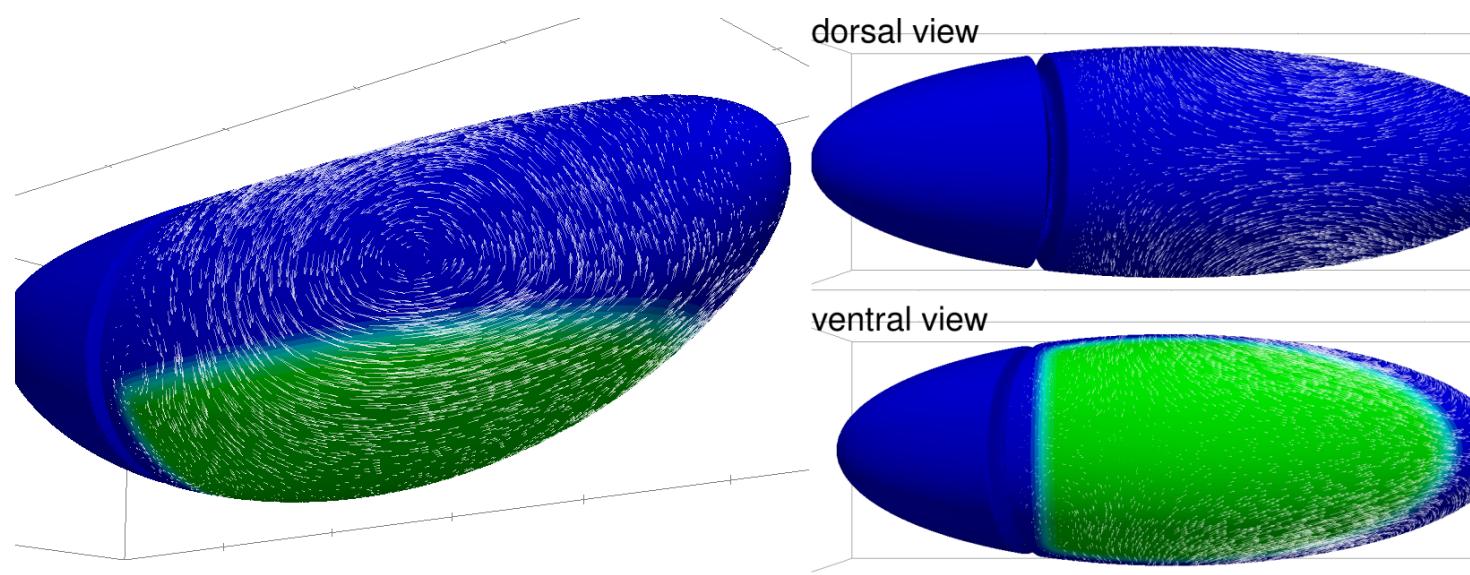
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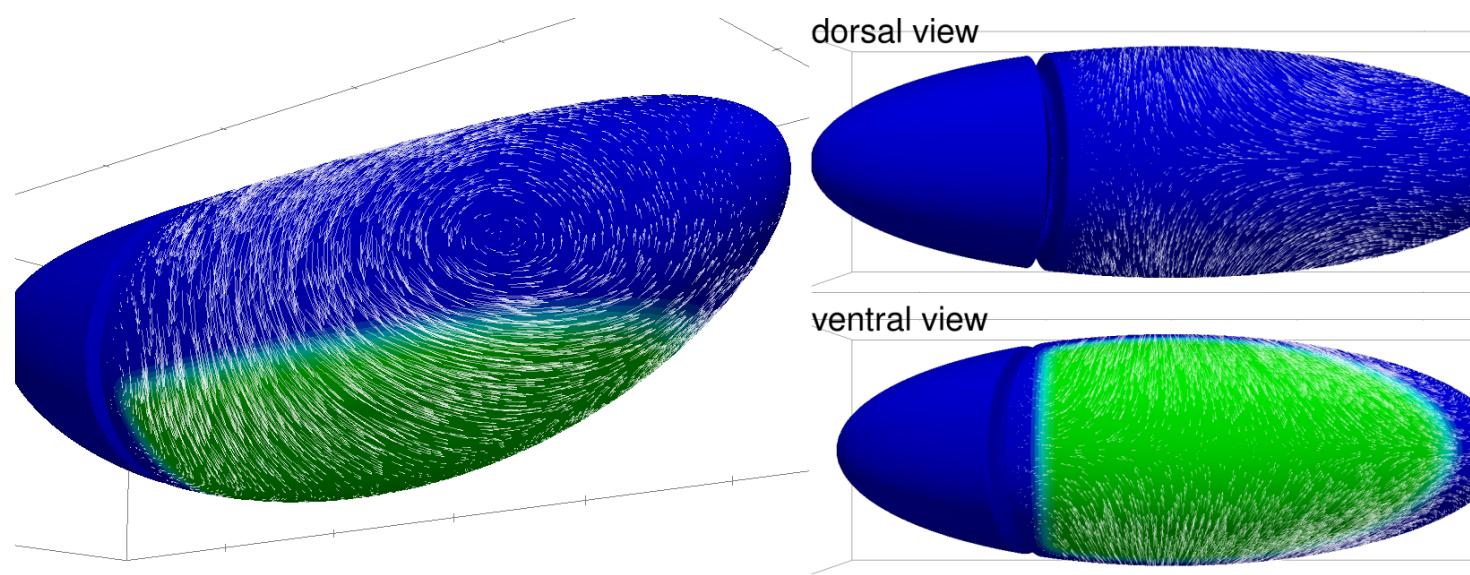
Resistance to changes of apical area and morphogenetic flow



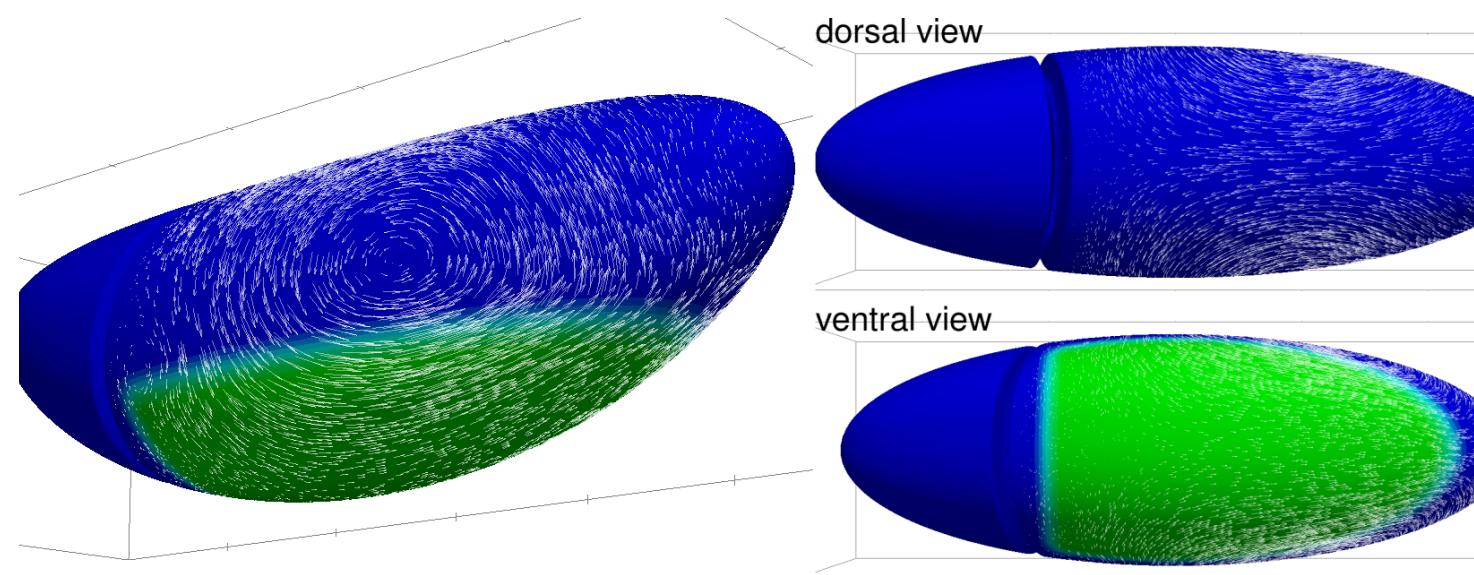
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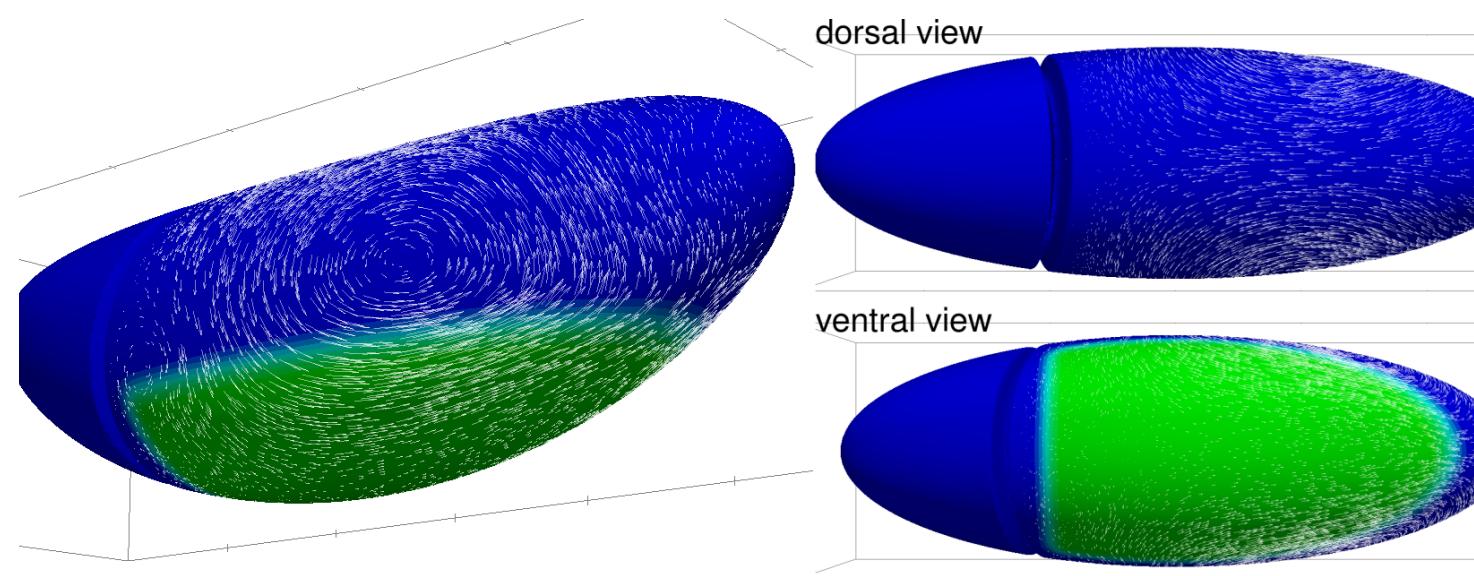
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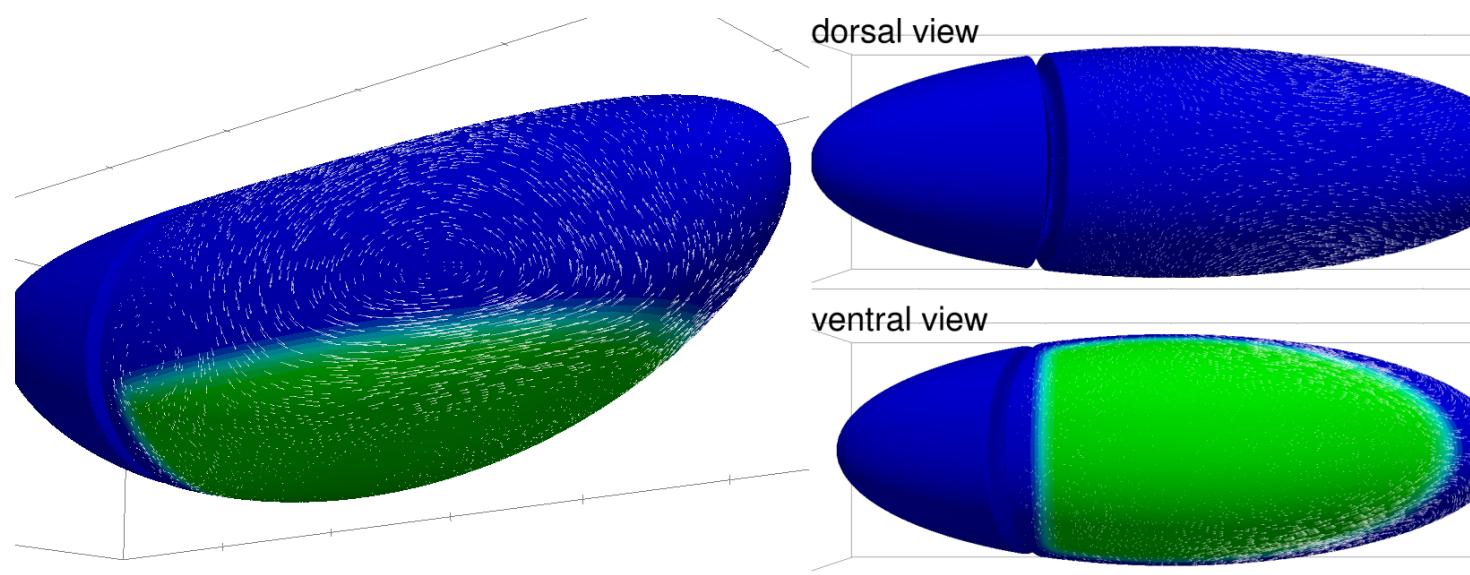
Hydrodynamic length and morphogenetic flow



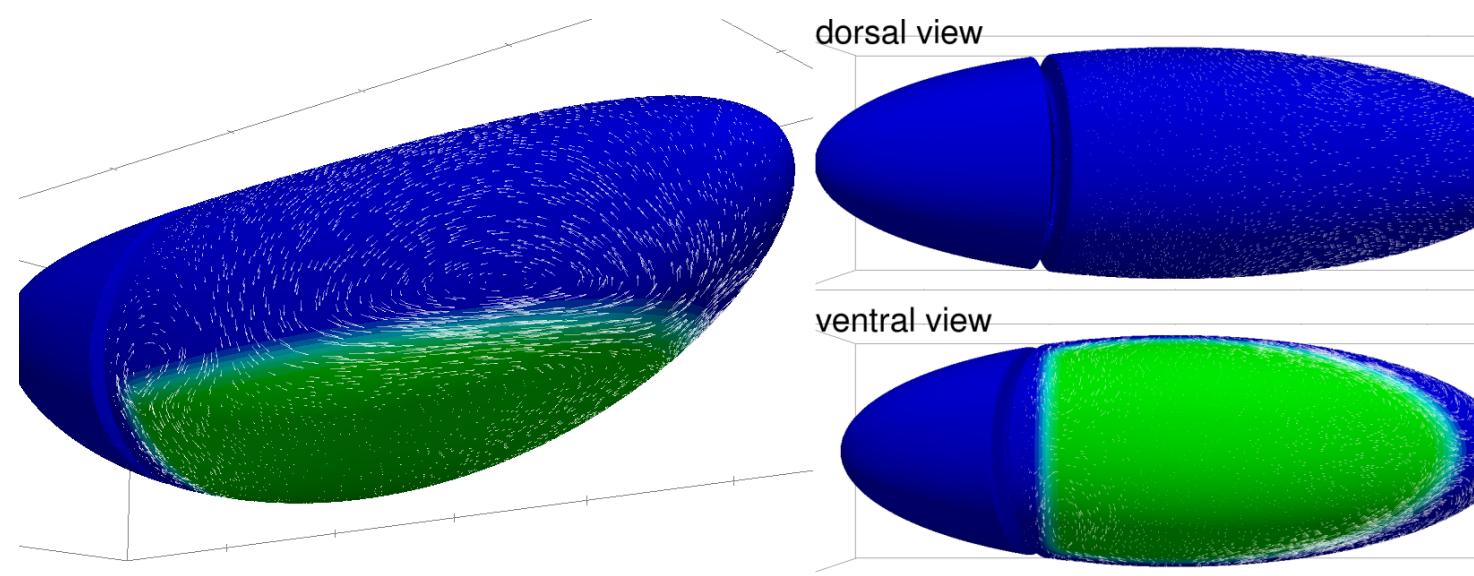
Hydrodynamic length and morphogenetic flow



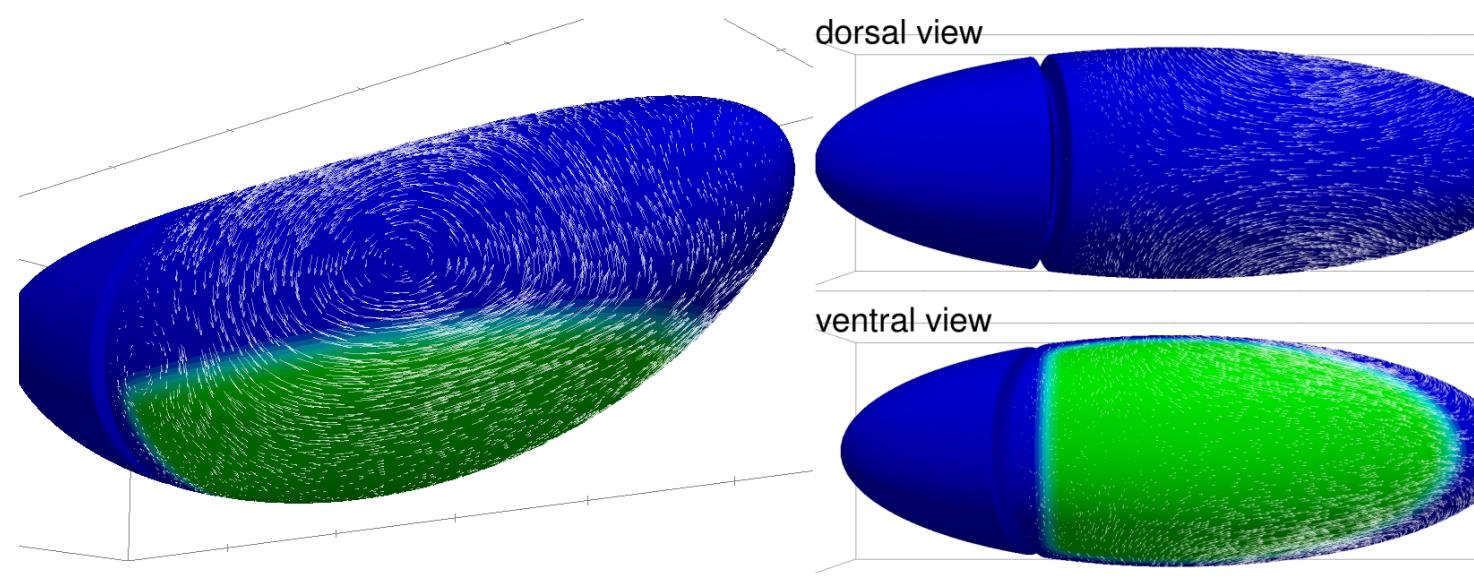
Hydrodynamic length and morphogenetic flow



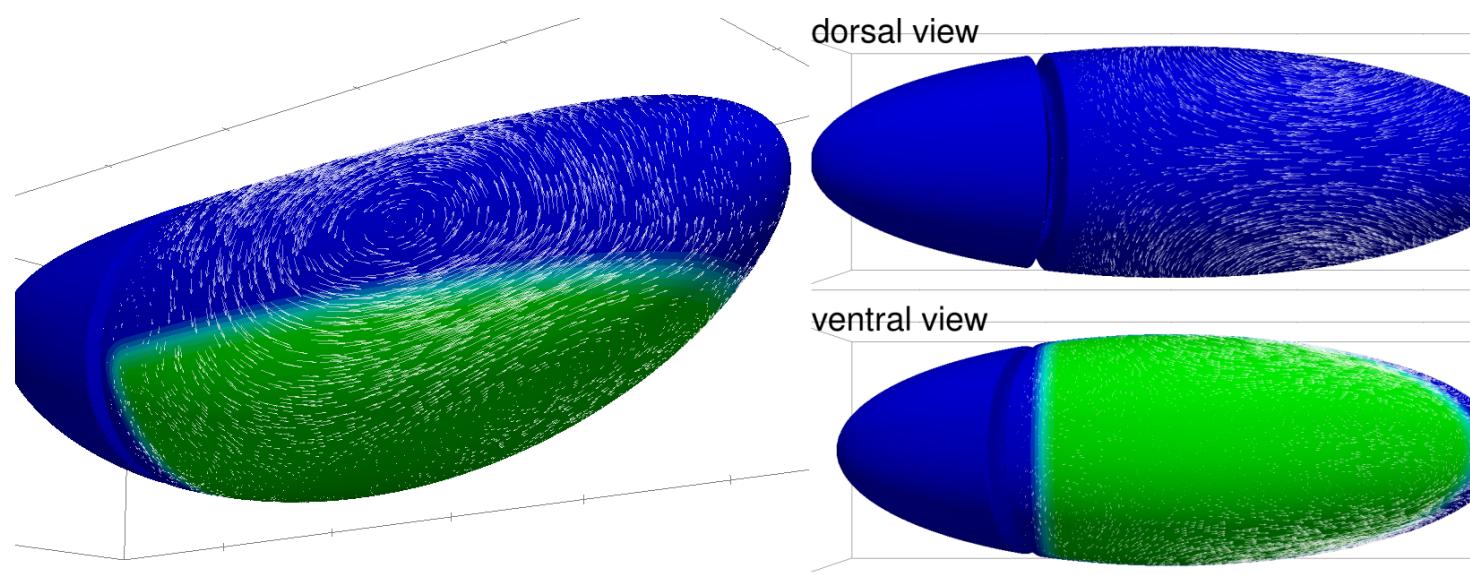
Hydrodynamic length and morphogenetic flow



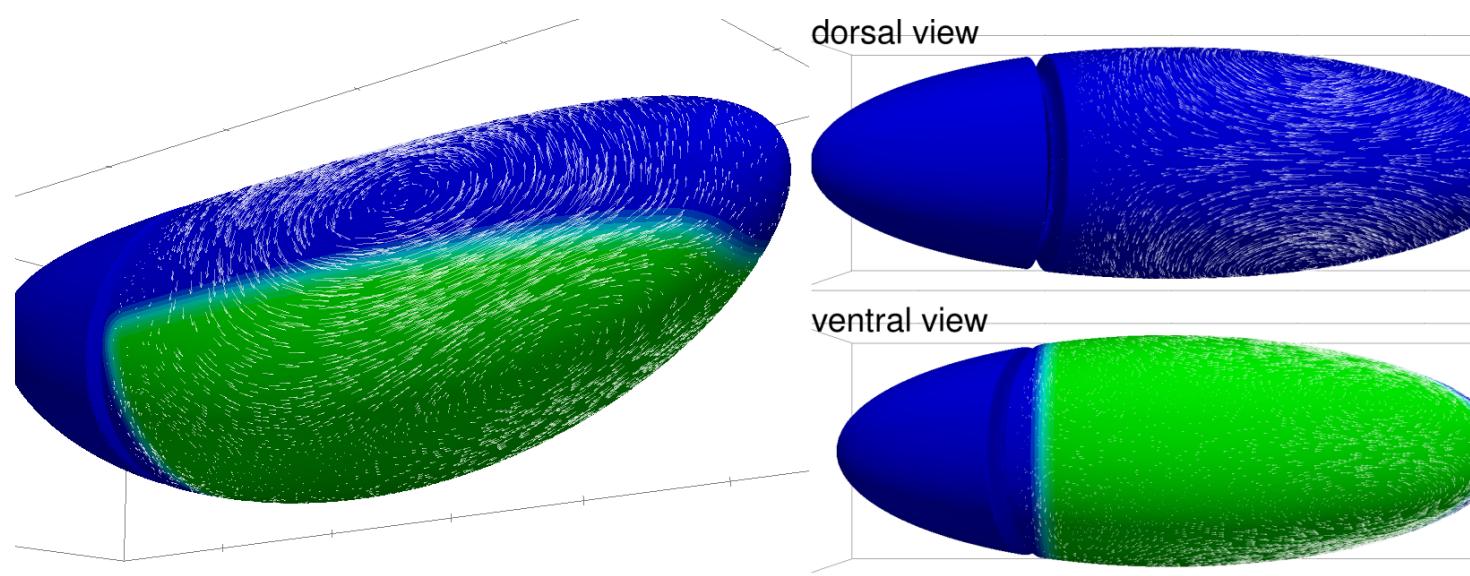
Geometry of myosin patterning and morphogenetic flow



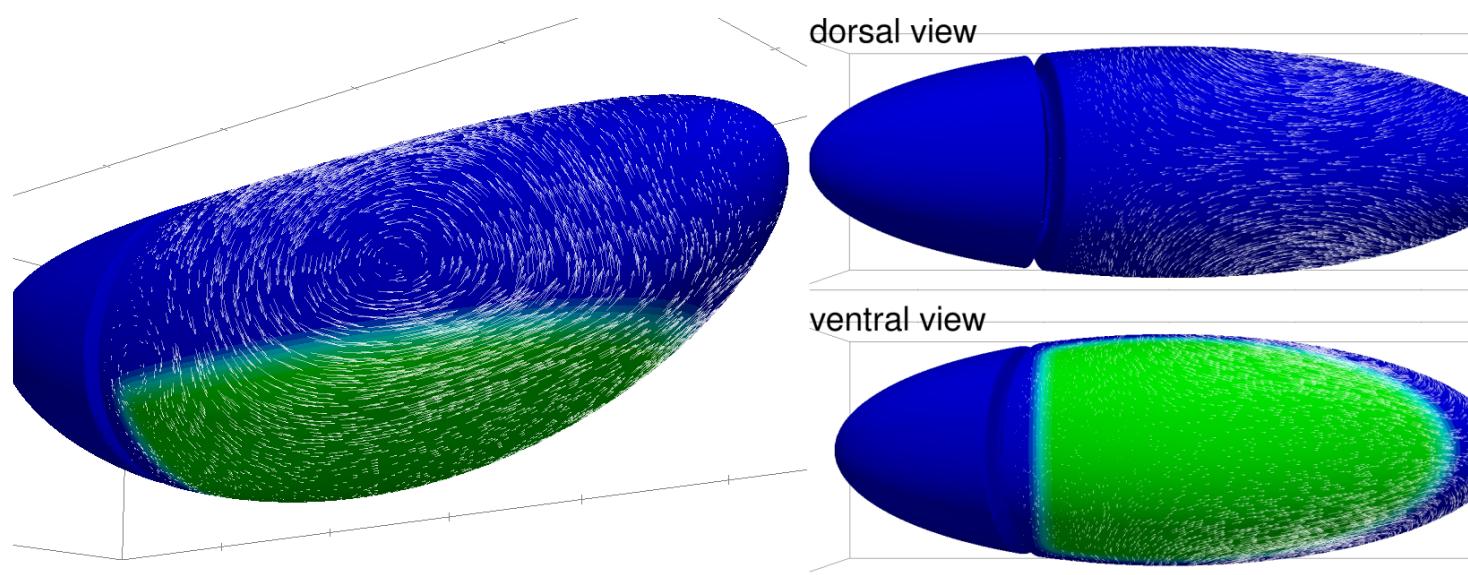
Geometry of myosin patterning and morphogenetic flow



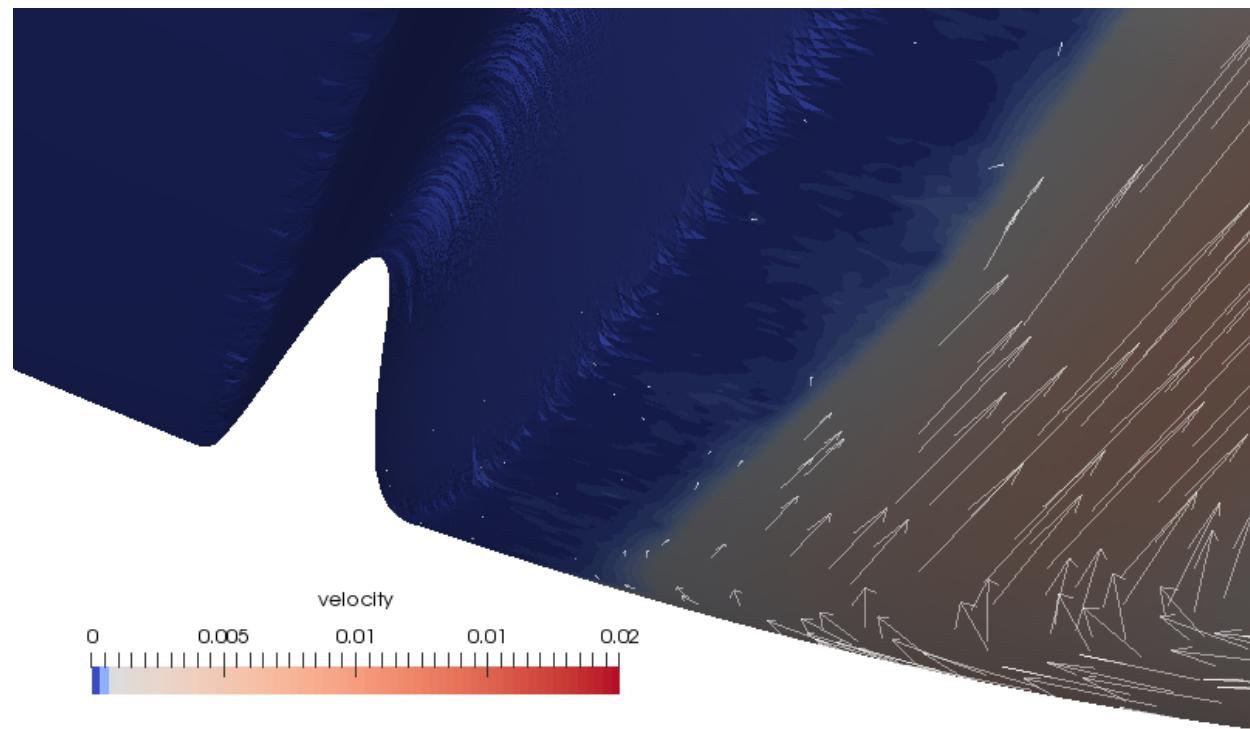
Geometry of myosin patterning and morphogenetic flow



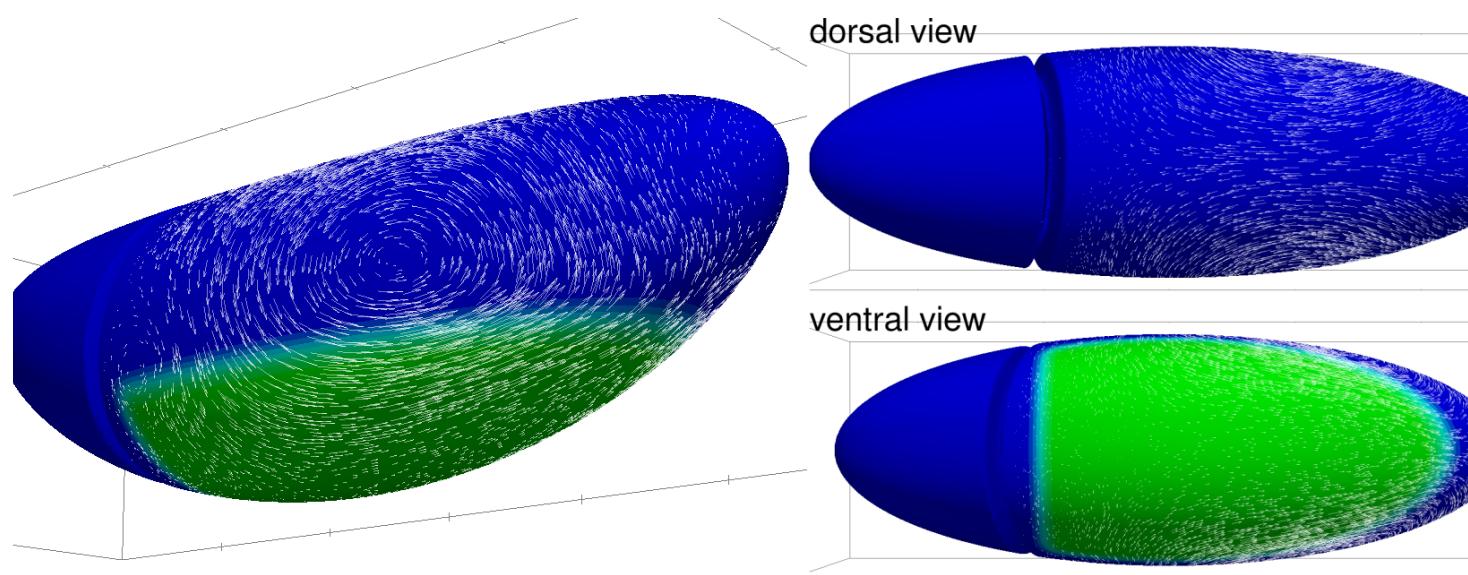
Cephalic furrow guides morphogenetic flow



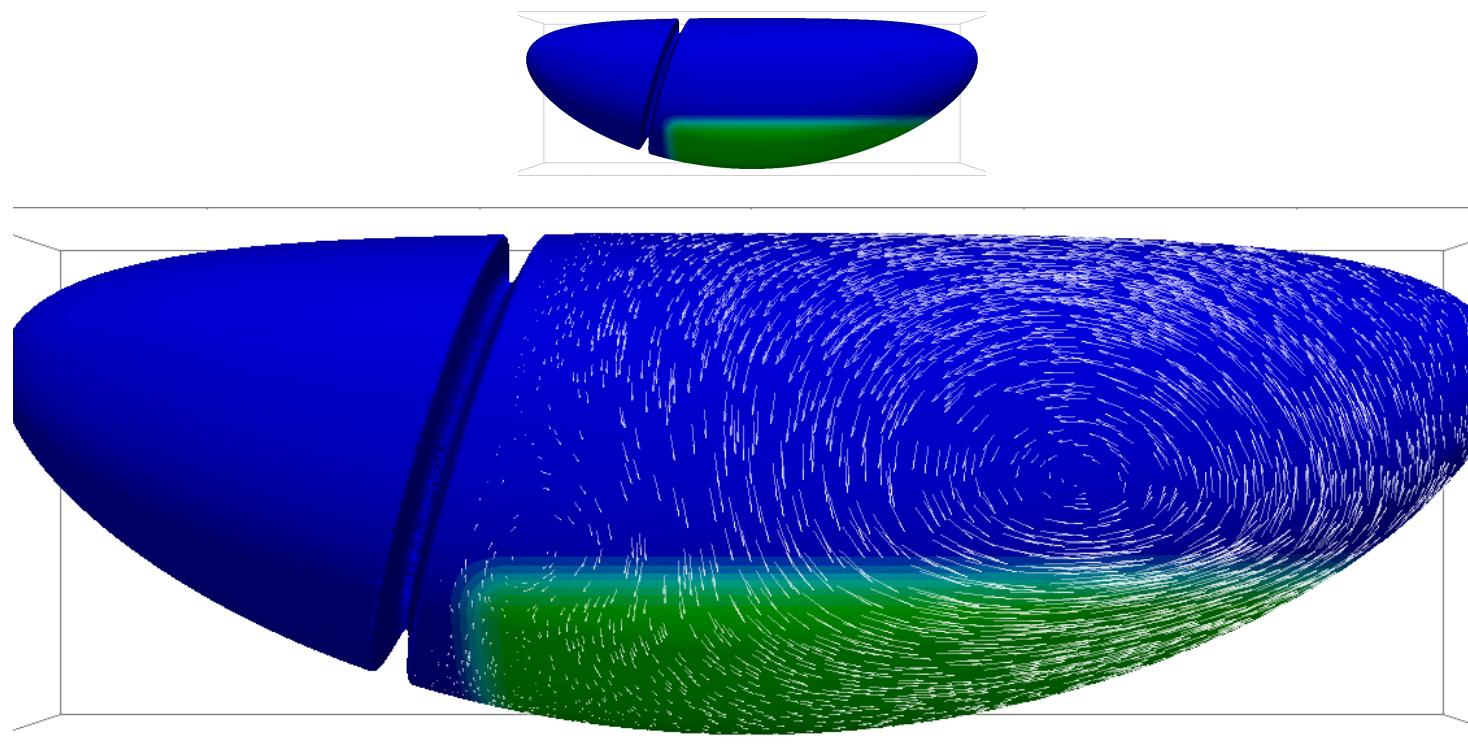
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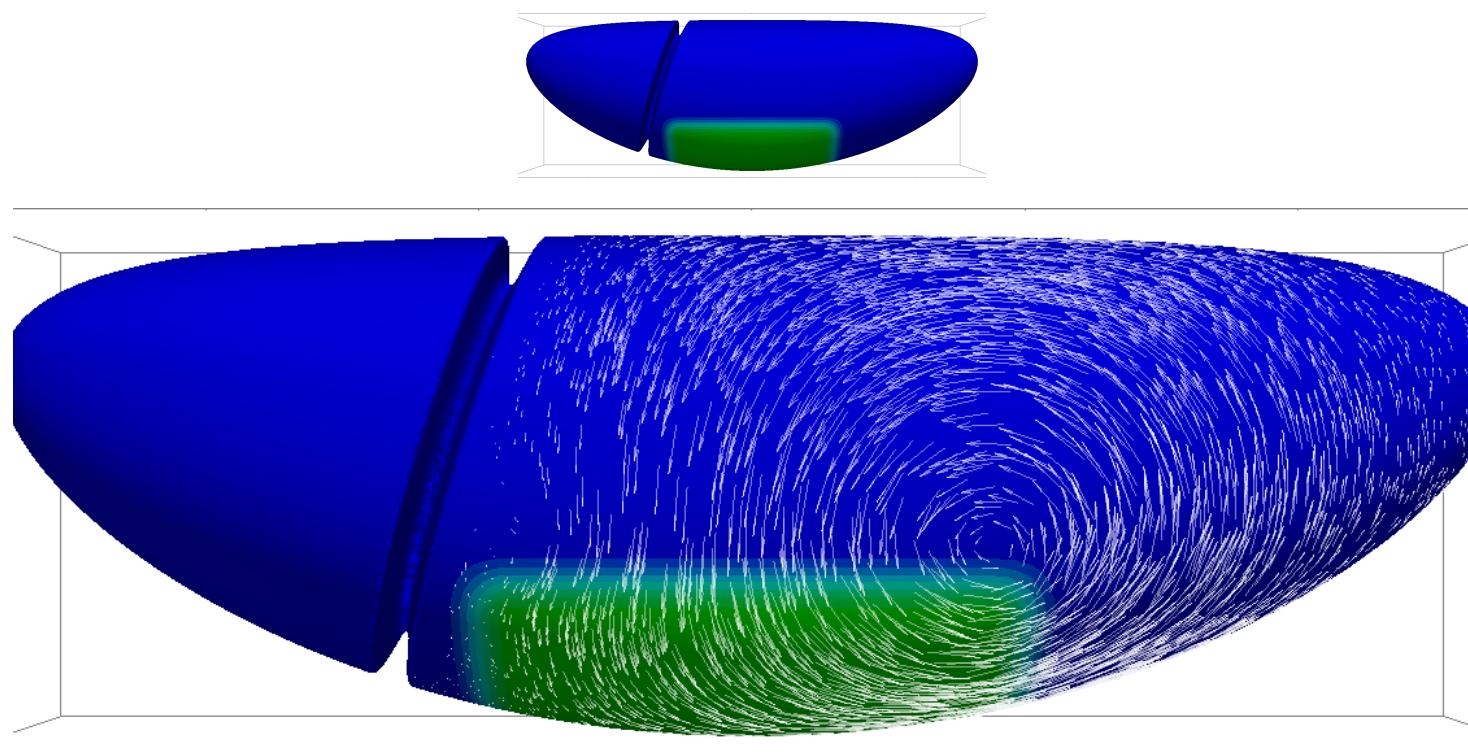
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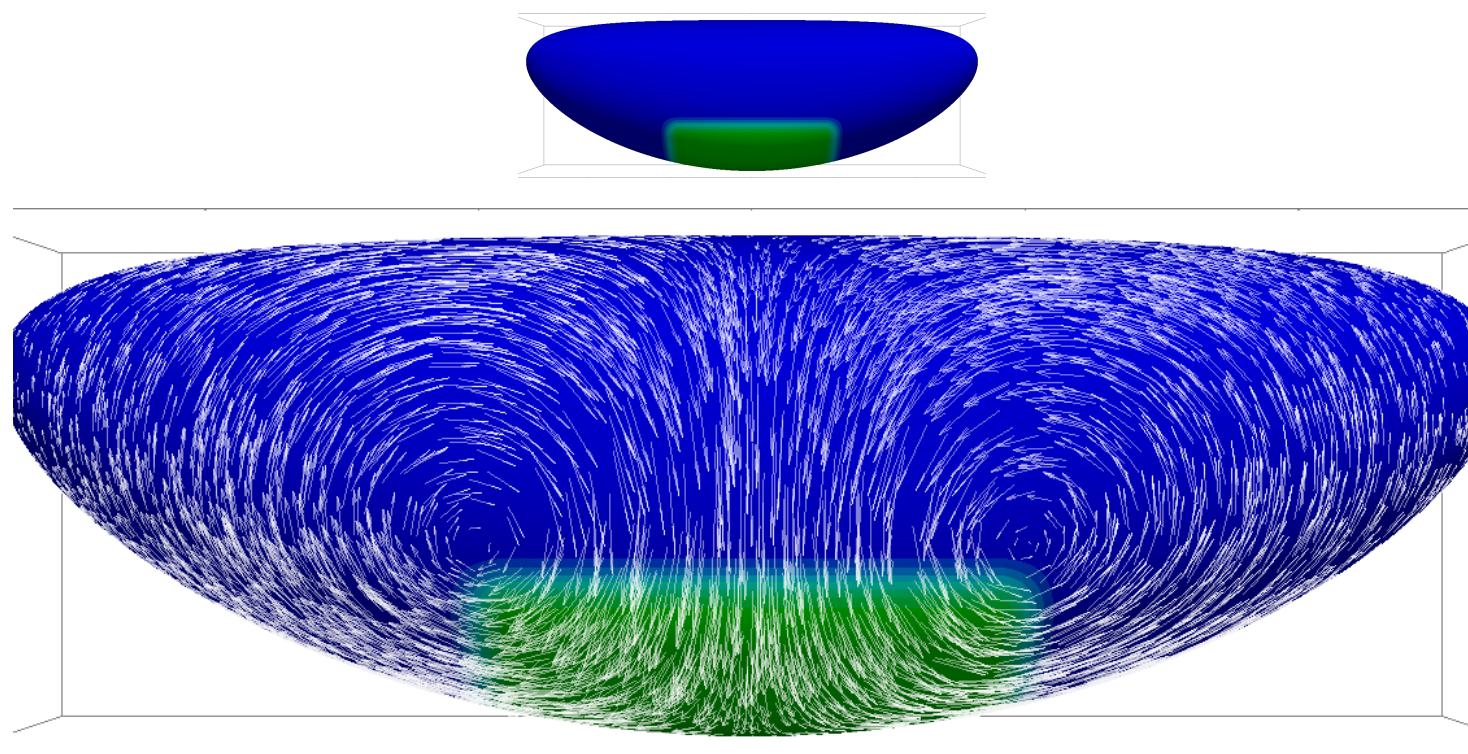
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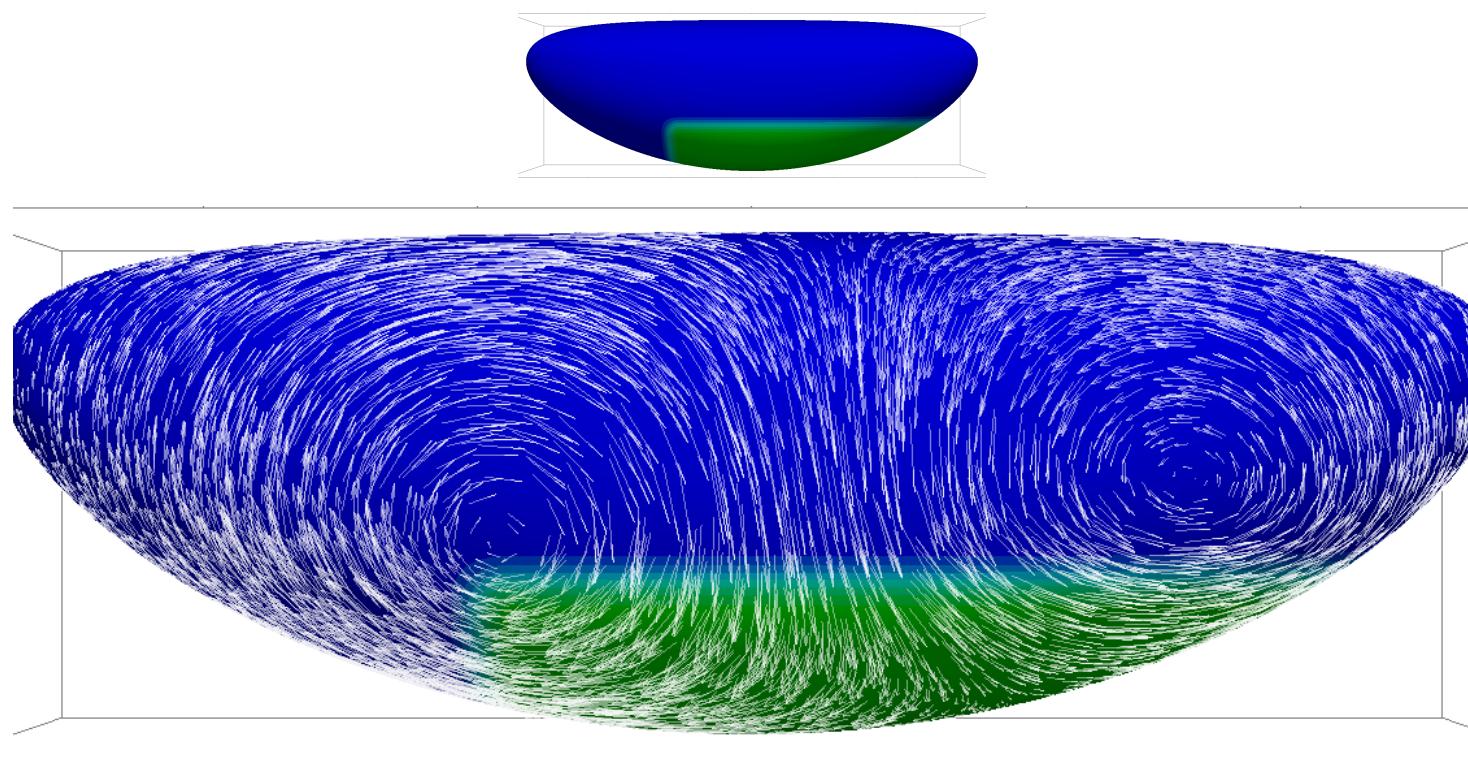
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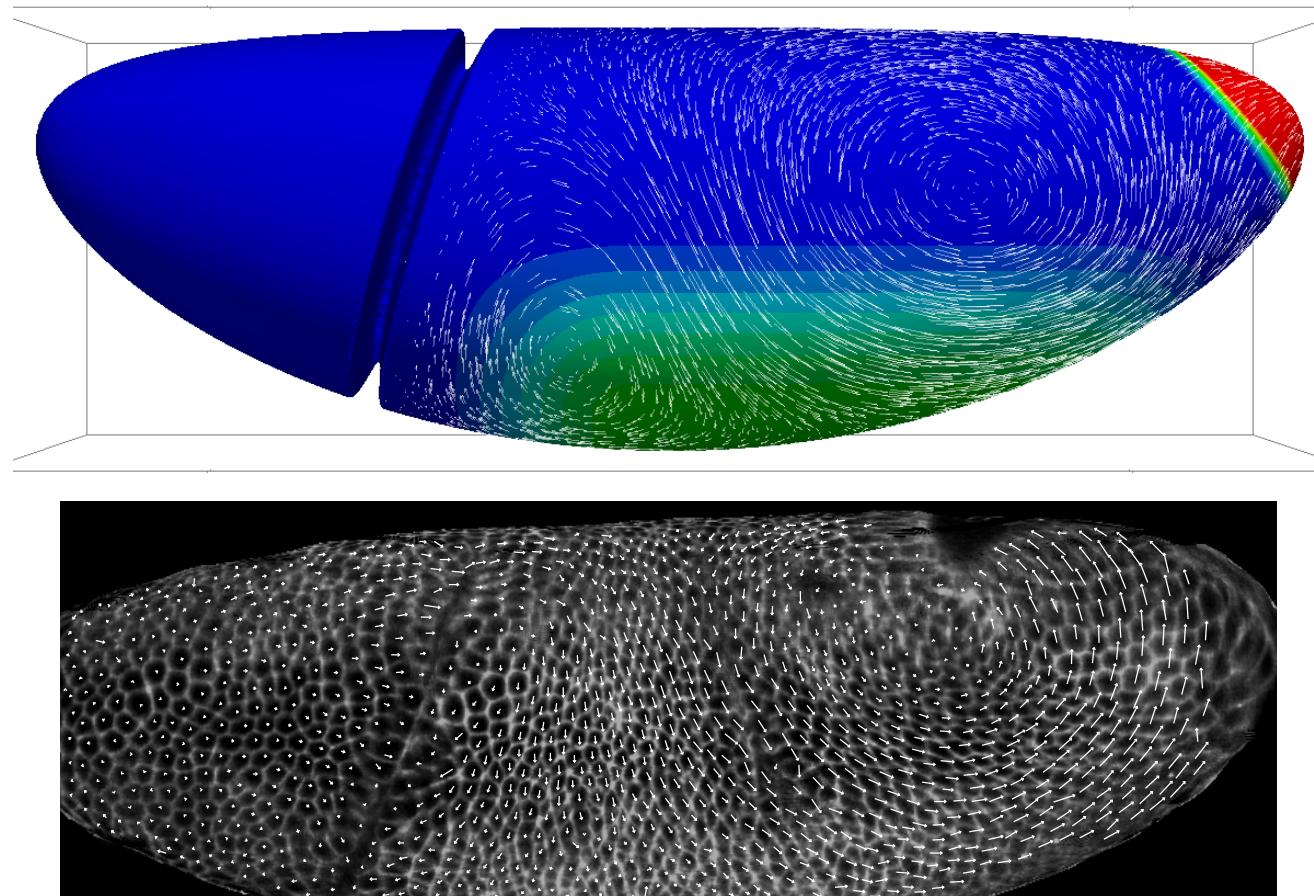
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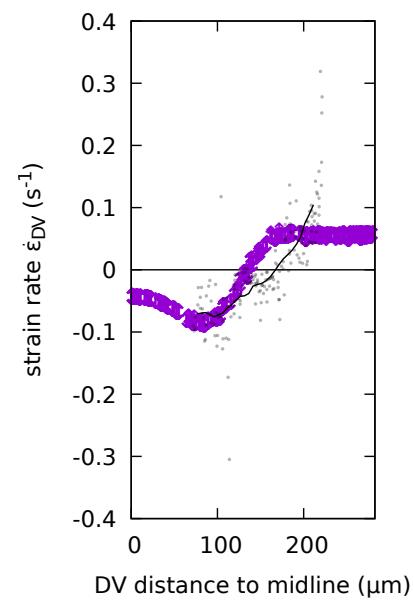
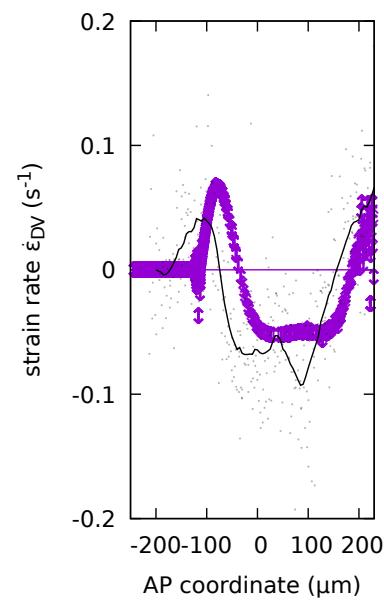
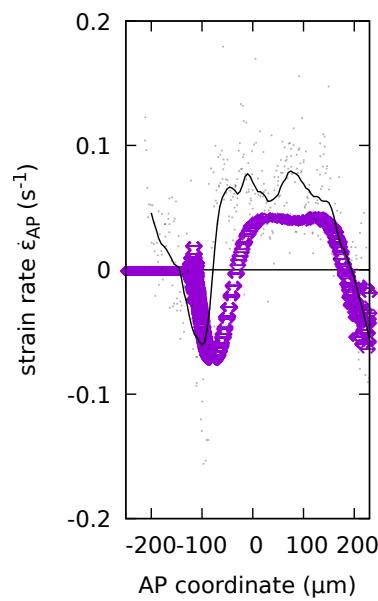
Cephalic furrow guides morphogenetic flow



Comparison with real data



Comparison with real data



Conclusions and perspectives

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Conclusions and perspectives

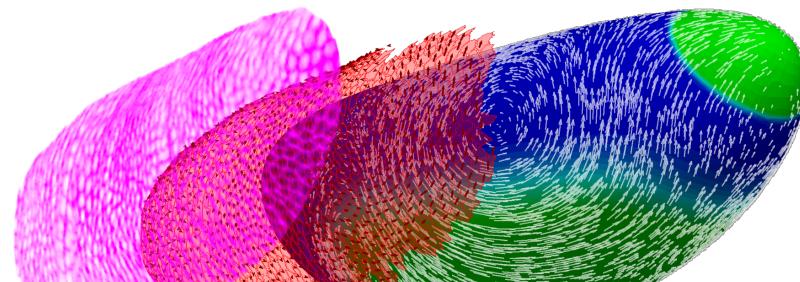
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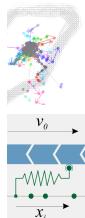
Conclusions and perspectives

- ▶ Whole embryo mechanics can be crucial for our understanding
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- ▶ Planar-polarisation may have more direct influence on global movement than intercalations
- ▶ Towards an integration with whole-embryo imaging: are geometry and myosin signal fully predictive of flows?



Co-workers

|PHY:Physics@Grenoble



Nilankur Dutta



Haythem Chelly



Pierre Recho



Claude Verdier



Catherine Quilliet



Philippe Marmottant

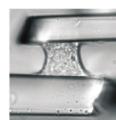


Alexandr Farutin



Chaouqi Misbah

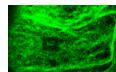
MSC:Physics@Paris



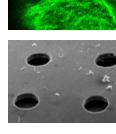
Atef Asnacios



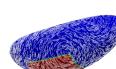
Grégoire Michaux



Sara Bouizakarne

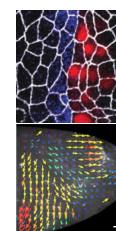


Alice Nicolas



Mahamar Dicko

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Bénédicte Sansor



Claire Lye



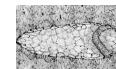
Guy Blanchard



Lukas Lang

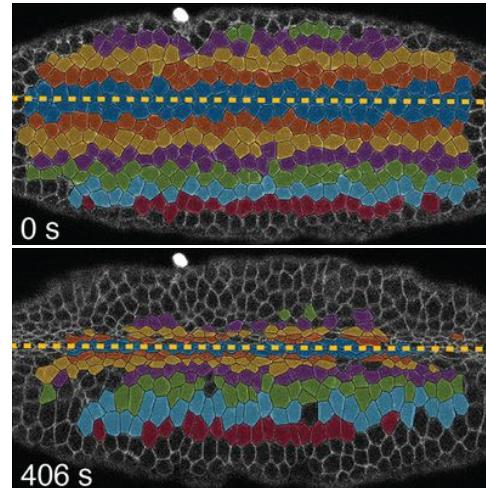
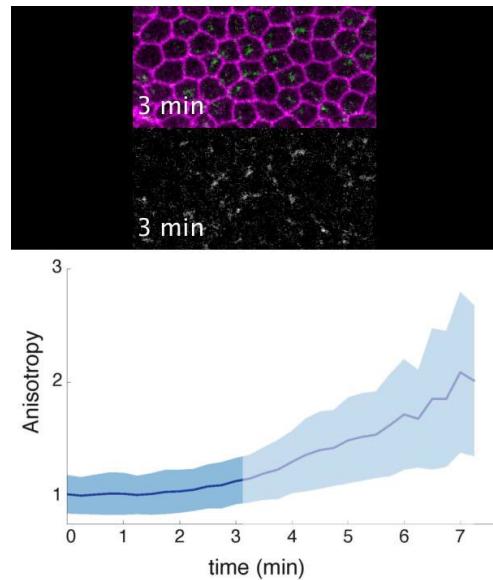


CSIC:DevBiol@Madrid



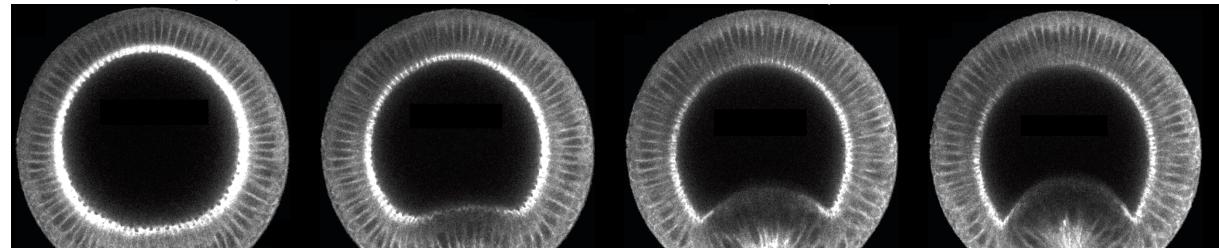
Nicole Gorfinkel

Contraction and ventral furrow formation

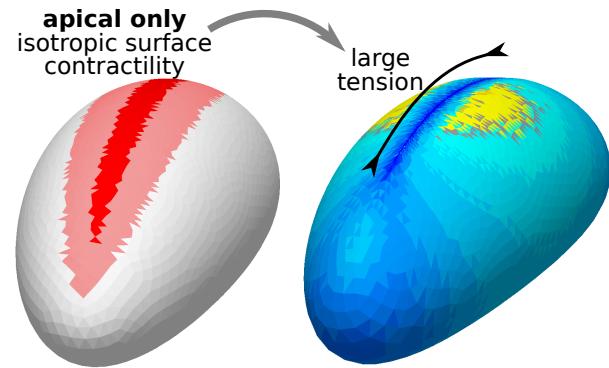


Heer et al., 2017

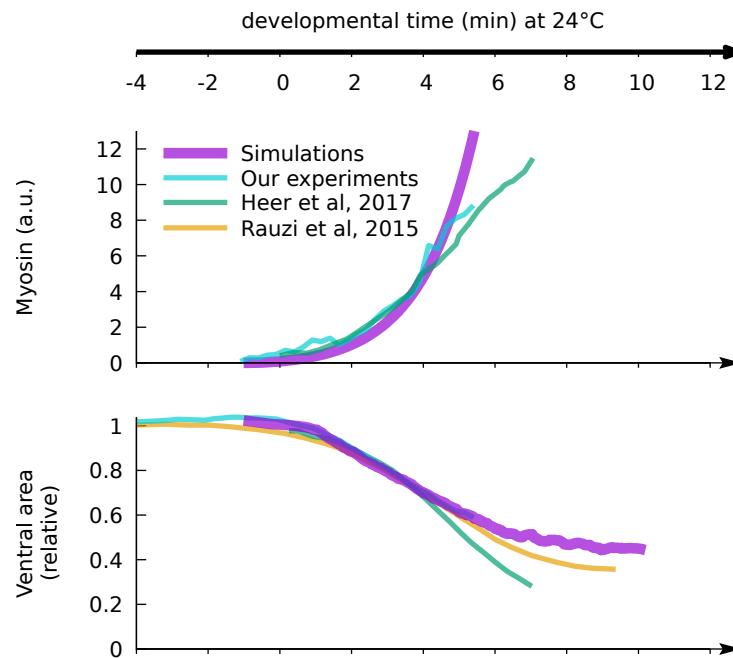
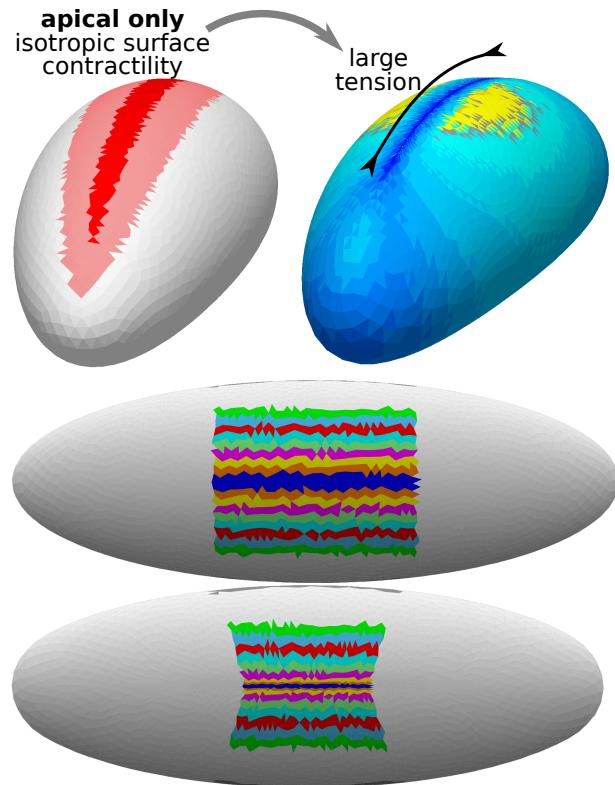
Chanet et al, 2017



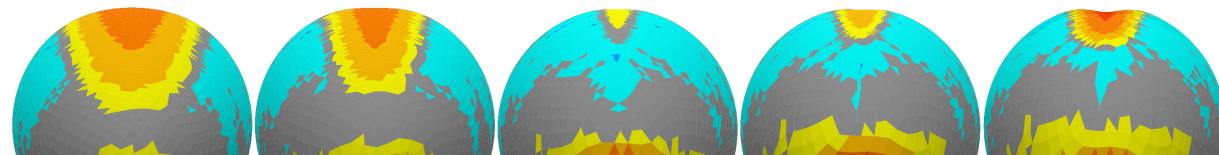
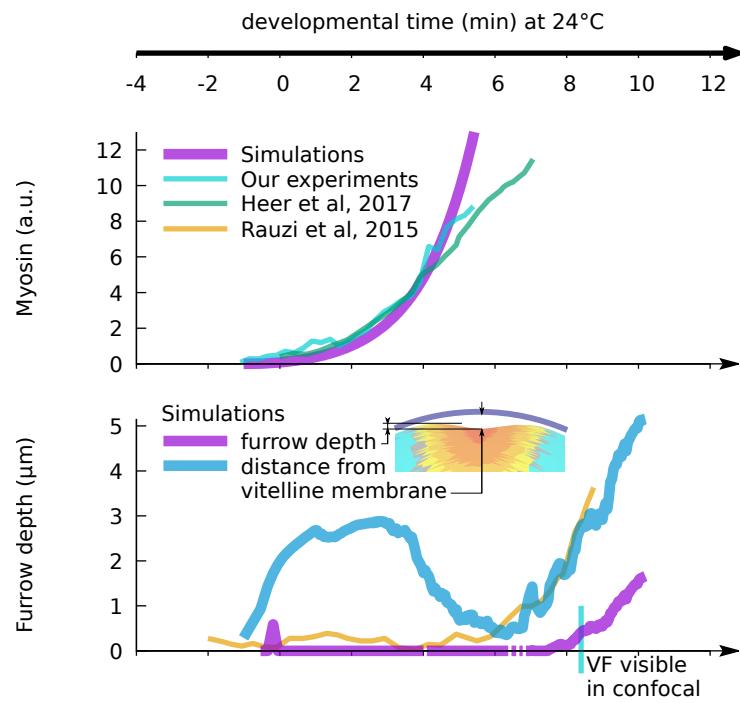
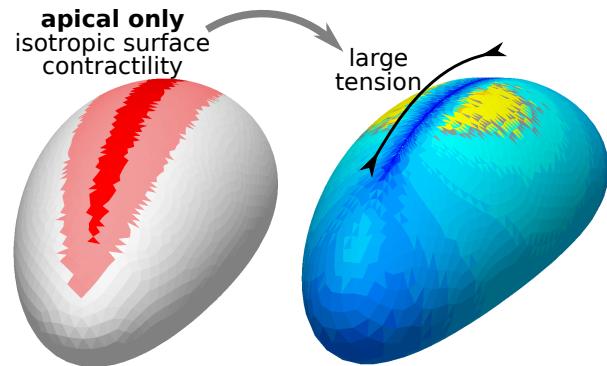
Apical drive of ventral furrow formation



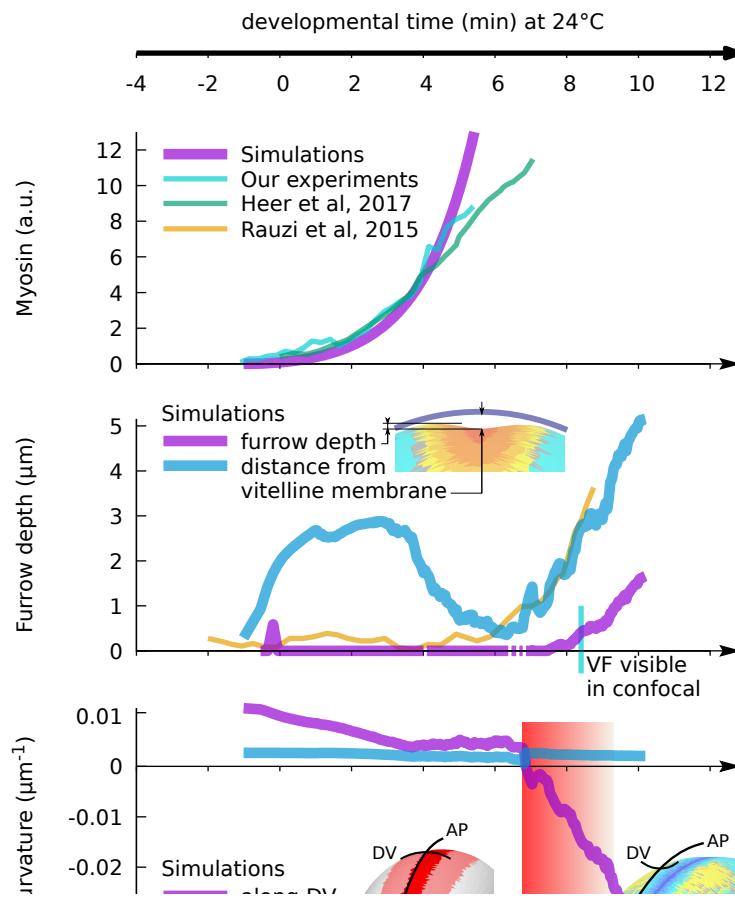
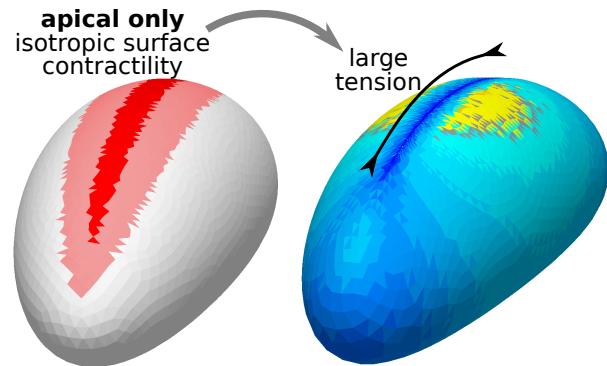
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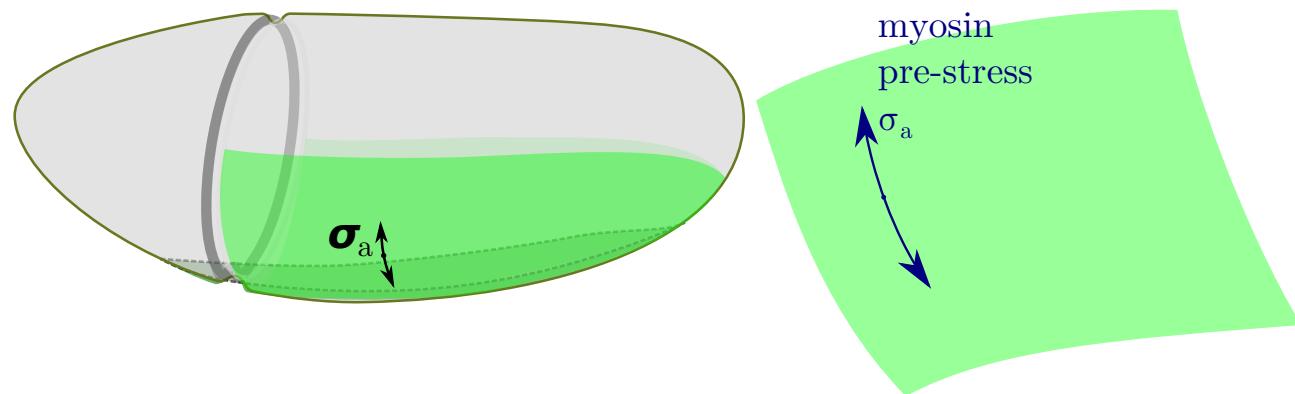
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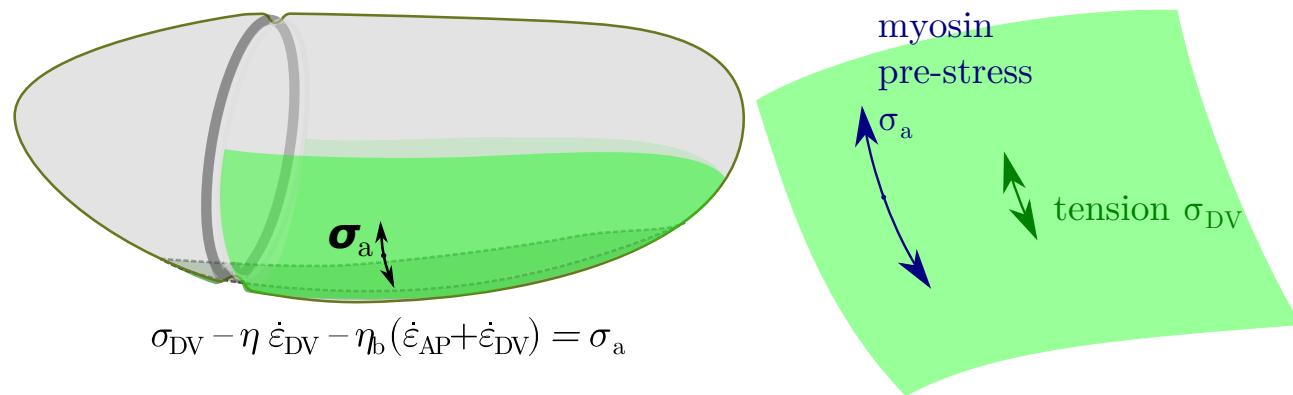


Germband extension modelling



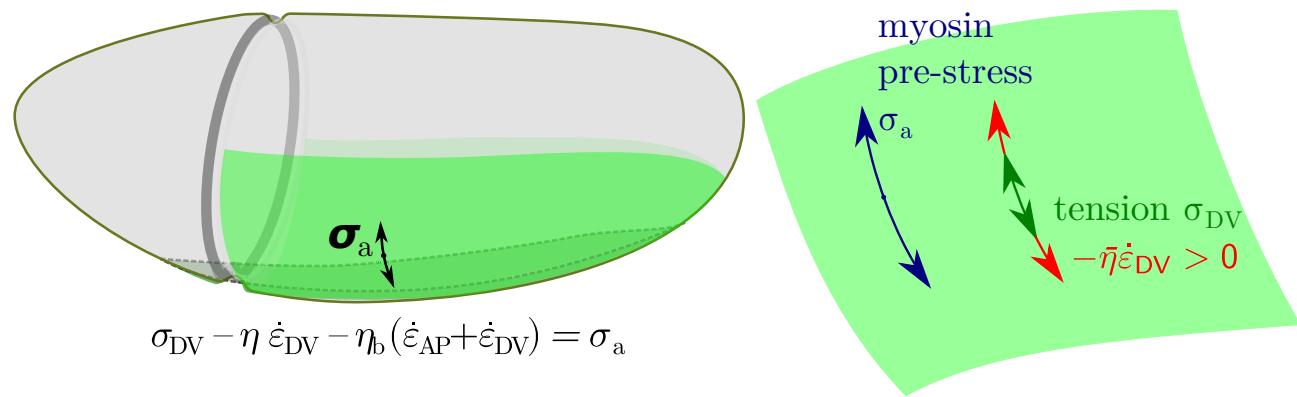
[Dicko et al. PLoS CR 2017]

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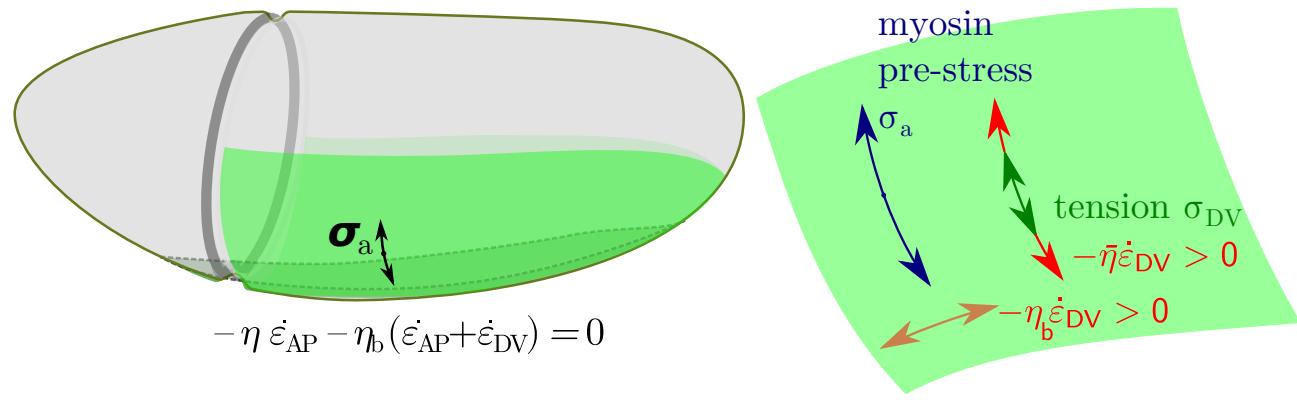
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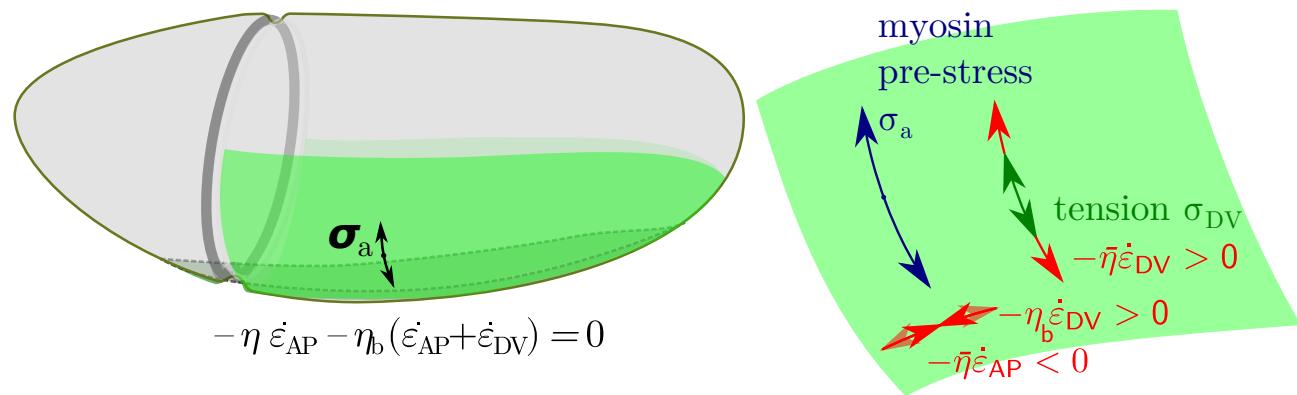
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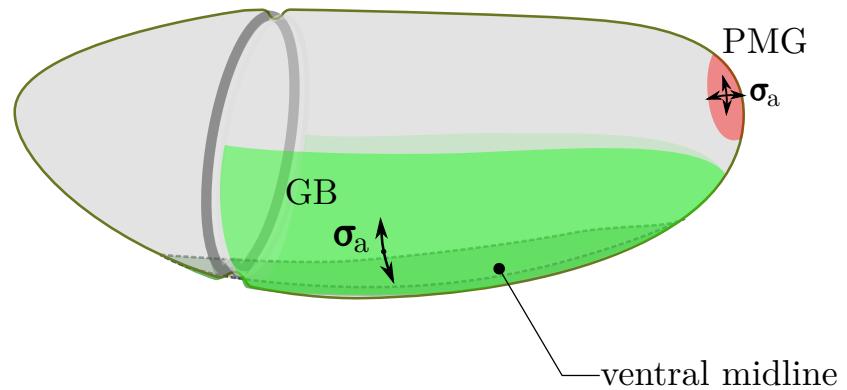
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