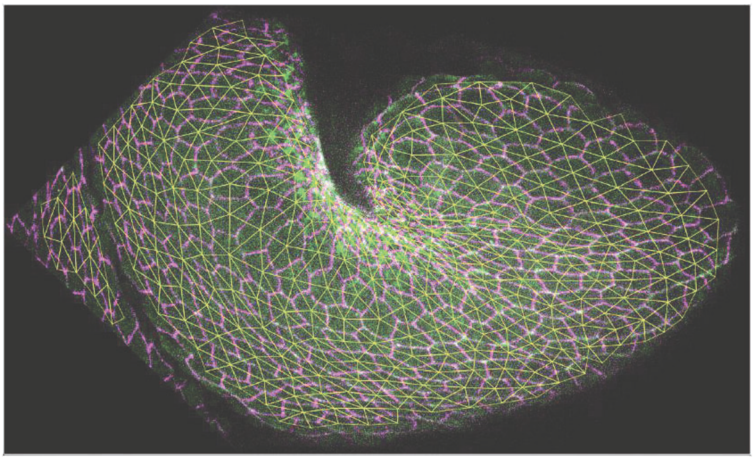
Morphogenesis: space, time, information

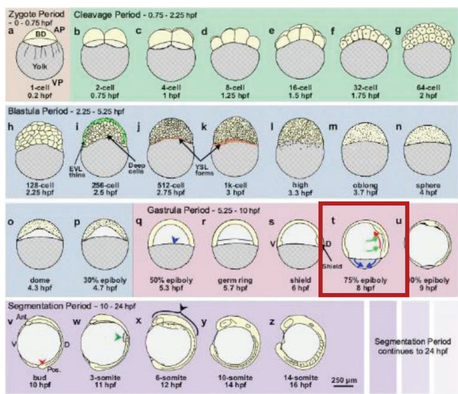


<u>Course 5:</u> Tissue morphogenesis - Geometry - Extension

Thomas Lecuit
chaire: Dynamiques du vivant

Introduction: Tissue Growth and Extension

- Tissue convergence/extension during embryogenesis



Introduction: Tissue Growth and Extension

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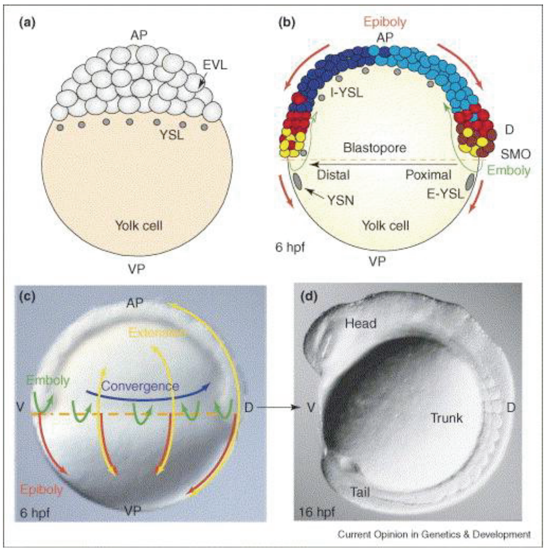
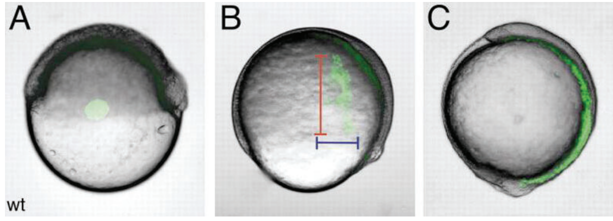


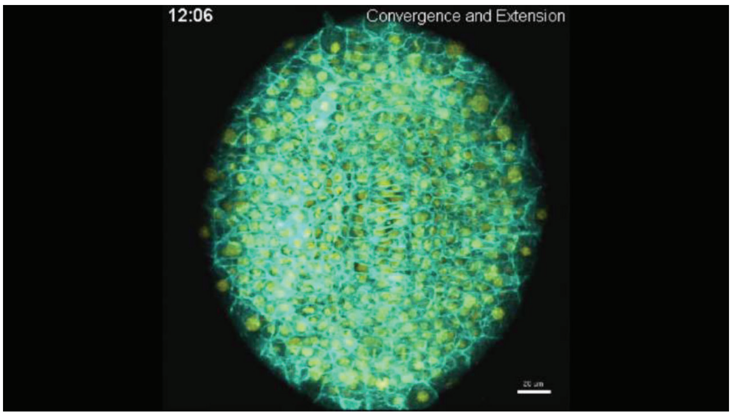
L Solnica-Krezel *COGD* 2006 16:433-441 doi.org/10.1016/j.gde.2006.06.009



J Bakkers et al. M. Hammerschmidt. *Development* 2004 131: 525-537; doi: 10.1242/dev.00954

Introduction: Tissue Growth and Extension

- Tissue convergence/extension during embryogenesis



Introduction: Tissue Growth and Extension

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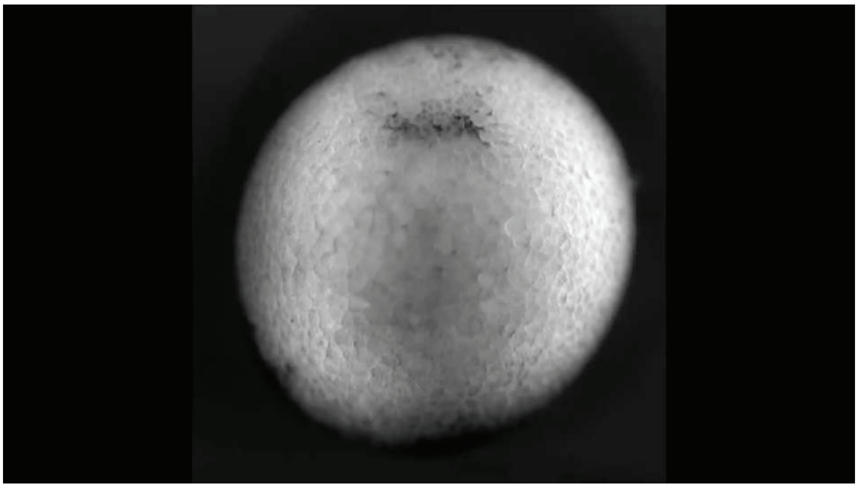

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Introduction: Tissue Growth and Extension

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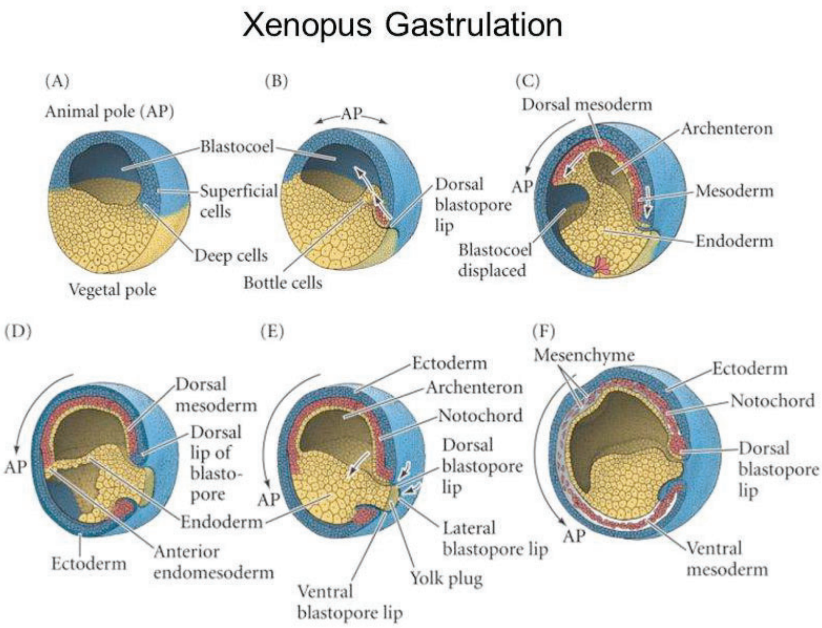

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Introduction: Tissue Growth and Extension

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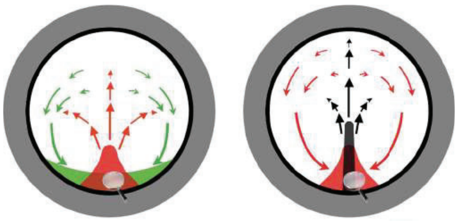
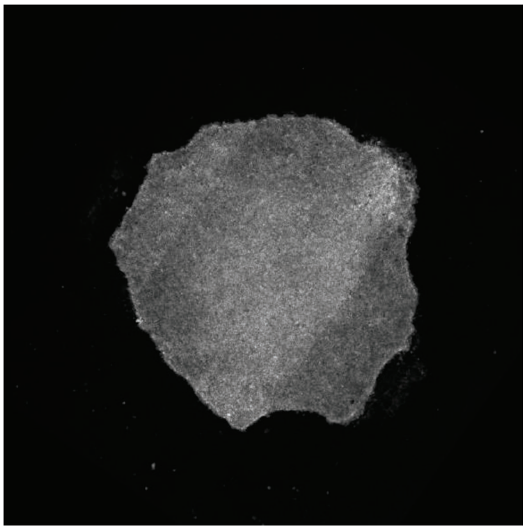


Voiculescu et al, and Stern C. *Nature* 449:1049. 2007



Firmino J. et al, and Gros J.
Dev. Cell. 36:249. 2016

Introduction: Tissue Growth and Extension

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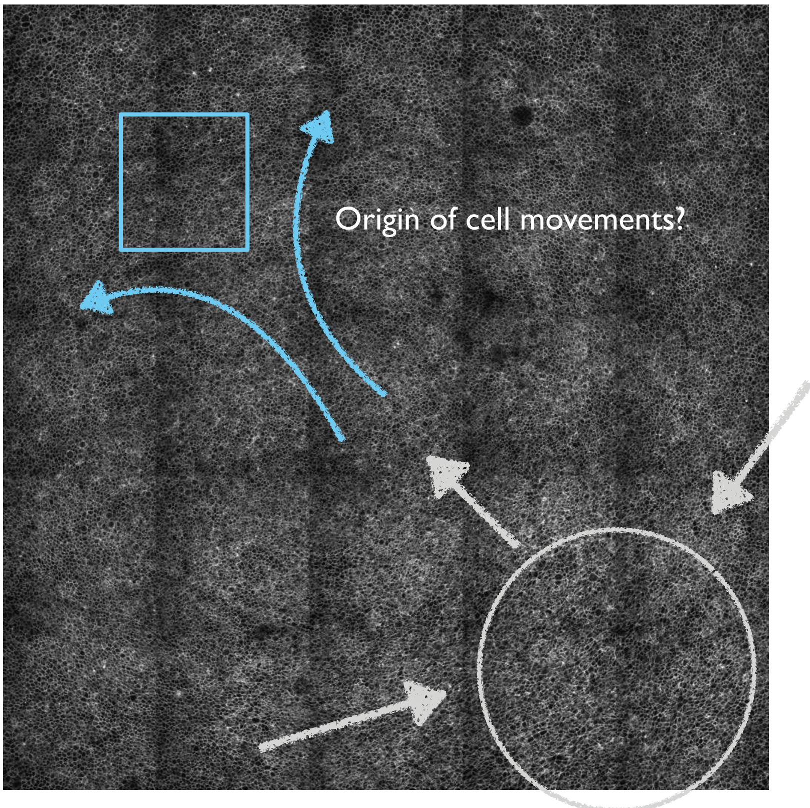

Firmino J. et al, and Gros J. *Dev. Cell*. 36:249. 2016

Introduction: Tissue Growth and Extension

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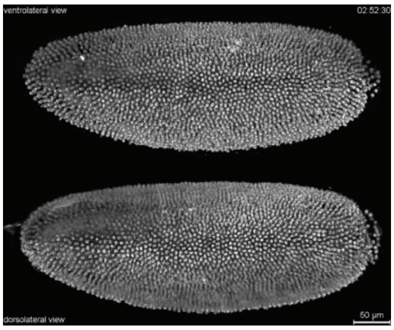
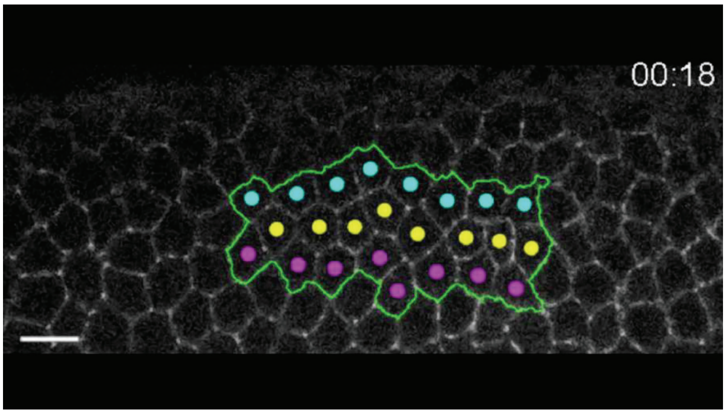
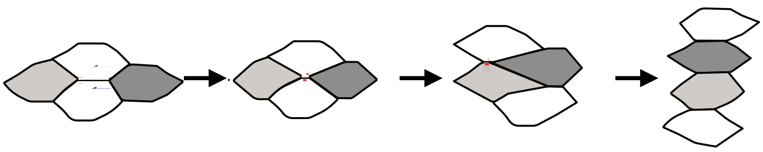


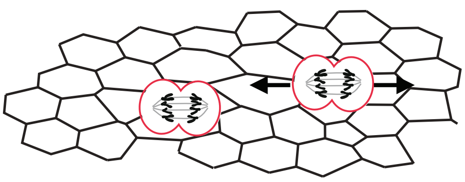


Introduction: cellular processes underlying tissue extension

- Polarised cell rearrangements drive tissue convergence/extension: Also called « cell intercalation »



- Polarised cell divisions drive tissue extension

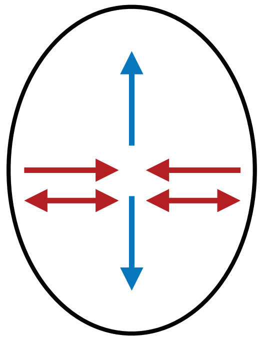


- Interplay between cell rearrangements and cell division

Introduction: Tissue Growth and Extension

Orientation/polarity: Information?

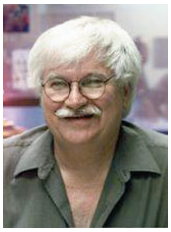
Origin of forces: Mechanics



Plan

1. Introduction: convergence/extension movements
   cell intercalation and cell division
2. Mechanics of intercalation: cell protrusions
3. Mechanics of intercalation: cortical tension
4. Tissue interactions
5. Roles of cell division in tissue extension
6. Planar polarisation of cell behaviours

2. Mechanics of cell intercalation: Polarised cell protrusions

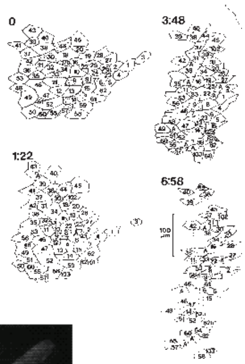


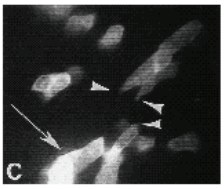
Ray Keller
Univ. of Virginia

- Non adherent mesenchymal cells

Cell motility driving mediolateral intercalation in explants of *Xenopus laevis*

JOHN SHIH* and RAY KELLER
Development 116, 901-914 (1992)

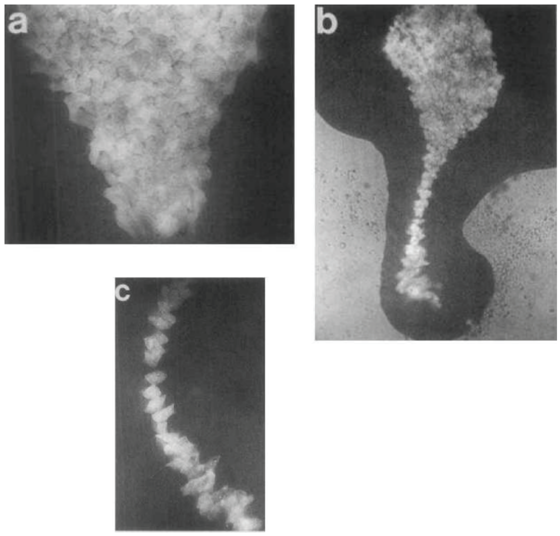




The Cellular Basis of the Convergence and Extension of the *Xenopus* Neural Plate

RAY KELLER, JOHN SHIH, AND AMY SATER
Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, California 94720

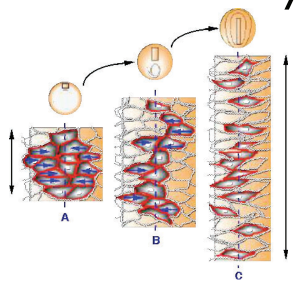
DEVELOPMENTAL DYNAMICS 193:199–217 (1992)

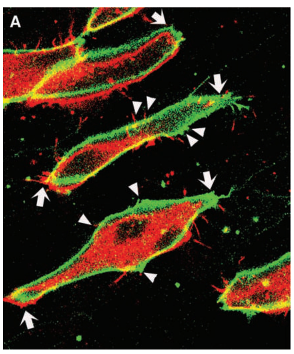


2. Mechanics of cell intercalation: Polarised cell protrusions

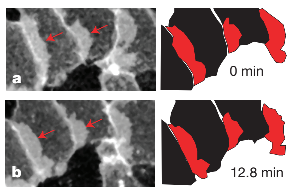
- Non adherent mesenchymal cells

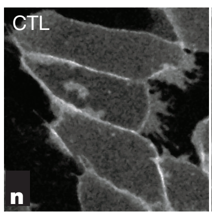
- Cells exhibit unipolar or bipolar cell protrusions characteristic of migrating cells
- Cell intercalation as a form of spatially biased cell migration

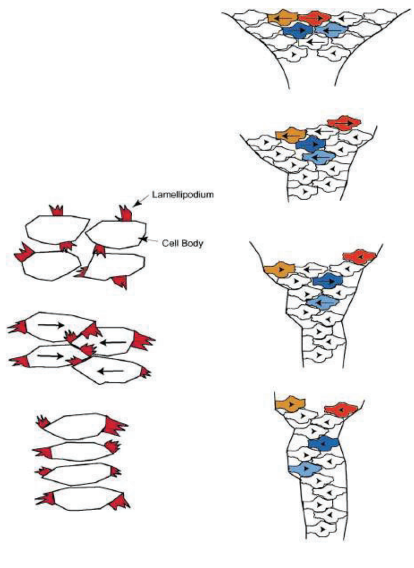




R. Keller *Science* 298:1950-1954 (2002)
(image: L. Davidson)







J. Wallingford et al. R. Harland. *Dev Cell* 405: 81-84 (2002)

J. Wallingford et al. R. Harland. *Nature* 405: 81-84 (2000)

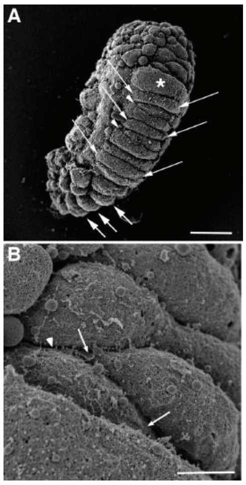
J. Shi and R. Keller. *Development* 116-901-914 (1992)

2. Mechanics of cell intercalation: Polarised cell protrusions

• Adherent epithelial cells

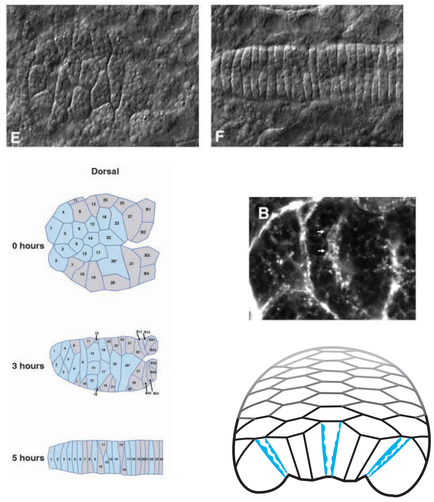
- Adherent epithelial cells also exhibit cell protrusions along their lateral surface.
- Cell protrusions are spatially biased.

Nematode Dorsal Hypodermis



Williams-Masson et al. and J. Hardin. *Dev. Biol*. 204, 263–276 (1998)

Urochordate Notochord



E. Munro and G. Odell. *Development* 129, 13-24 (2002)

2. Mechanics of cell intercalation: Polarised cell protrusions

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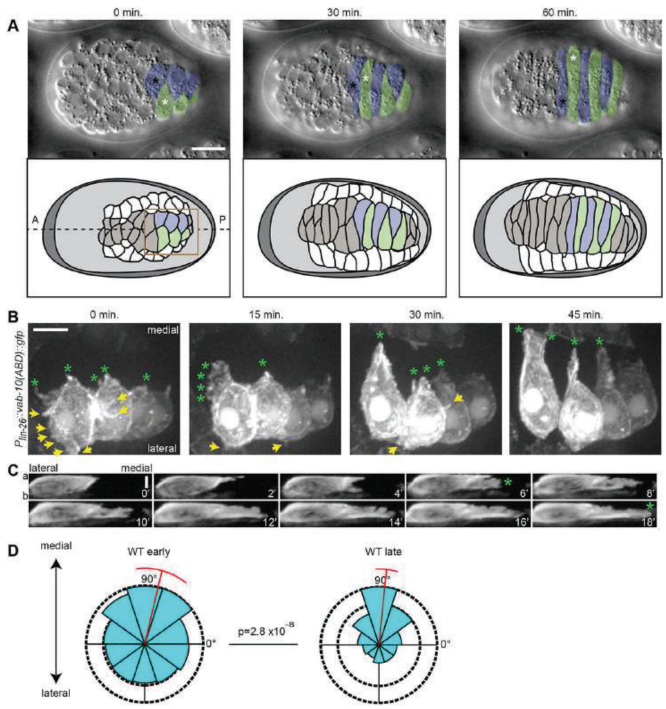
- Cell protrusions are spatially biased and depend on Rao activity.



E. Walck-Shannon, D. Reiner and J. Hardin *Development* (2015) 142, 3549-3560 doi:10.1242/dev.127597

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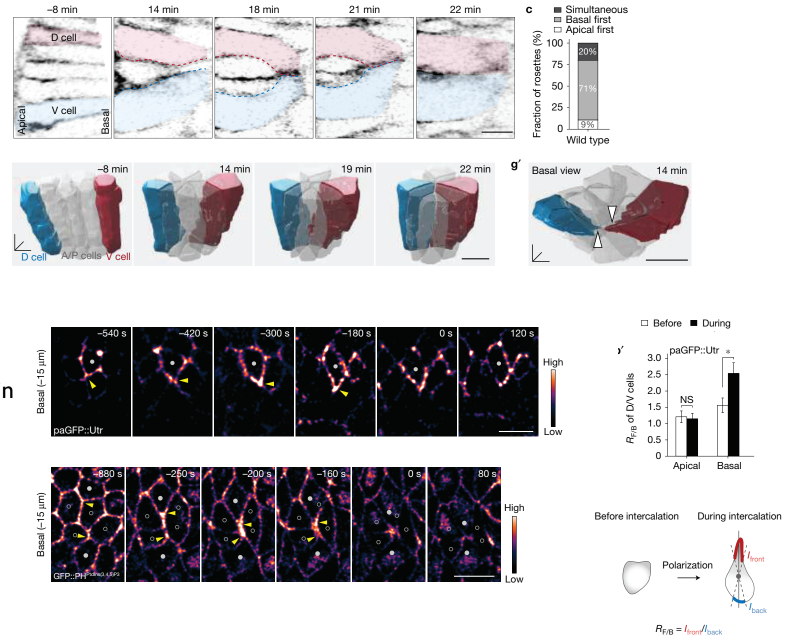


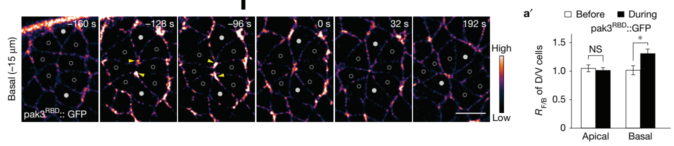
Z. Sun et al. and Y. Toyama. *Nat Cell Biol*. (2018) 20(4):503. doi: 10.1038/s41556-018-0069-4.

COLLÈGE DE FRANCE 1530

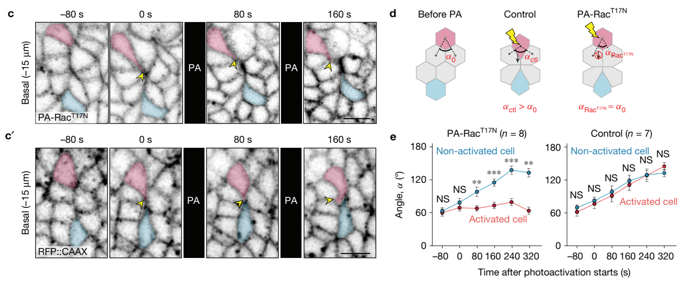
Thomas LECUIT 2018-2019

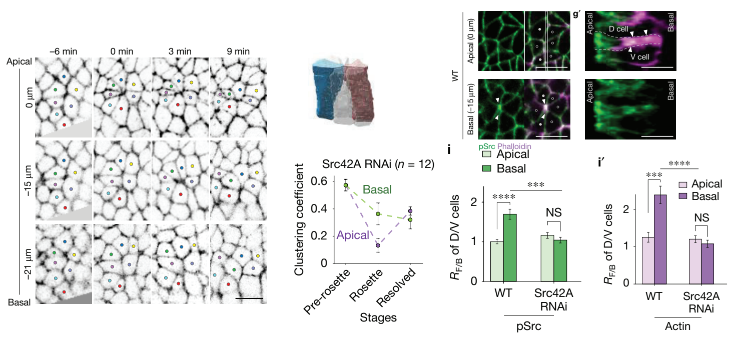
2. Mechanics of cell intercalation: Polarised cell protrusions

- Adherent epithelial cells



- Adherent epithelial cells also exhibit cell protrusions along their lateral surface.
- Cell protrusions are spatially biased.
- Blocking cell protrusive activity affects compaction of cell clusters associated with cell intercalation





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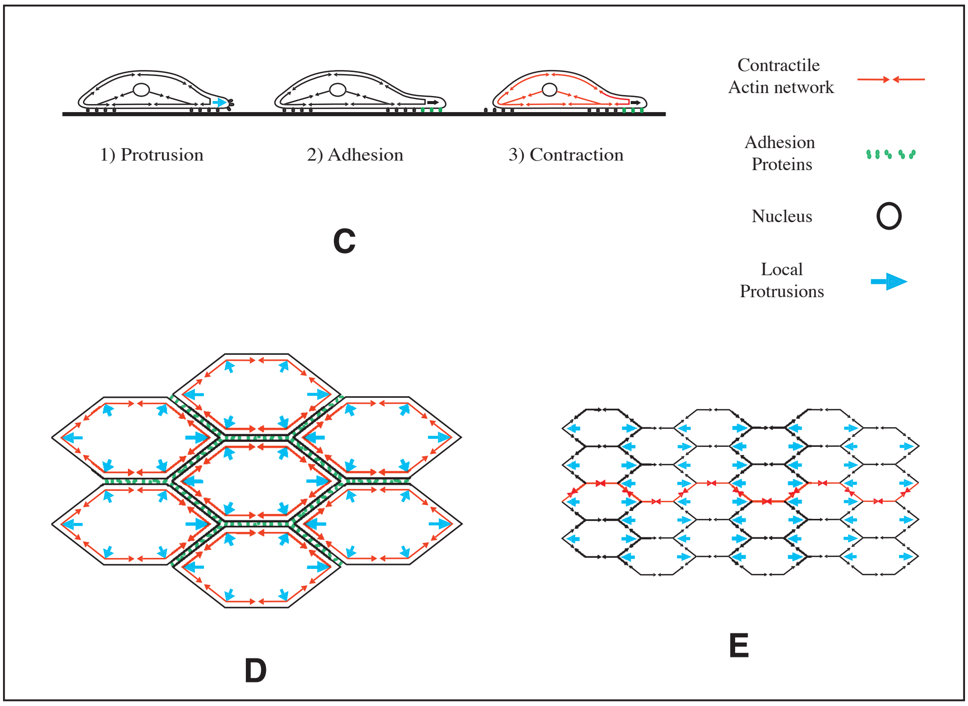
Z. Sun et al. and Y. Toyama. *Nat Cell Biol*. (2018) 20(4):503. doi: 10.1038/s41556-018-0069-4.

COLLÈGE DE FRANCE 1530

2. Mechanics of cell intercalation: Polarised cell protrusions

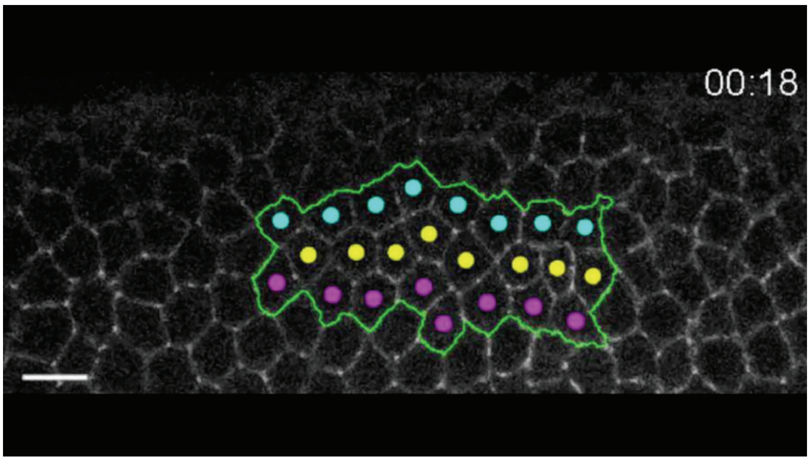
- Polarised protrusive forces in cell locomotion and intercalation



E. Munro and G. Odell. *Development* 129, 13-24 (2002)

2. Mechanics of cell intercalation:

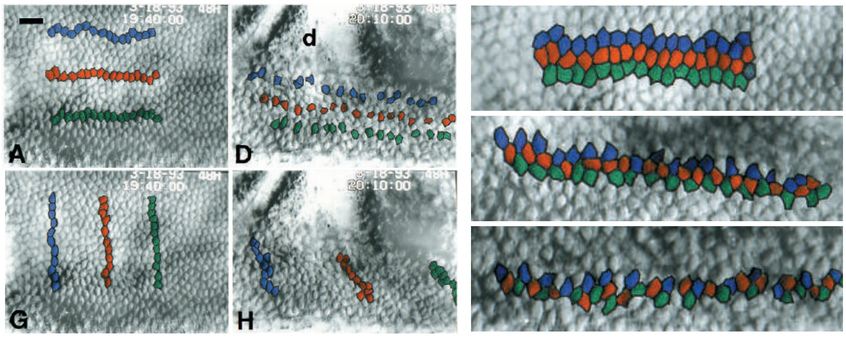
- Adherent epithelial cells

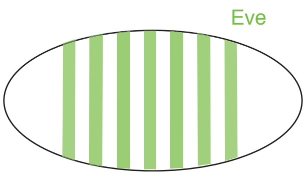


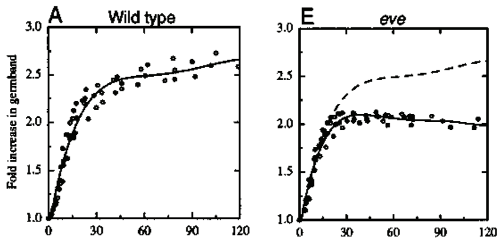
2. Mechanics of cell intercalation: Adhesion hypothesis

- Adherent epithelial cells

- Cells intercalate along media-lateral axis
- Cell intercalation is associated with tissue extension (germband extension)
- Embryo segmental patterning is required for this process







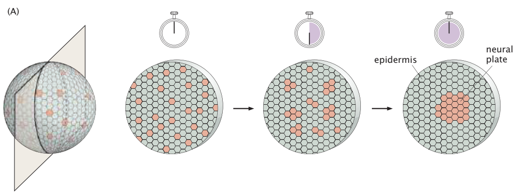
K. Irvine and E. Wieschaus. *Development* 120, 827-841 (1994)

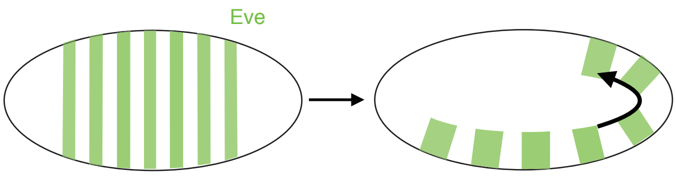
2. Mechanics of cell intercalation: Adhesion hypothesis

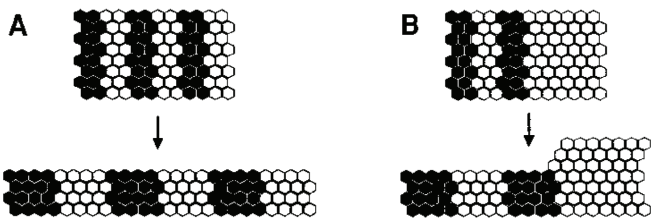
- Adherent epithelial cells

Differential Adhesion Hypothesis

- Tissues behave like viscous fluids
- Cells reorganise so as to minimise interfacial adhesion energy
- Tissue surface tension underlies cell aggregation behaviour







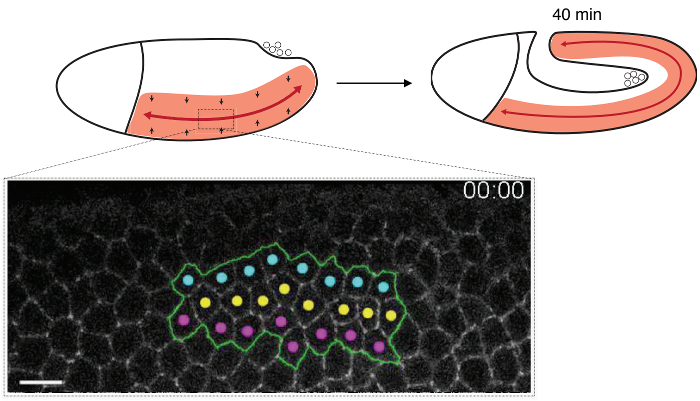
K. Irvine and E. Wieschaus. *Development* 120, 827-841 (1994)

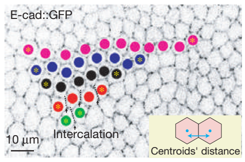
Department of Molecular Biology, Princeton University, Princeton NJ 08544, USA

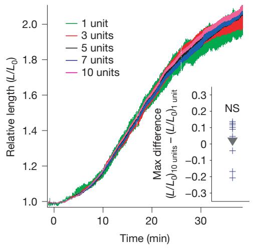
3. Mechanics of cell intercalation: Polarised Cortical tension

- Polarised neighbour exchange drives tissue extension

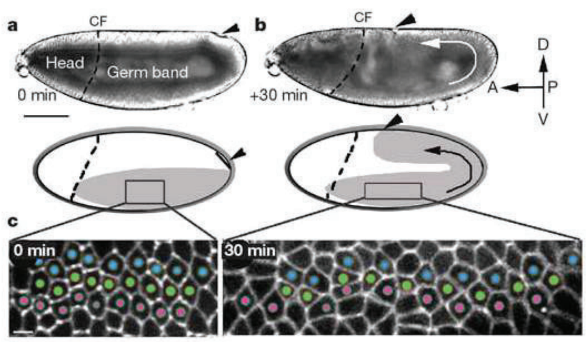
- Cells exchange neighbours
- Local cell displacement scales with tissue extension







C. Collinet et al. T. Lecuit. *Nature Cell Biol*. DOI: 10.1038/ncb3226 (2015)

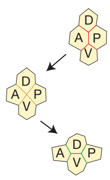


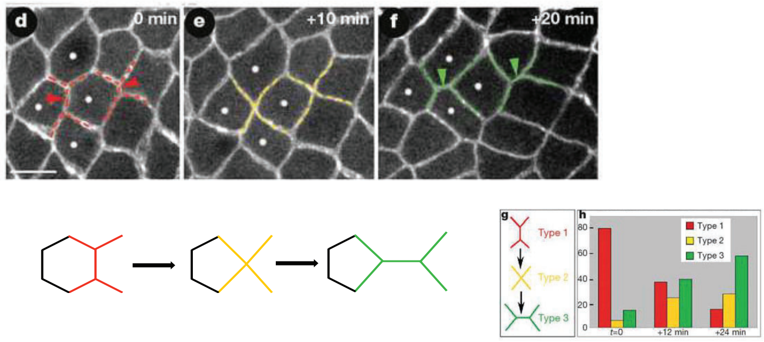
C. Bertet, L. Sulak and T. Lecuit. *Nature*. 429(6992):667-71. (2004)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Neighbour exchange is associated with planar polarised junction remodelling

T1 transition



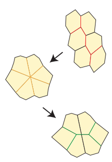


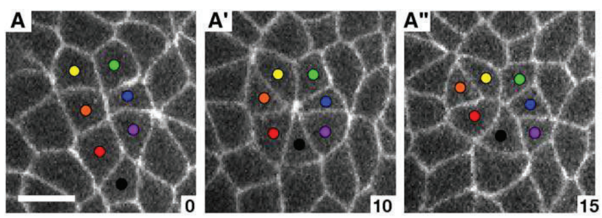
C. Bertet, L. Sulak and T. Lecuit. *Nature*. 429(6992):667-71. (2004)

Two sequential steps are spatially oriented:

- Polarised junction disassembly
- Polarised junction growth

Rosette

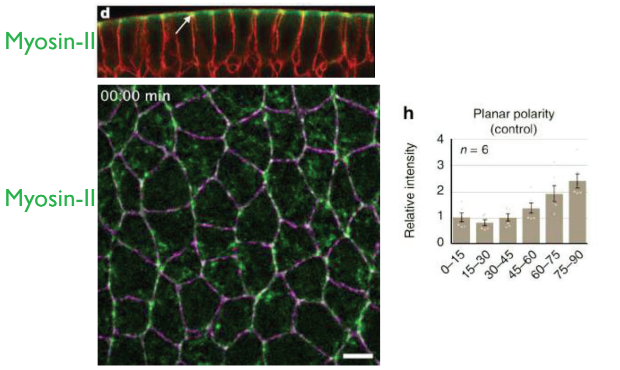




T. Blankenship et al, and J. Zallen *Dev Cell*. 11:459-70 (2006)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Junction remodelling requires planar polarised actomyosin cortical tension



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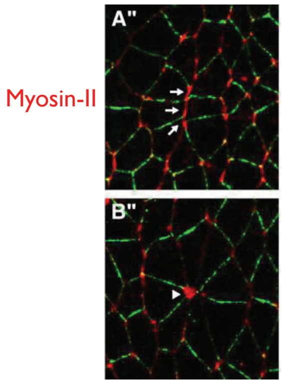
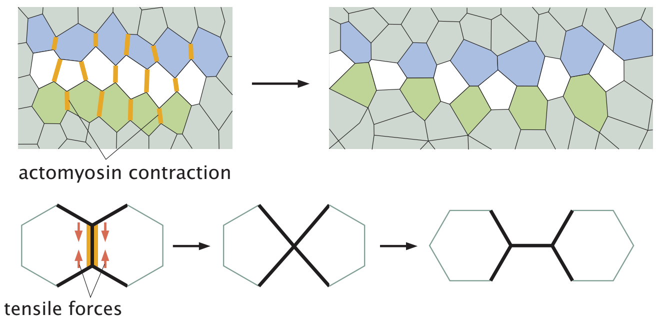
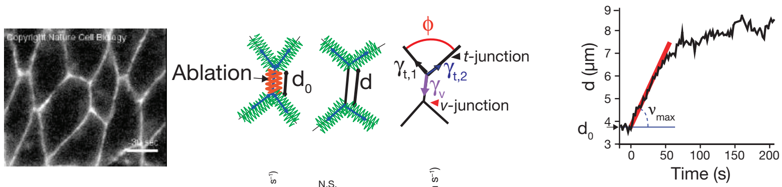


T. Blankenship et al, and J. Zallen *Dev Cell*. 11:459-70 (2006)



3. Mechanics of cell intercalation: Polarised Cortical tension

- Measurement of tension in vivo: laser nano ablation

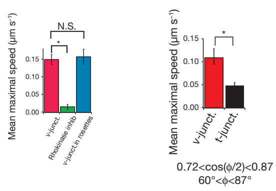


Force balance at vertices $(\vec{\gamma}_{t,1}+\vec{\gamma}_{t,2})(t=0^+)=\vec{\gamma}_v(t=0^-)$

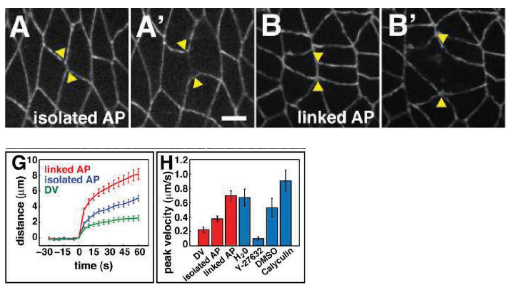
$V_{max}=\gamma_v/\mu$

μ : drag coefficient

γ_v : tension at t=0



M. Rauzi et al, T. Lecuit and PF-Lenne, *Nature Cell Biology*. 10: 1401-1410 (2008)



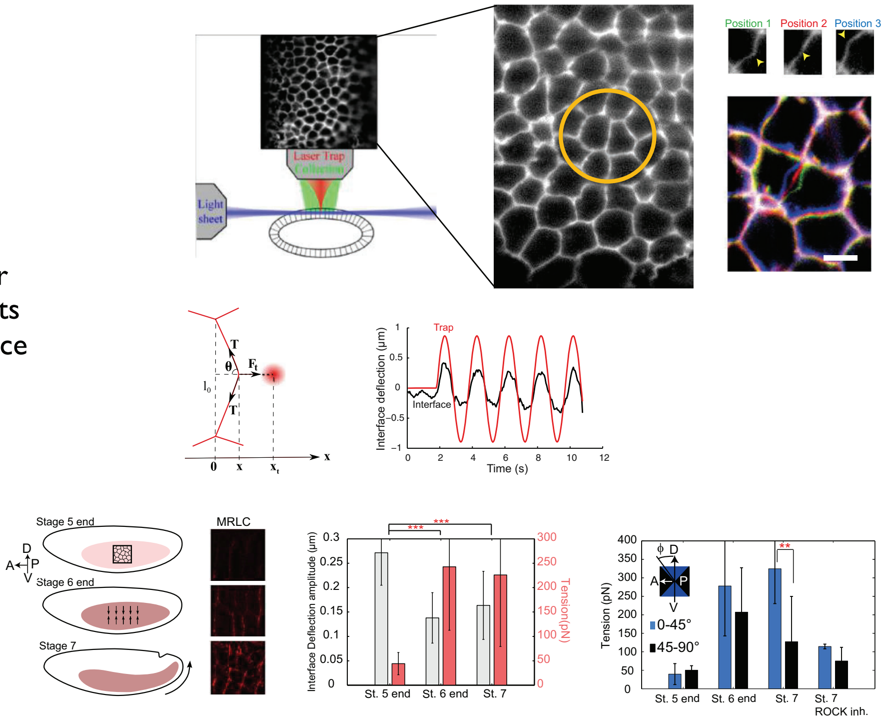
R. Fernandez-Gonzalez et al, J. Zallen. *Developmental Cell* 17, 736–743 (2009)

See Review on force and stress measurements in vivo:
K Sugimura, PF. Lenne and F. Graner *Development*. 143(2):186-96. (2016)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Measurement of tension in vivo: optical tweezers

200pN force range corresponds to a few bipolar MyosinII motor mini filaments to remodel a cell-cell interface



K. Bambardekar, R. Clément et al, PF. Lenne. *Proc Natl Acad Sci*. 112(5):1416-21 (2015)

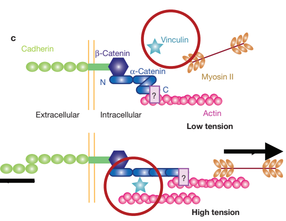
See Review on force and stress measurements in vivo:
K Sugimura, PF. Lenne and F. Graner *Development*. 143(2):186-96. (2016)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Measurement of tension in vivo: force sensor bioprobes

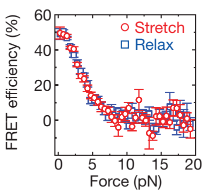
- Quantitative measurement of relative load on molecules

Vinculin is recruited at E-cadherin complexes under load exerted by contractile actomyosin networks



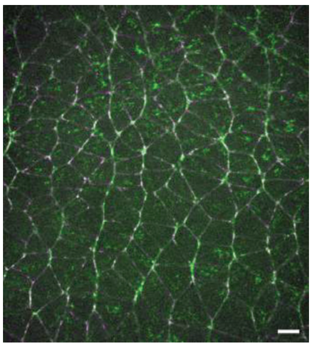
See also Course 14 Nov 2017

- Value of forces using FRET sensors

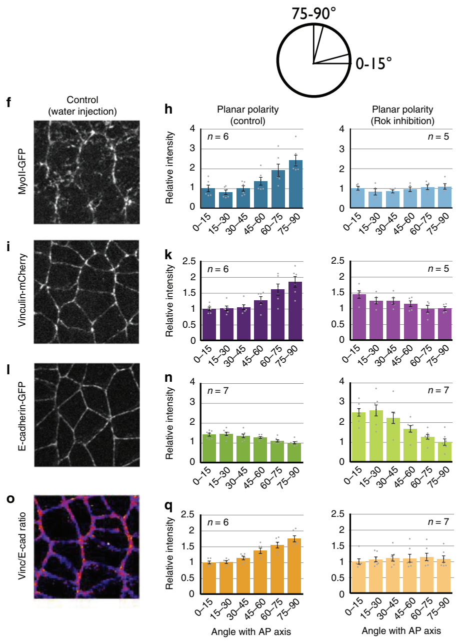


Grashoff C. et al., Schwartz M. , *Nature*, 466:263. 2010

Borghi N. et al Nelson WJ. and Dunn A., *PNAS*, 109:12568. 2012



MyoII::GFP
Vinculin::mCherry



Kale GR, Yang X, Philippe JM, Mani M, Lenne PF, Lecuit T. *Nat Commun*. 9(1):5021. doi: 10.1038/s41467-018-07448-8. (2018)

See Review on force and stress measurements in vivo:
K Sugimura, PF. Lenne and F. Graner *Development*. 143(2):186-96. (2016)

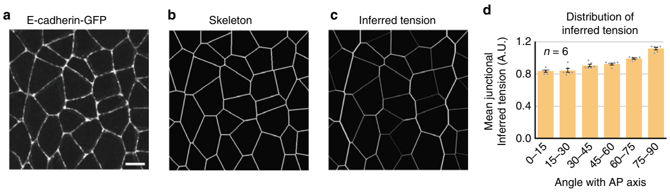
3. Mechanics of cell intercalation: Polarised Cortical tension

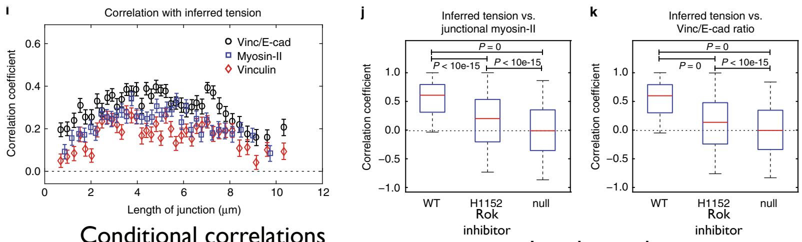
- Measurement of tension in vivo: force inference in equilibrium models

Assumes Force balance at cell vertices: a good approximation

Cell Geometry reflects distribution of forces acting on vertices

Relative values of forces





Conditional correlations (among junctions of same length)

Local correlations (among junctions of same cell)

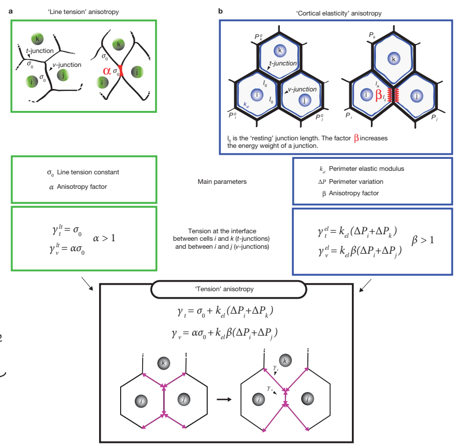
Kale GR, Yang X, Philippe JM, Mani M, Lenne PF, Lecuit T. *Nat Commun*. 9(1):5021. doi: 10.1038/s41467-018-07448-8. (2018)

Chiou, K. K., Hufnagel, L. & Shraiman, B. *PLoS Comput. Biol*. 8, e1002512 (2012).

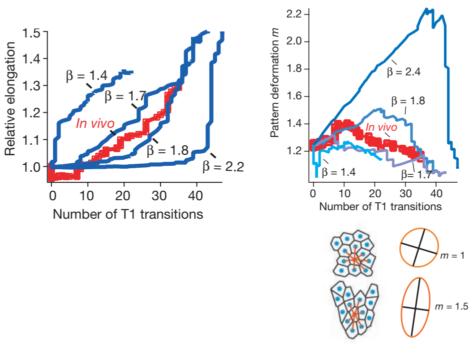
3. Mechanics of cell intercalation: Polarised Cortical tension

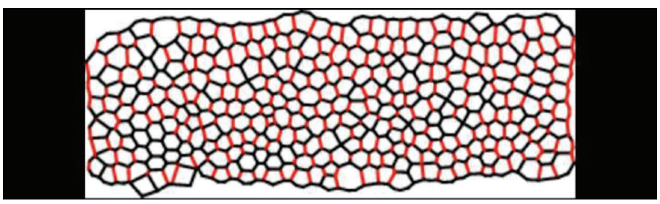
- Assessment of tension patterns in equilibrium models

Assumes Force balance at cell vertices. Change in cell configuration through minimisation of energy function E



$$E = \underbrace{\sum_{\text{junctions }(ij)} \sigma(\theta_{ij}) l_{ij}}_{\text{line energy}} + \underbrace{\frac{1}{2}\sum_{\text{cells } i} k_i^P \left(\sum_{\text{cells } j \text{ neighbours of } i} \beta(\theta_{ij}) l_{ij} - P_i^0 \right)^2}_{\text{cortical elastic energy}} + \underbrace{\frac{1}{2}\sum_{\text{cells } i} k_i^A (A_i - A_i^0)^2}_{\text{area elastic energy}}$$

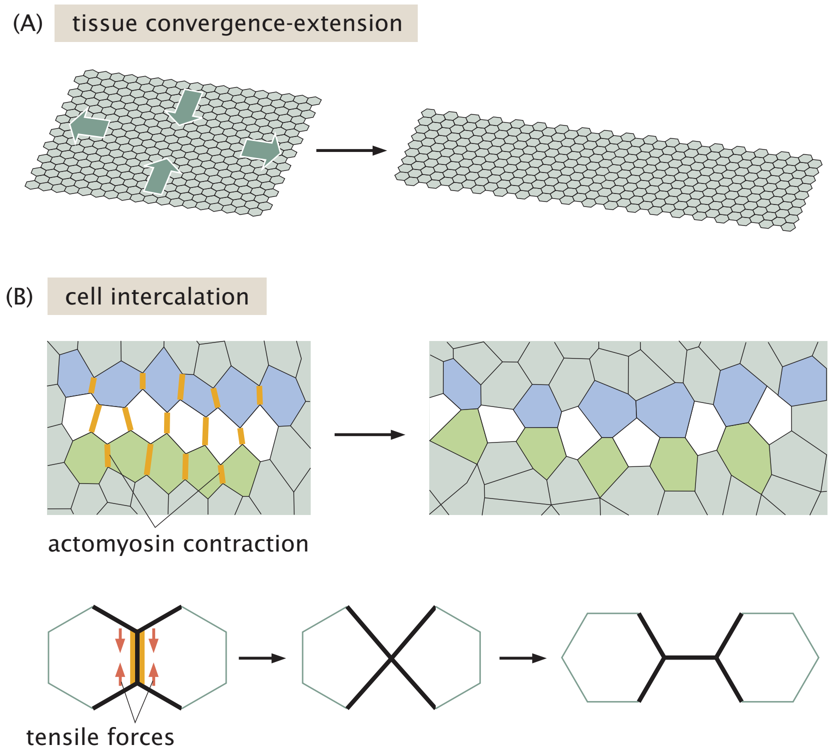




M. Rauzi et al, T. Lecuit and PF-Lenne, *Nature Cell Biology*. 10: 1401-1410 (2008)

3. Mechanics of cell intercalation: Polarised Cortical tension

- The « universality » of polarised cortical tension driving cell intercalation

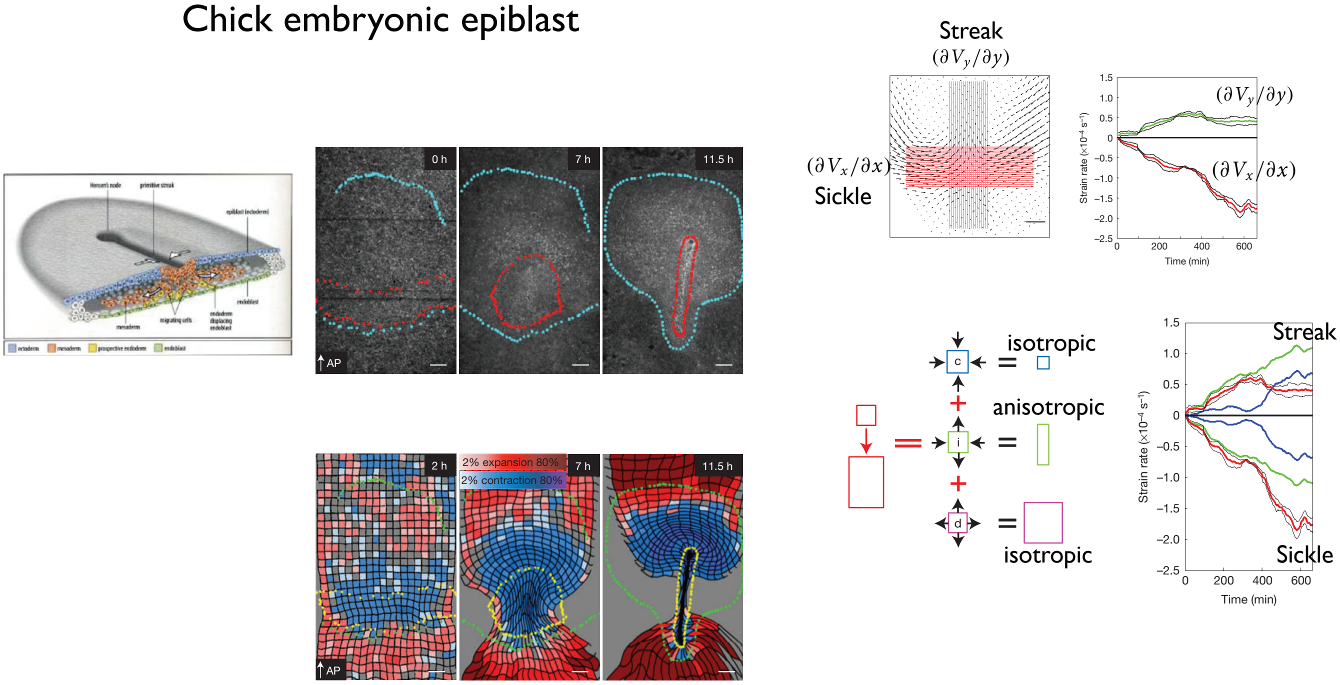


Nigel Orme

3. Mechanics of cell intercalation: Polarised Cortical tension

- The « universality » of polarised cortical tension driving cell intercalation

Chick embryonic epiblast

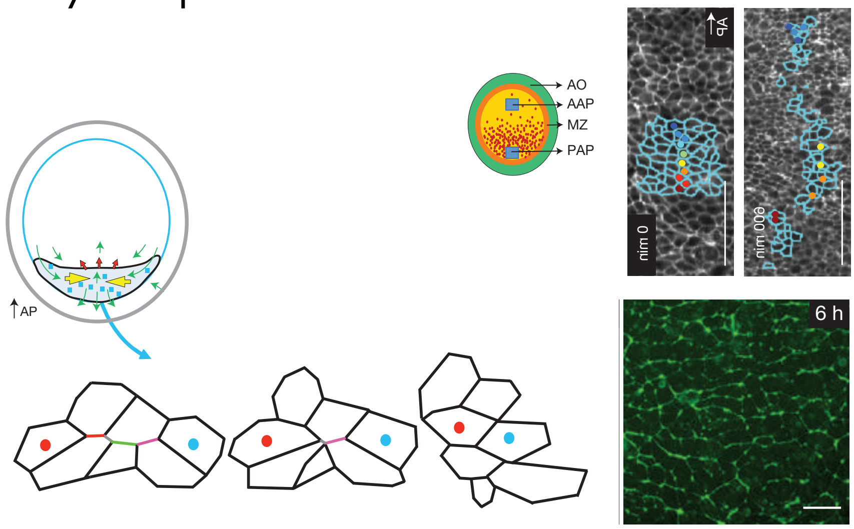


Rozbicki E. et al, and Weijer CI. *Nature Cell Biol*. 17:397. 2015

3. Mechanics of cell intercalation: Polarised Cortical tension

- The « universality » of polarised cortical tension driving cell intercalation

Chick embryonic epiblast



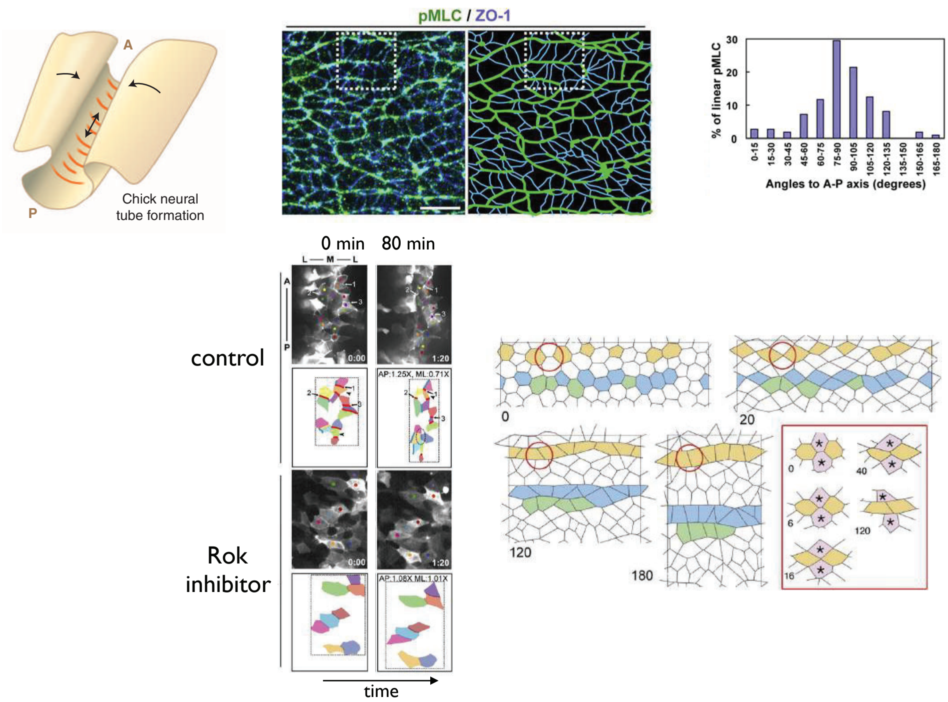
phospho-MRLC (Myosin-II)

Rozbicki E. et al, and Weijer CI. *Nature Cell Biol*. 17:397. 2015

3. Mechanics of cell intercalation: Polarised Cortical tension

- The « universality » of polarised cortical tension driving cell intercalation

Vertebrate neurulation

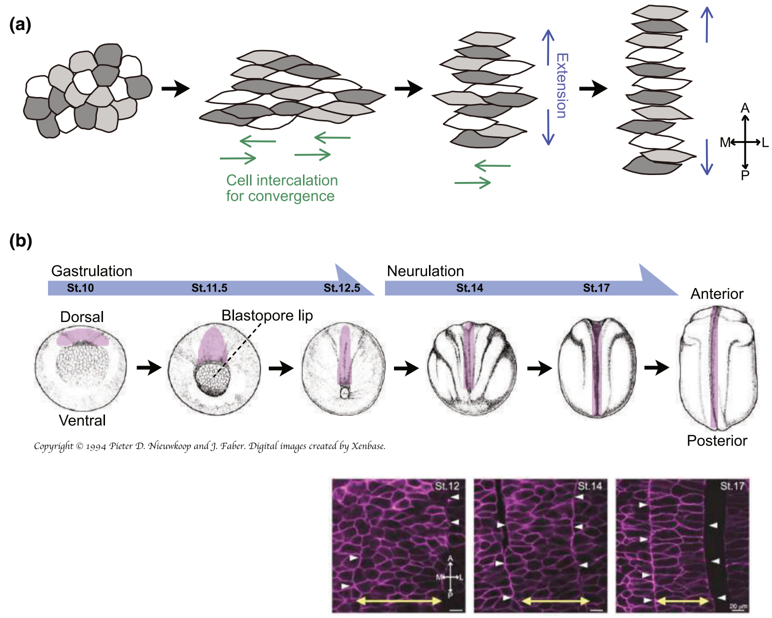


T. Nishimura, H. Honda and M. Takeichi *Cell 149*, 1084–1097 (2012)

3. Mechanics of cell intercalation: Polarised Cortical tension

- The « universality » of polarised cortical tension driving cell intercalation

Cortical tension underlies intercalation in mesenchymal cells: Xenopus

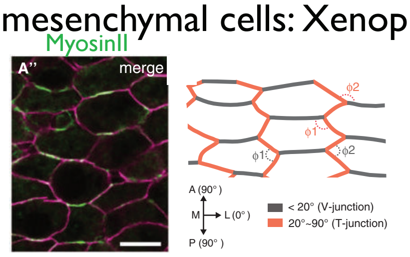


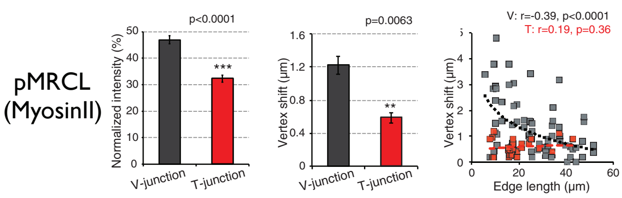
A. Shindo *WIREs Dev Biol*, e293. doi: 10.1002/wdev.293 (2017)

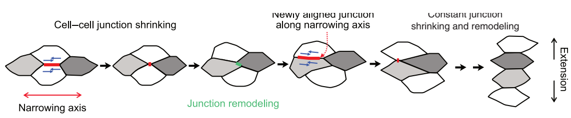
3. Mechanics of cell intercalation: Polarised Cortical tension

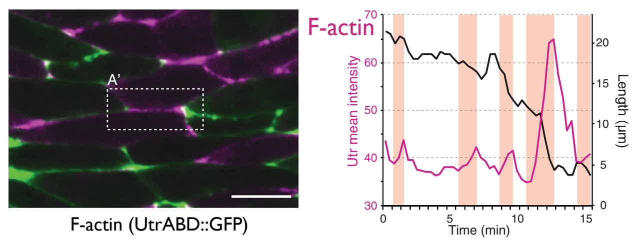
- The « universality » of polarised cortical tension driving cell intercalation

Cortical tension underlies intercalation in mesenchymal cells: Xenopus





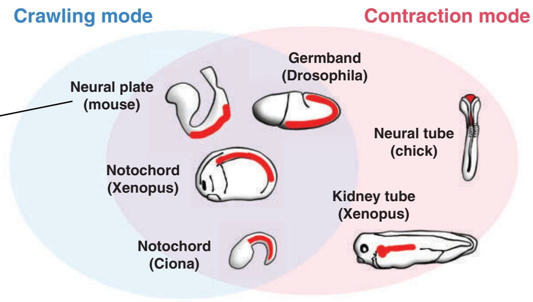




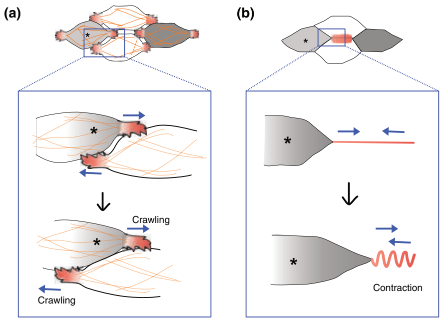
A. Shindo and J. Wallingford Science 343:649-652 (2014)

Cellular Mechanics of Intercalation

- Two force producing modes underly tissue extension in different organisms and tissues



M. Williams et al. A. Sutherland. *Developmental Cell* 29:34–46,(2014)



A. Shindo *WIREs Dev Biol*, e293. doi: 10.1002/wdev.293 (2017)

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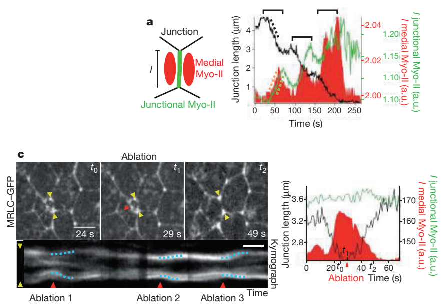
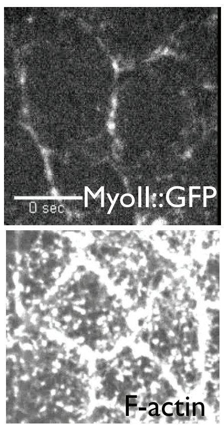
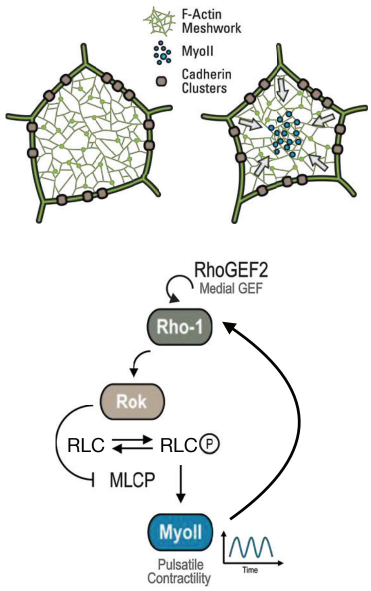
3. Mechanics of cell intercalation: Polarised Cortical tension

- Pulsatile contractile actomyosin drives junction shrinkage



M. Rauzi, PF. Lenne, T. Lecuit. *Nature*. 468:1110-4 (2010)





Martin, Kaschube, Wieschaus, *Nature* 2009
Rauzi, Lenne, Lecuit. *Nature* 2010
Vasquez et al. *JCB* 2014
Munjal et al. *Nature* 2015
Banerjee, Munjal Lecuit &. Rao M *Nature Comm* 2017

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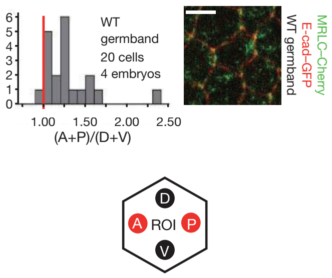
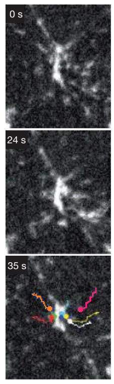
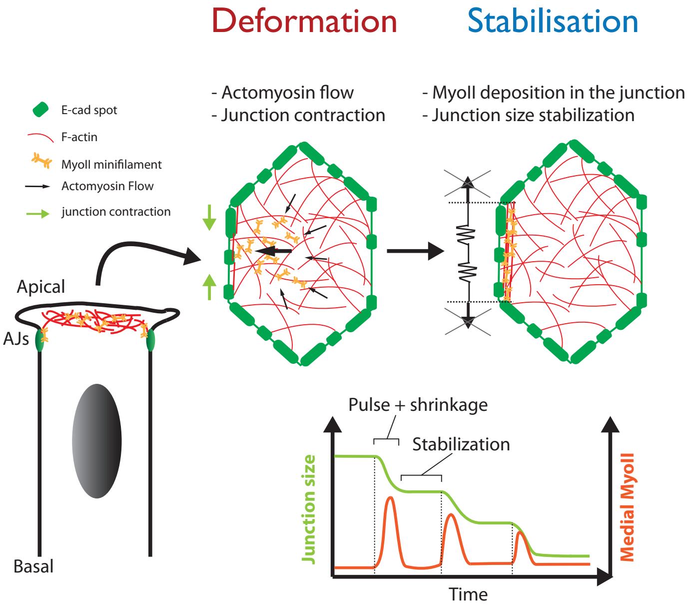
3. Mechanics of cell intercalation: Polarised Cortical tension

- Anisotropic flow of actomyosin orients junction shrinkage
- Sequential deformation and stabilisation of junction length ensures persistent cell intercalation





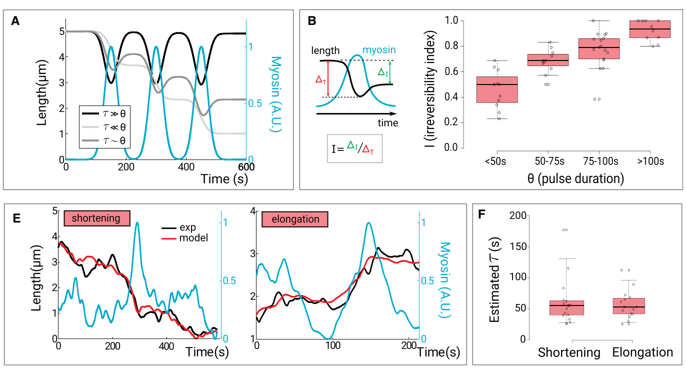


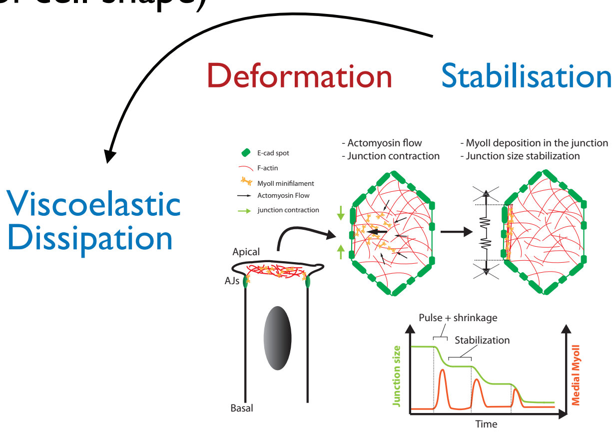
M. Rauzi, PF. Lenne, T. Lecuit. *Nature*. 468:1110-4 (2010)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Viscoelastic dissipation at cell junctions underlies the irreversibility of cell deformation (stabilisation of cell shape)

Maxwell model of viscoelasticity: τ :dissipation time scale
θ : pulse duration





-E-cadherin turnover?

-Cortical actomyosin turnover?

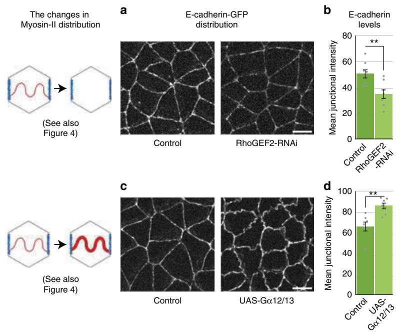
M. Rauzi, PF. Lenne, T. Lecuit. *Nature*. 468:1110-4 (2010)

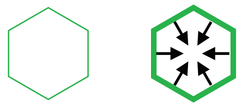
Clément R, Dehapiot B, Collinet C, T. Lecuit, PF. Lenne *Curr Biol*. 27:3132-3142 (2017)

3. Mechanics of cell intercalation: Polarised Cortical tension

- Differential effect of tensile and shear stress on E-cadherin dynamics

1. tensile stress stabilises E-cadherin

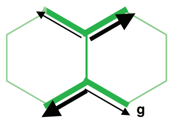


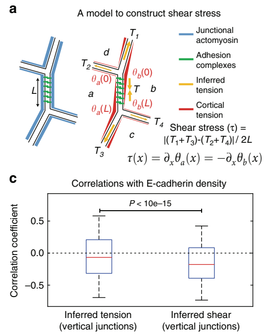


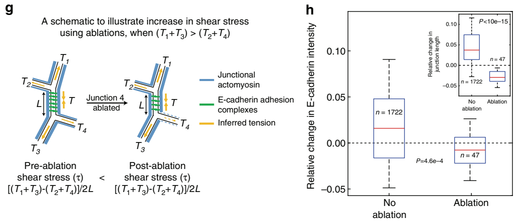
- Need to explore further the potential link between shear and viscoelastic dissipation at cell junctions
- See Course 14 Nov 2017 on Adhesion

2. shear stress de-stabilises E-cadherin

- Inferred shear at cell junctions anti-correlates with E-cadherin density
- Causal effect of shear: increase in shear (following ablation) leads to reduced E-cadherin density although junction length is reduced (no dilution effect).



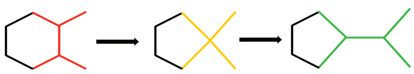




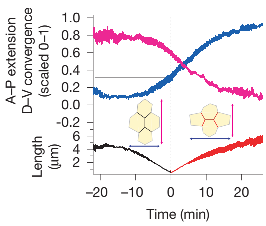
Kale GR, Yang X, Philippe JM, Mani M, Lenne PF, Lecuit T. *Nat Commun*. 9(1):5021. doi: 10.1038/s41467-018-07448-8. (2018)

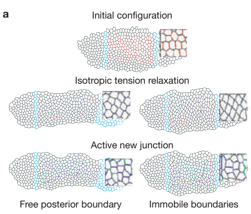
3. Mechanics of cell intercalation: Polarised Cortical tension

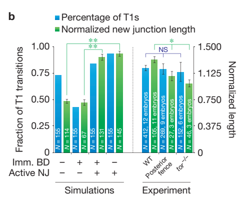
- Pulsatile contractile actomyosin drives junction extension



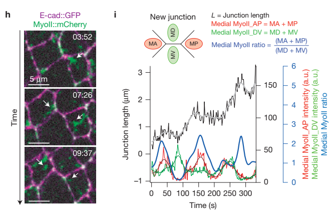
- Local extension is mostly associated with junction growth
- Fixed boundaries prevent cell intercalation when modelling isotropic tension relaxation
- Active new junction growth rescues intercalation within fixed boundaries

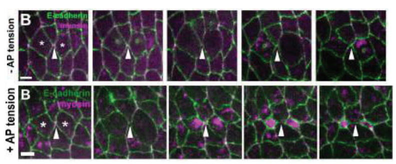


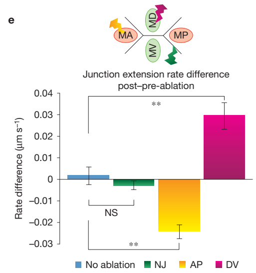




- Polarised Actomyosin pulses correlate with and are required for steps of junction growth.







Other mechanisms:

- Myosin-II depletion in new junction (mediated by PTEN): Bardet P-L et al, and Y. Bellaïche *Dev Cell* 25:534-546. (2013)
- E-cadherin glycosylation (?) Zhang et al. J. Grosshans. *Dev. Biol*. 390:208–220 (2014)

C. Collinet et al. T. Lecuit. *Nature Cell Biol*. 17:1247-58. DOI: 10.1038/ncb3226 (2015)

Yu JC, Fernandez-Gonzalez R:. *Elife* 5. pii: e10757. (2016)

Hara Y, Shagirov M, Toyama Y: *Curr Biol* 26:2388-2396 (2016)

Plan

1. Introduction: convergence/extension movements
   cell intercalation and cell division

2. Mechanics of intercalation: cell protrusions
3. Mechanics of intercalation: cortical tension

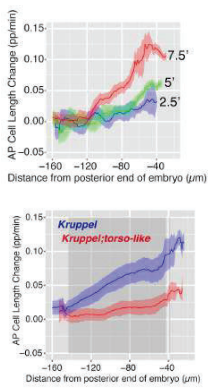
4. Tissue interactions

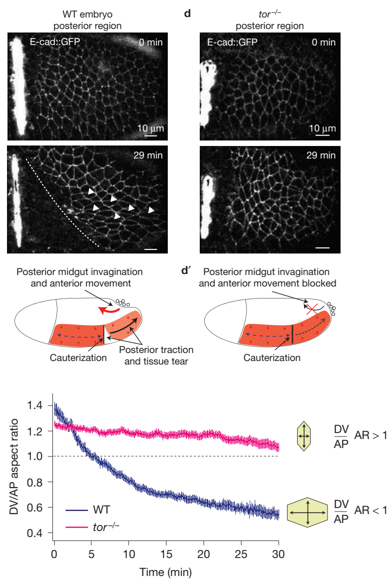
5. Roles of cell division in tissue extension

6. Planar polarisation of cell behaviours

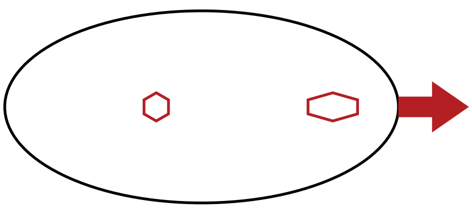
4. Mechanical tissue interactions: non-locality

- Embryonic axis elongation in *Drosophila* requires pulling forces acting at tissue boundaries





- Cells are stretched along the anteroposterior axis: Cell deformation and tissue tearing.
- Cell stretching depends on the posterior endoderm

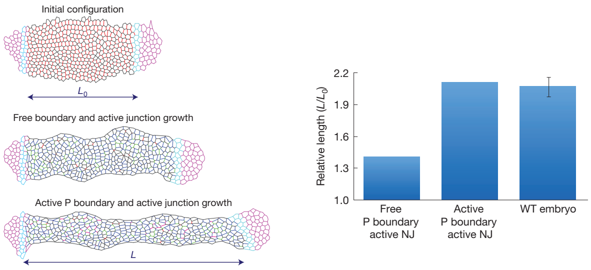


C. Collinet et al. T. Lecuit. *Nature Cell Biol*. 17:1247-58. DOI: 10.1038/ncb3226 (2015)

C. Lye and B. Sanson. PLOS Biology | DOI:10.1371/journal.pbio.1002292 (2015)

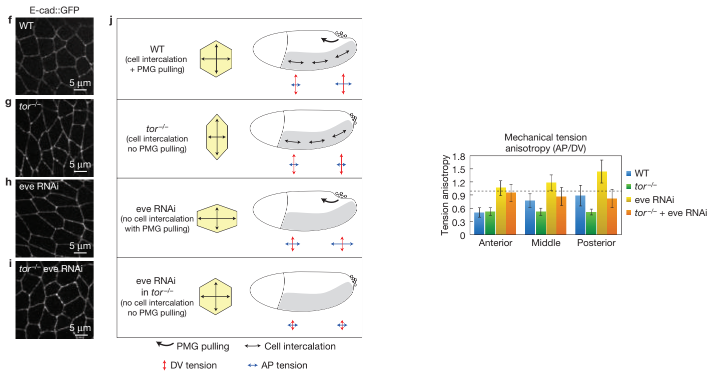
4. Mechanical tissue interactions: non-locality

- Embryonic axis elongation in *Drosophila* requires pulling forces acting at tissue boundaries



  - Simulations: Active (pulling) posterior boundary increases tissue extension

  - Ablation experiments reveal tissue level tension acting in the posterior of the embryo

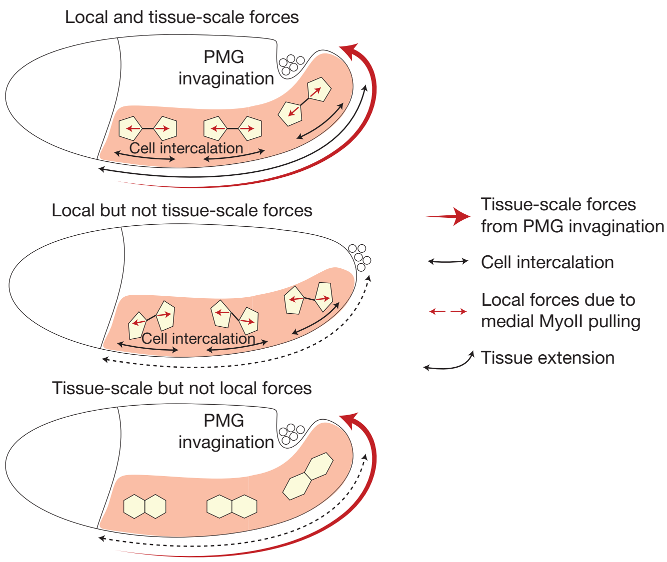


C. Collinet et al. T. Lecuit. *Nature Cell Biol*. 17:1247-58. DOI: 10.1038/ncb3226 (2015)

4. Mechanical tissue interactions: non-locality

- Embryonic axis elongation in *Drosophila* requires pulling forces acting at tissue boundaries

- Tissue scale pulling forces orient junction growth associated with cell intercalation.
- Polarized local and non-local stresses unsure viscous flow of tissue along the antero-posteriro axis.

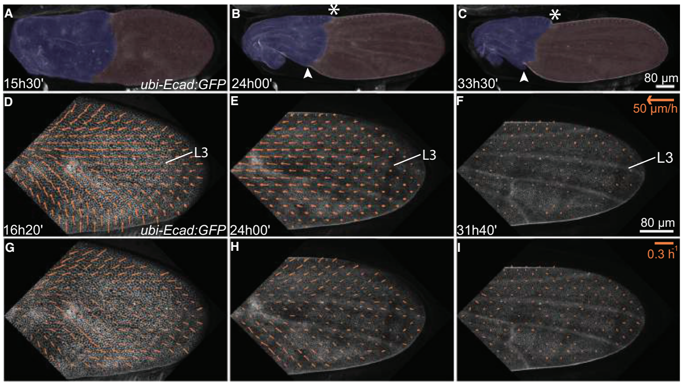


C. Collinet et al. T. Lecuit. *Nature Cell Biol*. 17:1247-58. DOI: 10.1038/ncb3226 (2015)

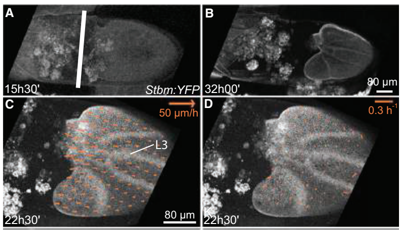
C. Lye and B. Sanson. PLOS Biology | DOI:10.1371/journal.pbio.1002292

4. Mechanical tissue interactions: non-locality

- Proximodistal extension of the *Drosophila* wing: proximal contraction and distal mechanical anchoring/coupling



- Cellular flows are oriented along the proximo-distal axis.
- Active contraction of the proximal hinge tissue (blue) blocks cellular flow and axis elongation.

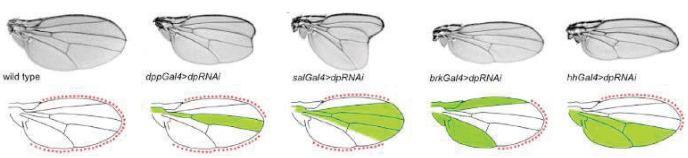


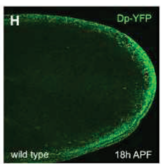
B. Aigouy et al. F. Jülicher and S. Eaton. *Cell* 142, 773–786 (2010)

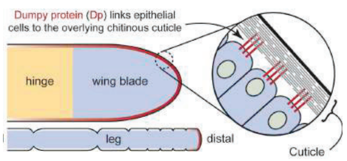
4. Mechanical tissue interactions: non-locality

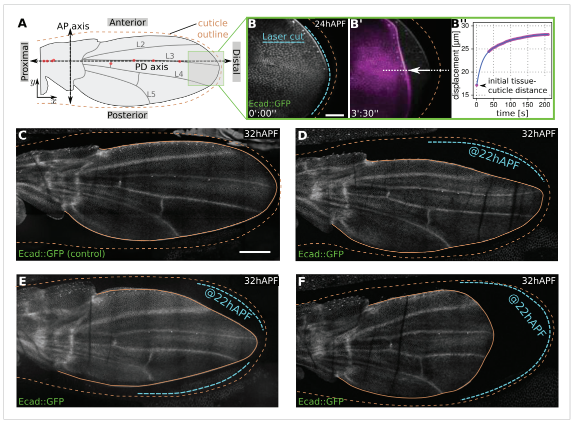
- Wing shape: Proximodistal extension of the *Drosophila* wing.
- Proximal contraction and distal mechanical anchoring/coupling

- Mechanical coupling at the distal end of the wing by the ECM (extra cellular matrix) is required for axis elongation
- The pattern of mechanical coupling at the distal end of the wing shapes the wing







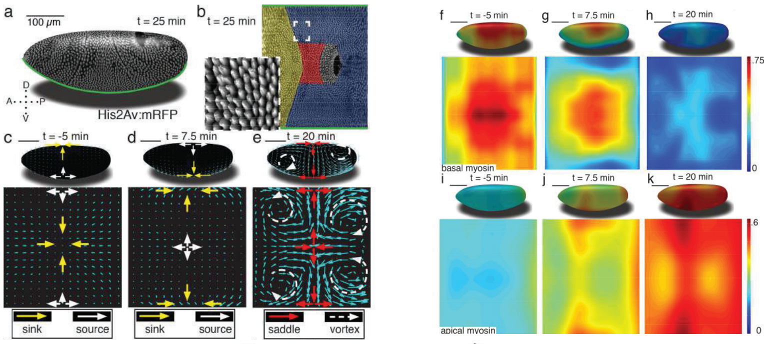


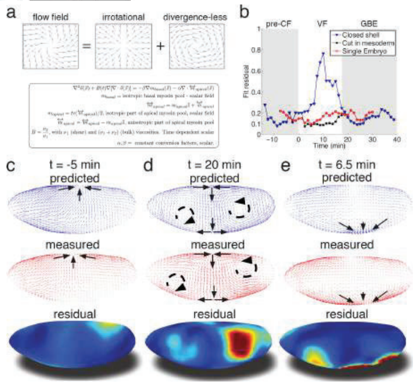
R. Ray et al., B. Thompson. *Developmental Cell* 34, 310–322 (2015)

R. Etournay et al. F. Jülicher and S. Eaton. *eLife* 4:e07090. (2015)

4. Mechanical tissue interactions: non-locality

- Prediction of large scale tissue flows from the pattern of actomyosin contractility





- Viscous flow emerge from gradients of contractility and stress in the basal and apical regions of cells: eg. ventral depletion of Myosin-II at the base causes dorsal ward flow which behaves as a « sink ».
- Non-locality of stress stems from:

1. non-compressibility of material and local forcing.
2. mechanical feedbacks (eg. ventral to lateral ectoderm).

Streichan et al. B. Shraiman *eLife*;7:e27454. (2018)

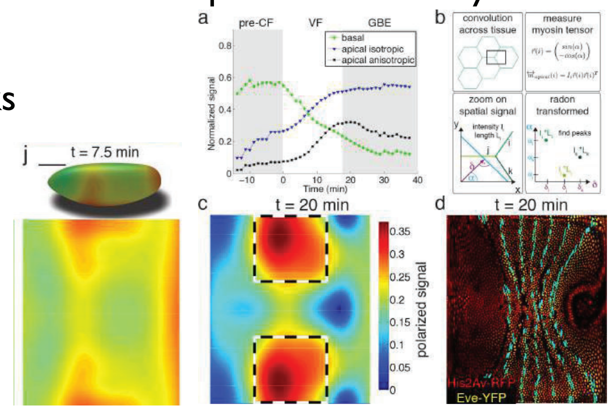
M. Dicko et al, B. Sanson and J. Etienne. PLOS Computational Biology | https://doi.org/10.1371/journal.pcbi.1005443 (2017)

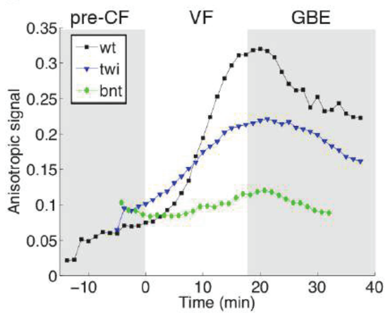
4. Mechanical tissue interactions: non-locality

- Prediction of large scale tissue flows from the pattern of actomyosin contractility

Non-locality via mechanical feedbacks across tissues: MyosinII anisotropy

Myosin-II anisotropic distribution in the lateral ectoderm is reduced when mesoderm invagination is affected





Streichan et al. B. Shraiman *eLife*;7:e27454. (2018)

see also: Butler LC et al. and B. Sanson. *Nature Cell Biology* 11:859–864.

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Plan

1. Introduction: convergence/extension movements
   cell intercalation and cell division

2. Mechanics of intercalation: cell protrusions
3. Mechanics of intercalation: cortical tension

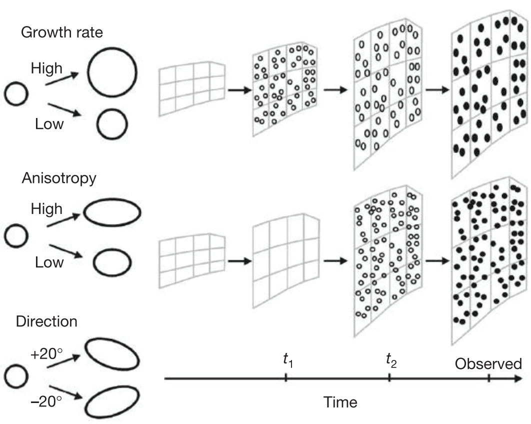
4. Tissue interactions

5. Roles of cell division in tissue extension

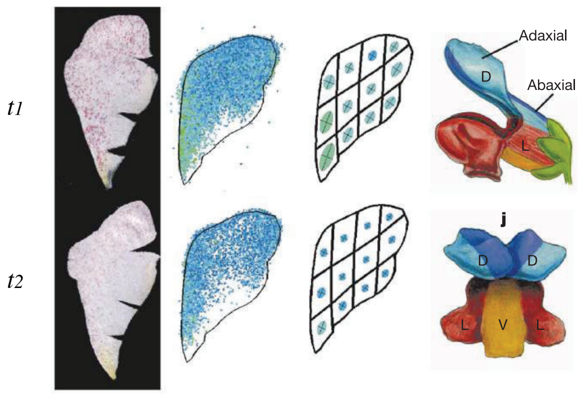
6. Planar polarisation of cell behaviours

5. Roles of cell division during tissue extension

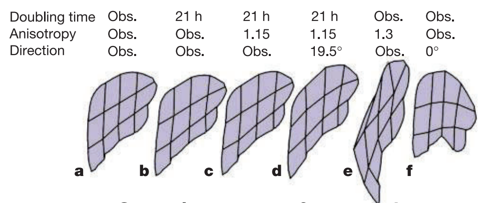
- Growth (cell growth and cell division) underlies tissue shape in plants



Growth parameters



Observations: clonal analysis



Simulations of growth

Rolland-Lagan AG. et al. and Coen E. *Nature*. 422:161. (2003)

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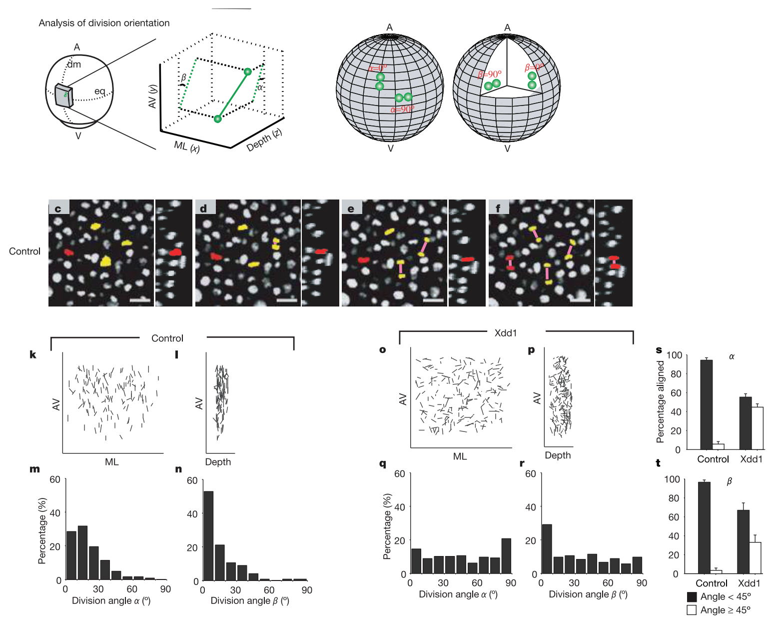
5. Roles of cell division during tissue extension

- In animals, though cells move, cell division is also essential for tissue morphogenesis, in particular tissue extension

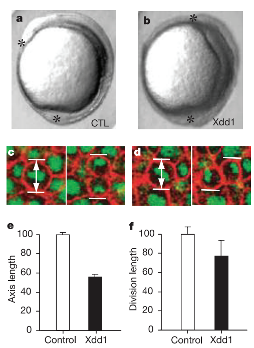
- Cell division orientation
- Tissue fluidisation
- Interplay between cell division and cell intercalation

5. Roles of cell division during tissue extension

- Cell division orientation



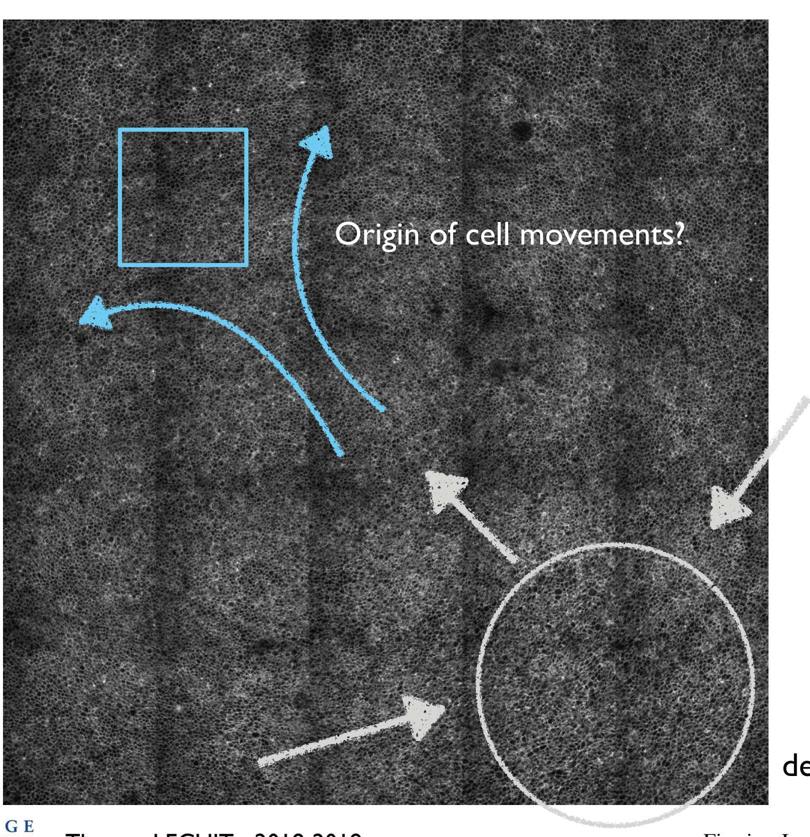
- Embryonic axis elongation in the Zebrafish requires oriented cell division.

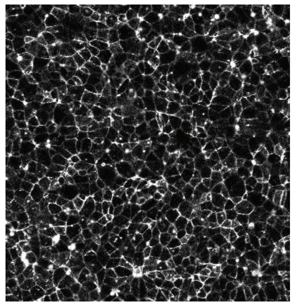


Y. Gong, C. Mo and S. Fraser. *Nature*. 430:689-693 (2004)

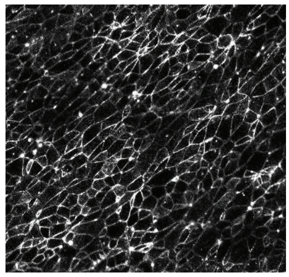
5. Roles of cell division during tissue extension

- Tissue fluidisation by cell division





Myosin-II

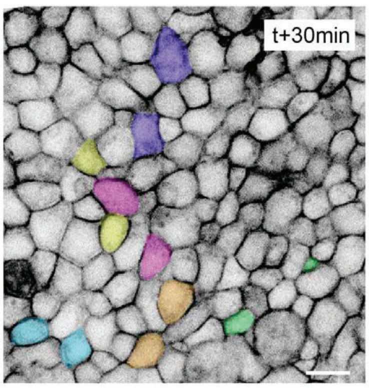


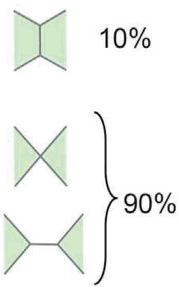
Convergence/Extension driven by Myosin-II dependent cell intercalation

Firmino J. et al, and Gros J. *Dev. Cell*. 36:249. 2016

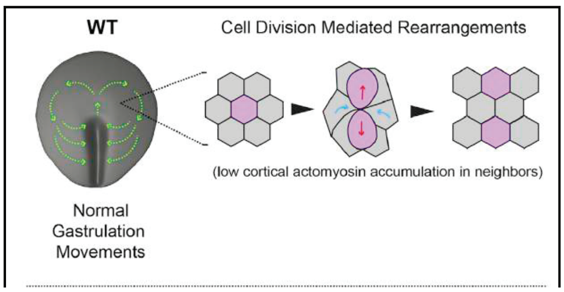
5. Roles of cell division during tissue extension

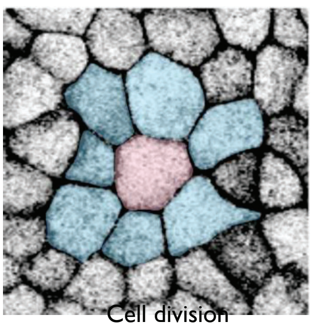
- Tissue fluidisation by cell division



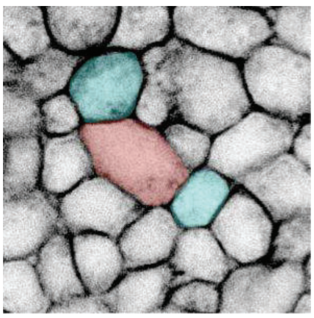


Associated with cell intercalation





Cell division without cell intercalation

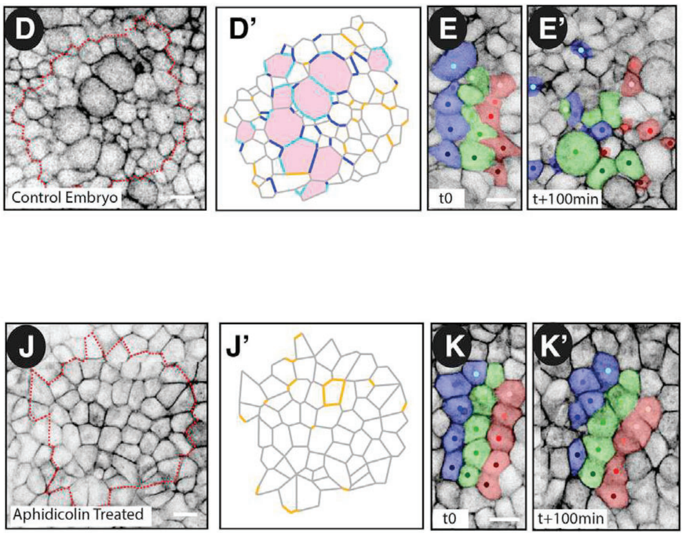


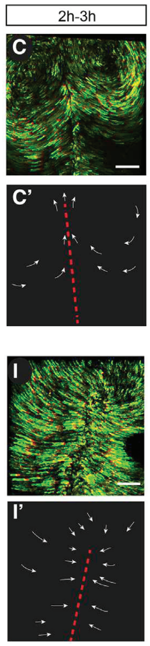
Intercalary cell division

Firmino J. et al, and Gros J. *Dev. Cell*. 36:249. 2016

5. Roles of cell division during tissue extension

- Contribution of intercalary cell divisions to cell movements





Inhibitor of DNA replication/cell cycle (arrest in S phase)

Firmino J. et al, and Gros J. *Dev. Cell*. 36:249. 2016

5. Roles of cell division during tissue extension

Define Strain tensor (**G**) characterising tissue growth and morphogenesis.
G is decomposed into Geometric (**S**) and Topological (**T**) strain components
All strain tensors are dimensionless, spatially averaged based on statistics of centroid links, and vanish for translation and rotation).

- Geometric strain tensor: Cell shape (**S**)
- Topological strain tensor: Cell Division (**D**) + Intercalation (**R**) +Apoptosis (**A**)

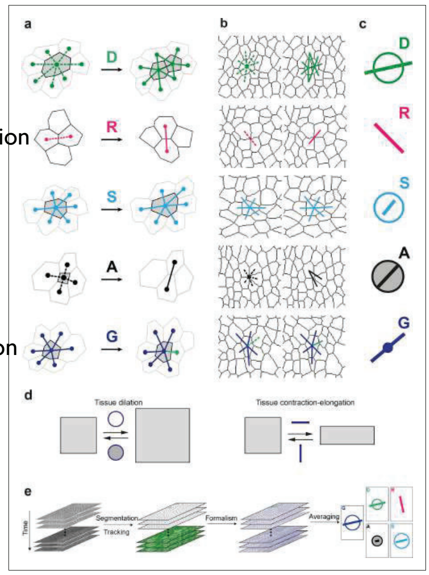
Compute strain rates (1/h) (averaged over time interval).

$$\mathbf{G} = \mathbf{D} + \mathbf{R} + \mathbf{S} + \mathbf{A}$$

Tensorial definition of strain with amplitude , anisotropy and direction

Cell: Division, Intercalation, Shape, Death

Tissue Deformation



Guirao et al. K. Sugimura, F. Graner and Y. Bellaïche. *eLife* 4:e08519 (2015)
F. Graner et al. *European Physical Journal E* 25:349–369 (2008)

see also: R. Etournay et al. F. Jülicher and S. Eaton. *eLife* 4:e07090. (2015)

5. Roles of cell division during tissue extension

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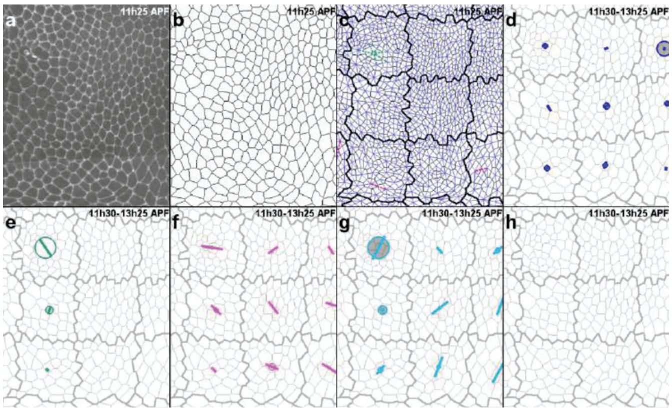
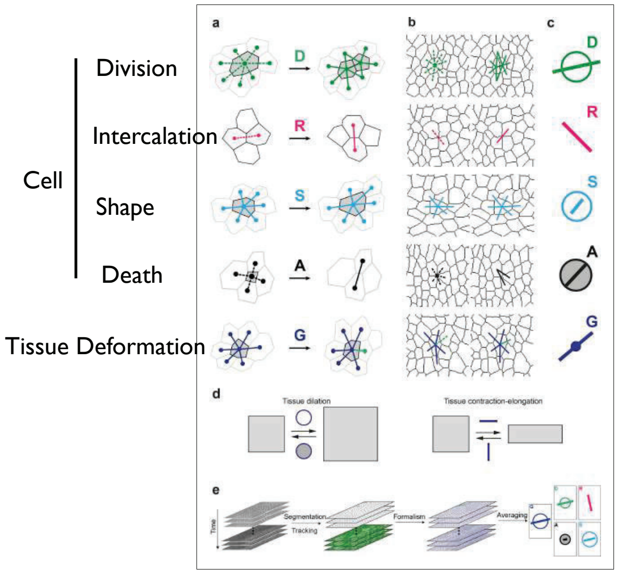


Tensorial definition of strain with amplitude , anisotropy and direction



Guirao et al. K. Sugimura, F. Graner and Y. Bellaïche. *eLife* 4:e08519 (2015)

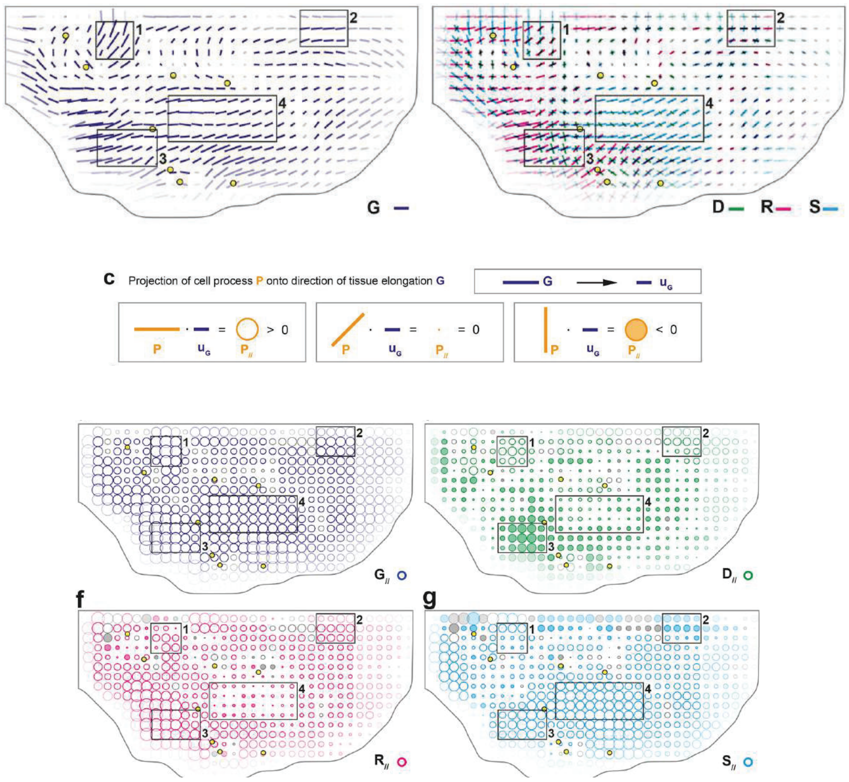
F. Graner et al. *European Physical Journal E* 25:349–369 (2008)

see also: R. Etournay et al. F. Jülicher and S. Eaton. *eLife* 4:e07090. (2015)

5. Roles of cell division during tissue extension

- Contributions of cell division, intercalation and cell shape changes to tissue deformation vary across the tissue

- In some cases (region 1), cell **division plays a positive contribution to local tissue strain.**
- But in other cases (region 3) cell **division contributes negatively to local tissue strain,** while cell rearrangements have a major role.



Guirao et al. K. Sugimura, F. Graner and Y. Bellaïche. *eLife* 4:e08519.(2015)

5. Roles of cell division during tissue extension

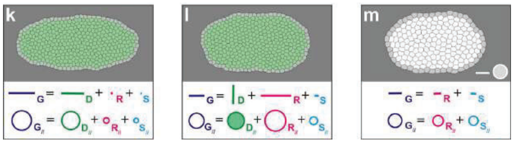
Comparaison of tissue deformation in control tissues (G_{wt}) and tissues in which cell division is blocked (G_{trbl}):
$\Delta G = G_{wt} - G_{trbl}$

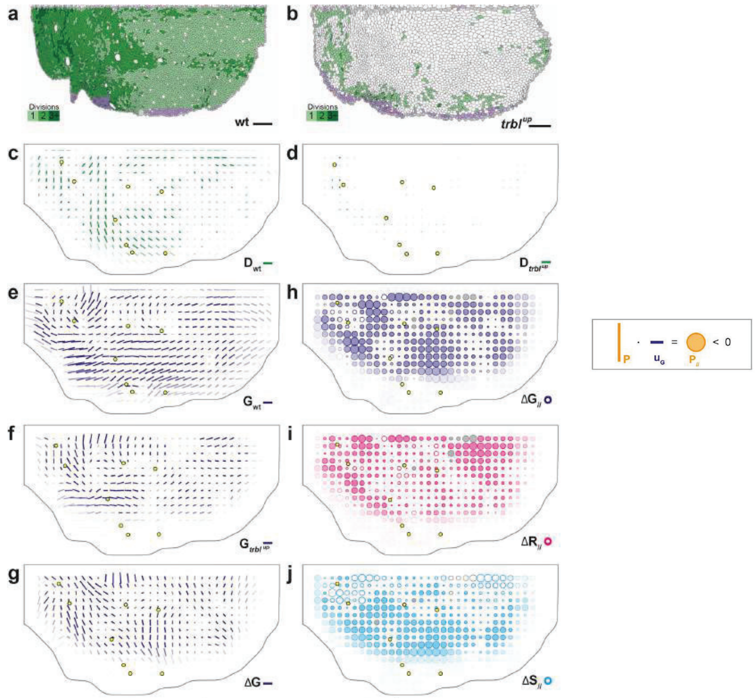
$\Delta G_{//}$: projection onto principal axis of strain in the wild-type. Measures whether block of cell division increases or counteracts tissue extension.

Throughout the tissue, block of cell division reduces tissue extension, even in regions where cell division is not oriented along axis of tissue deformation.

Blocking cell division affects cell intercalation.

Cell division drives tissue extension via its orientation (tensorial property) and cell proliferation per se.



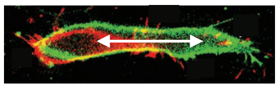


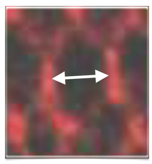
Guirao et al. K. Sugimura, F. Graner and Y. Bellaïche. *eLife* 4:e08519.(2015)

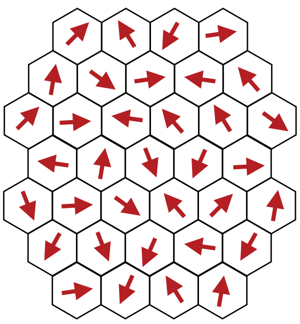
6. Planar polarisation of cell behaviours

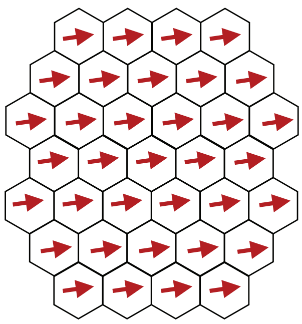
Planar cell polarisation entails:

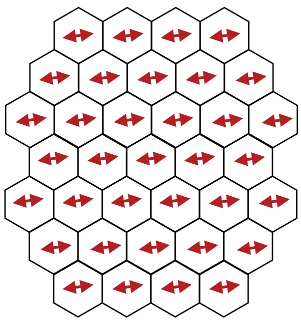
- Local symmetry breaking
- Cell-cell coupling/coordination









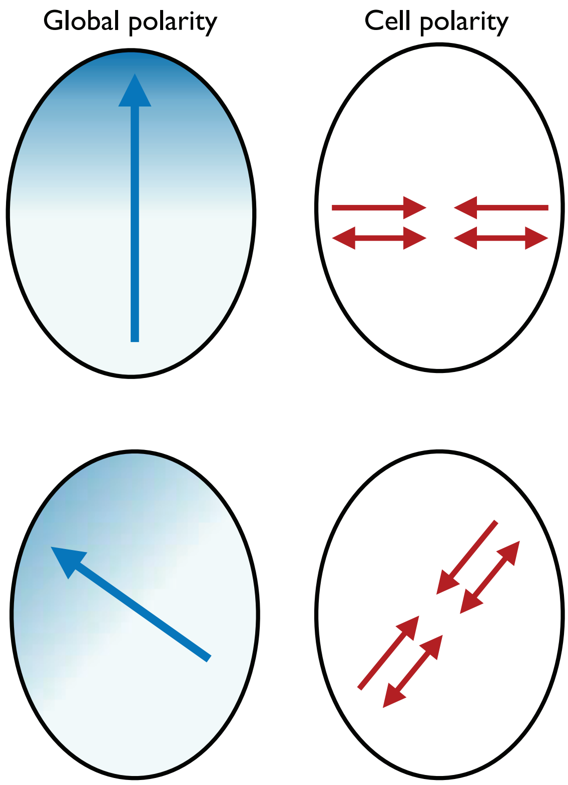


- Local symmetry breaking
- Cell-cell coupling/coordination
- Unipolar or Bipolar Polarity

6. Planar polarisation of cell behaviours

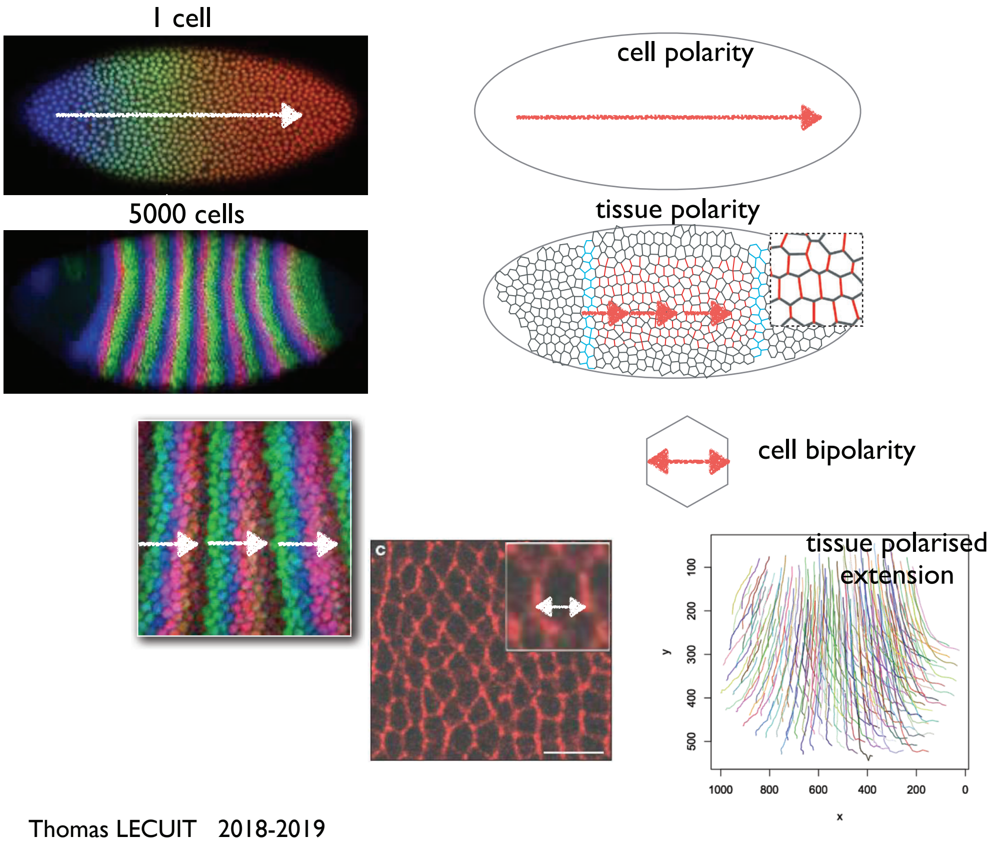
Planar cell polarisation entails:

- Local symmetry breaking
- Cell-cell coupling/coordination
- Coupling between global information and local information: the primary axis of the embryo must orient cell behaviours



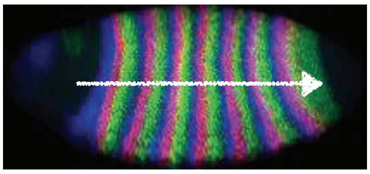
6. Planar polarisation of cell behaviours

- Cascading polarities underly global and local polarity coupling

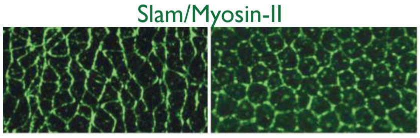


6. Planar polarisation of cell behaviours

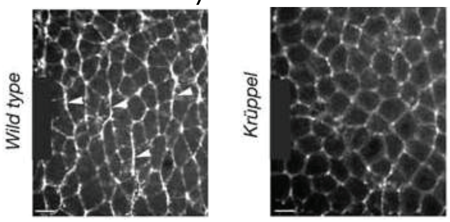
- Embryonic patterning is required for the establishment of cell bipolarity



Slam/Myosin-II

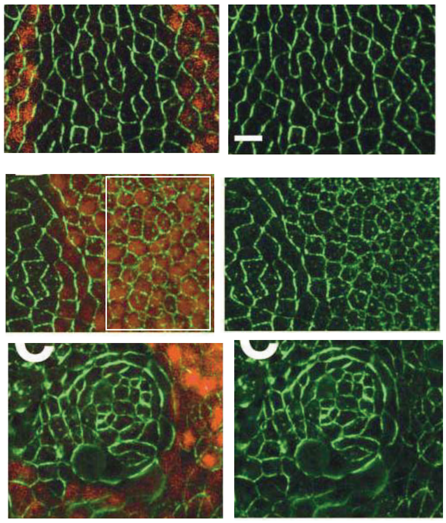


Myosin-II



C. Bertet, L. Sulak and T. Lecuit. *Nature*. 429(6992):667-71. (2004)

Slam/Myosin-II Eve



Eve
mis expression

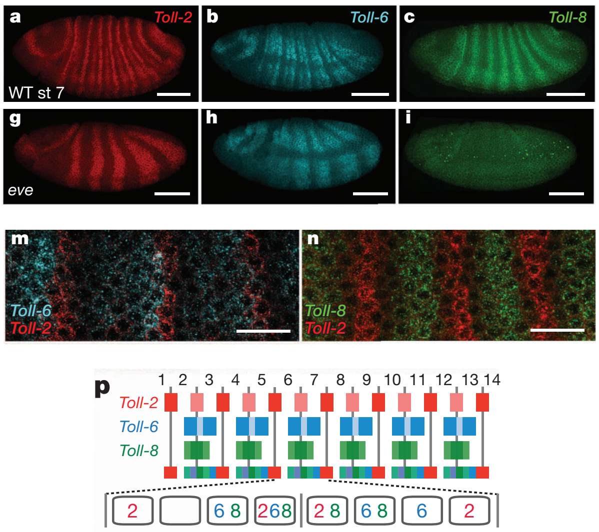
Eve
mis expression

J. Zallen and E. Wieschaus *Developmental Cell*, Vol. 6, 343–355

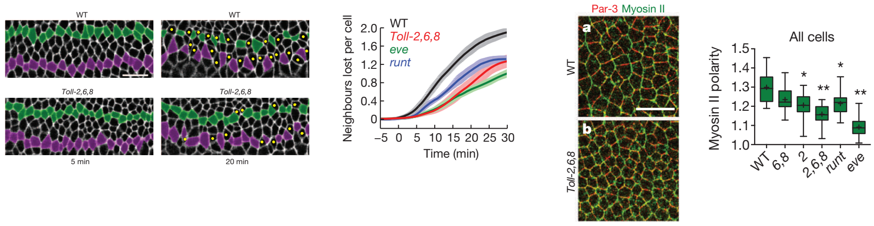
6. Planar polarisation of cell behaviours

- Striped expression of Toll like receptors is required for cell bipolarity

- Toll receptors are regulated by upstream pair-rule genes
- Tolls produce an interfacial information
- This **interfacial information** is an output of positional information



- Tolls are required for Myosin-II polarisation and cell intercalation

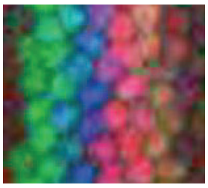


AC Paré, et al. and J. Zallen. *Nature*. 515:523-527 (2014)

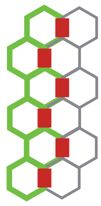
6. Planar polarisation of cell behaviours

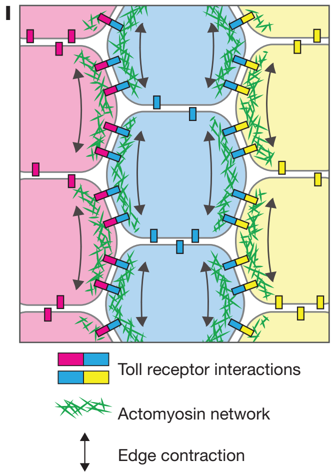
- Striped expression of Toll like receptors is required for cell bipolarity
  - Toll mediated **interfacial information** is an output of positional information
  - Hypothesis: combinatorial information at cell interfaces.

Positional Information



Interfacial Information





AC Paré, et al. and J. Zallen. *Nature*. 515:523-527 (2014)

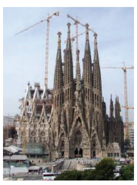
Programmed tissue extension

The spatial program controlling cell intercalation

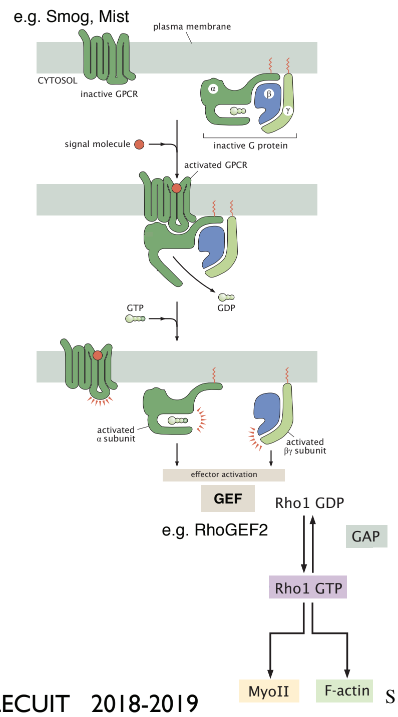
Information (genetics/ biochemistry)

↓

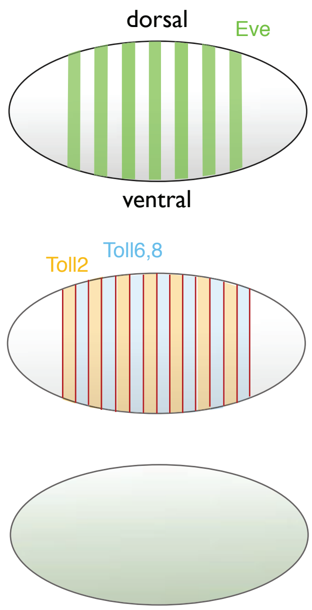
Mechanics



The pathway:
GPCR and G protein signalling underlies Myosin2 activation



The program:
Embryonic prepattern spatially controls signalling

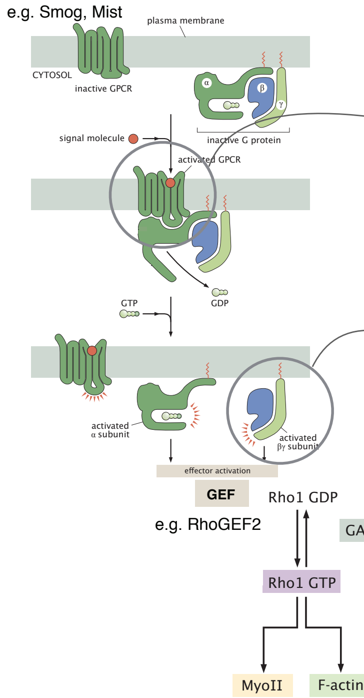


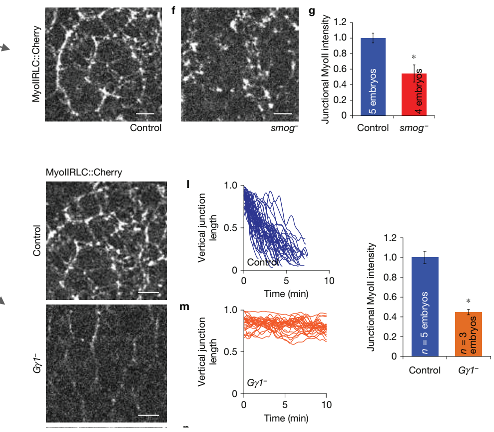
S. Kerridge and A. Munjal et al, and T. Lecuit. *Nat Cell Biol*. 2016 Mar;18(3):261-70
Manning et al. *Sci Signal*. 12;6(301):ra98 (2013)

6. Planar polarisation of cell behaviours

The spatial program controlling cell intercalation

The pathway:
GPCR and G protein signalling underlies
Myosin2 activation

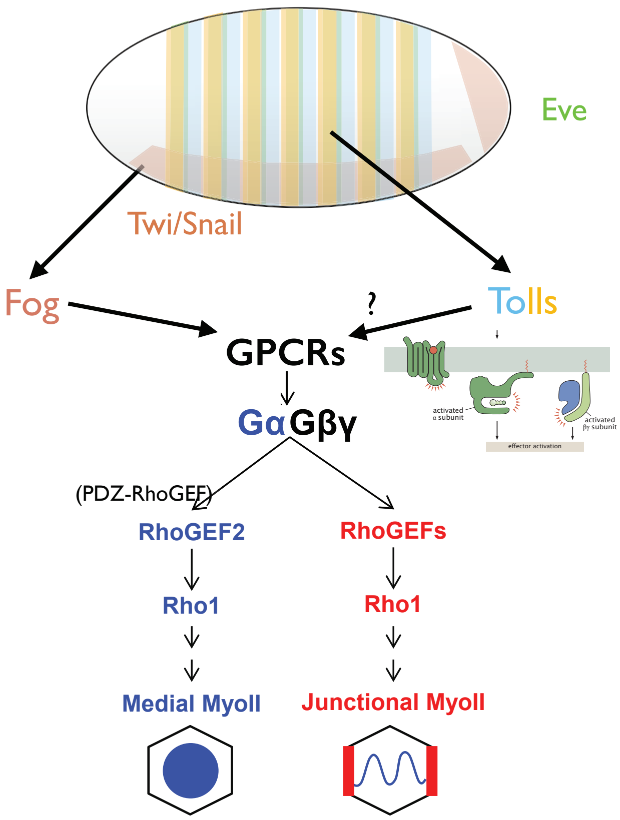




S. Kerridge and A. Munjal et al, and T. Lecuit. *Nat Cell Biol*. 2016 Mar;18(3):261-70

6. Planar polarisation of cell behaviours

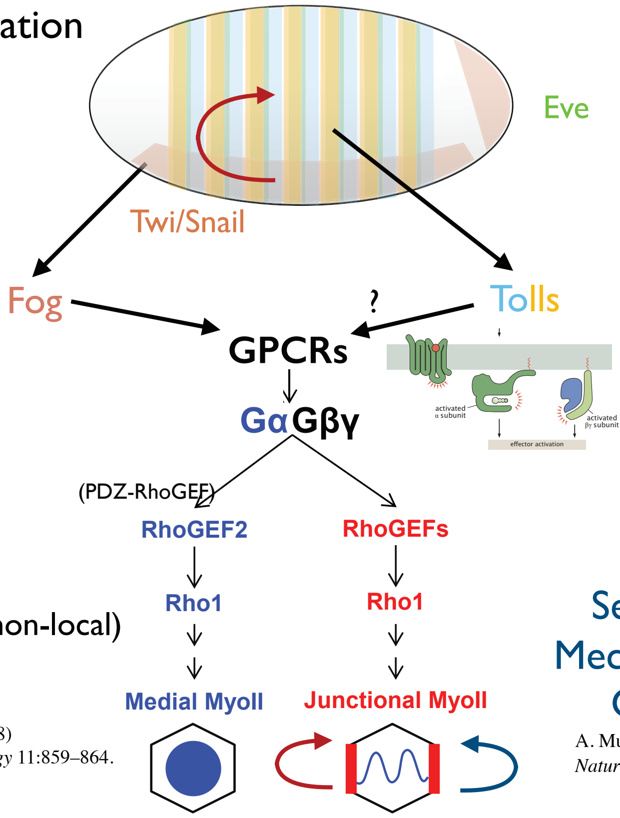
Programmed polarisation of cortical mechanics



S. Kerridge and A. Munjal et al, and T. Lecuit. *Nat Cell Biol*.18(3):261-70 (2016)
Manning et al. *Sci Signal*. 12;6(301):ra98 (2013)

6. Planar polarisation of cell behaviours

Programmed polarisation of cortical mechanics and self-organisation



Mechanical Amplification (local and non-local)

R. Fernandez-Gonzalez et al, J. Zallen. *Developmental Cell* 17, 736–743 (2009)

Streichan et al. B. Shraiman *eLife*;7:e27454. (2018)
Butler LC et al. and B. Sanson. *Nature Cell Biology* 11:859–864.

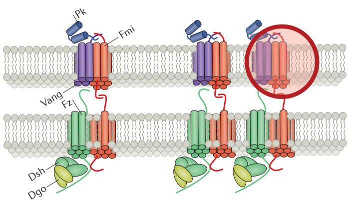
Self-organised Mechano-chemical Oscillations

A. Munjal et al, and T. Lecuit. *Nature*. 524:351-355 (2015)

S. Kerridge and A. Munjal et al, and T. Lecuit. *Nat Cell Biol*.18(3):261-70 (2016)
Manning et al. *Sci Signal*. 12;6(301):ra98 (2013)

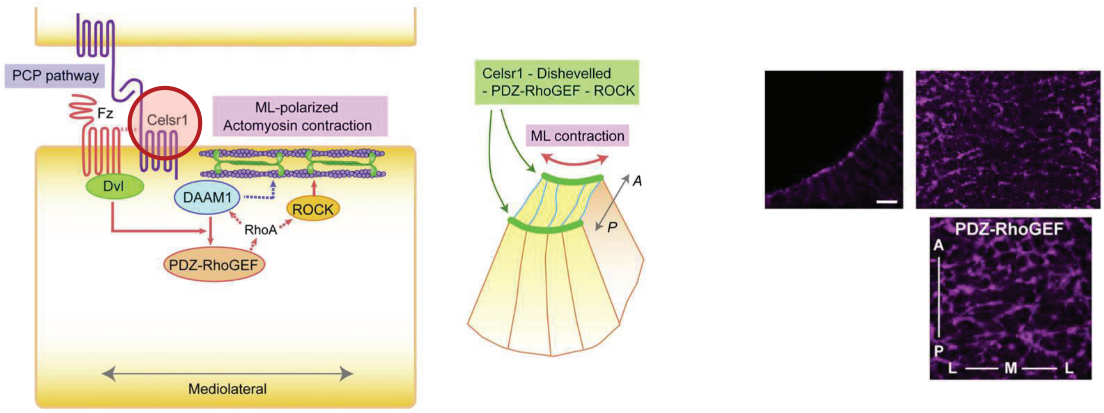
6. Planar polarisation of cell behaviours

Planar polarisation of actomyosin contractility in vertebrates requires activity of the planar cell polarity (PCP) pathway



- The GPCR Fmi/Celsr1 activates the Rho1 pathway

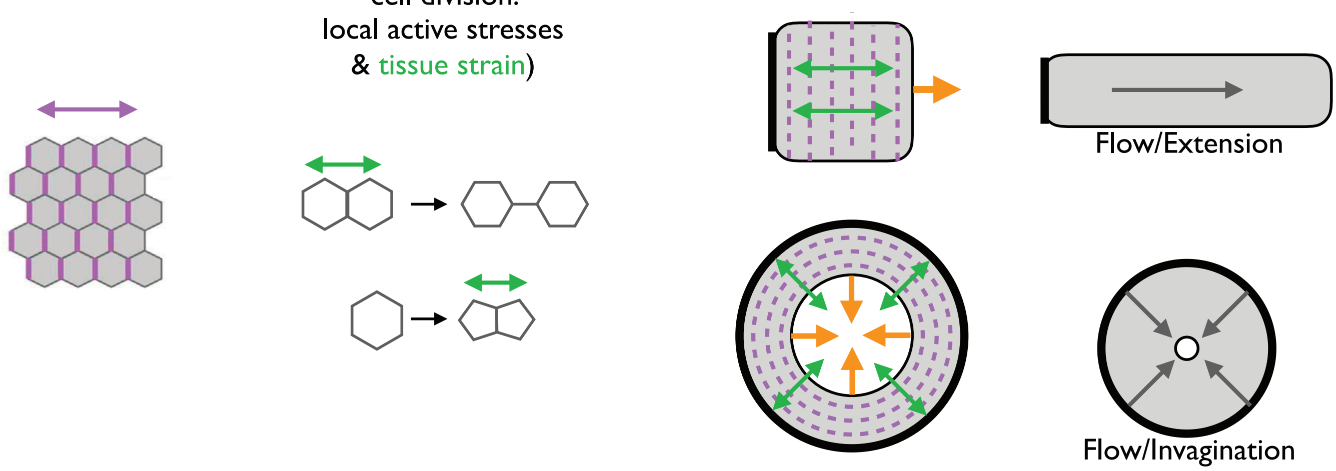
MC. Butler and J. Wallingford. *Nat Rev Mol Cell Biol*. 18(6):375-388. (2017)



T. Nishimura, H. Honda and M. Takeichi *Cell 149*, 1084–1097 (2012)

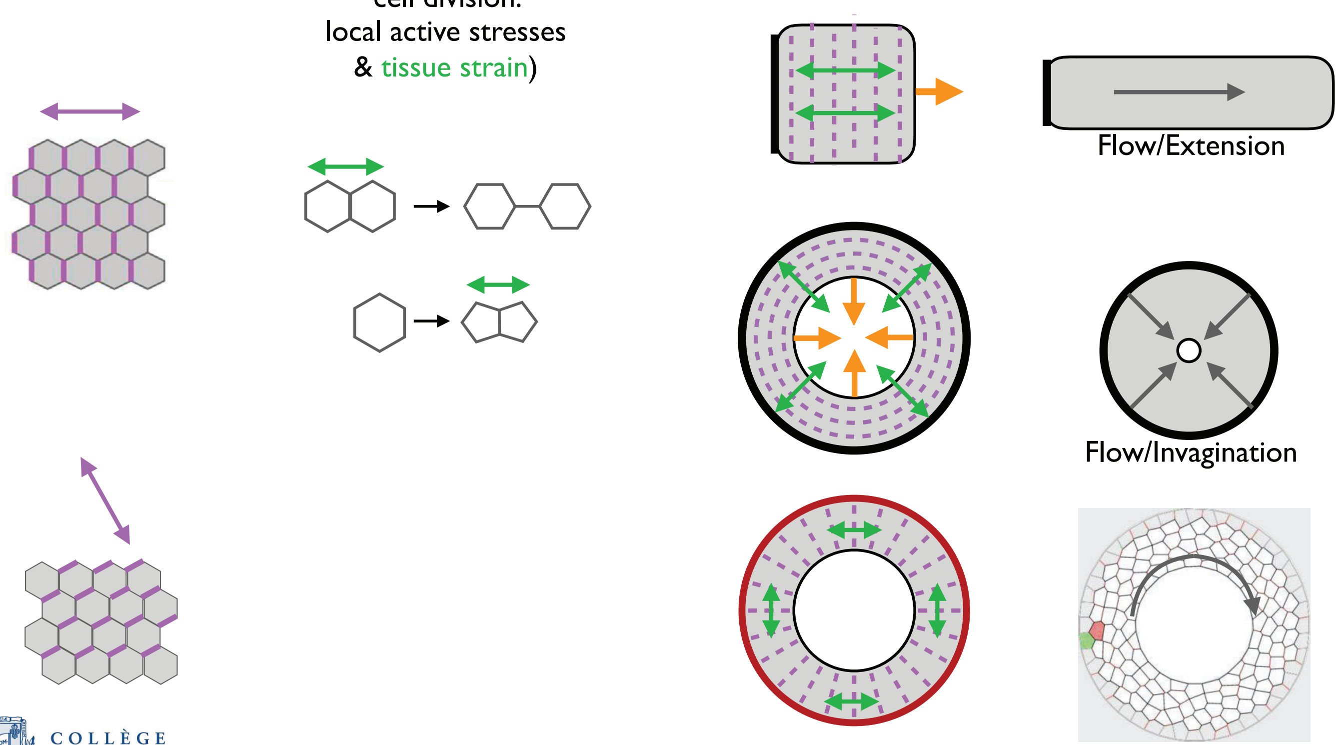
Summary

Orientation of bipolarity + Cell Mechanics (cell intercalation, cell division: local active stresses & tissue strain) + Geometry & Boundary conditions (tissue scale stress, friction, …) = Tissue Morphogenesis



Summary

Orientation of bipolarity + Cell Mechanics (cell intercalation, cell division: local active stresses & tissue strain) + Geometry & Boundary conditions (tissue scale stress, friction, …) = Tissue Morphogenesis

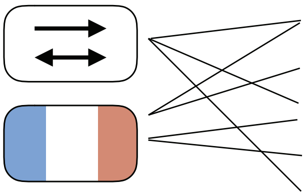


Flow/Rotation

K. Sato et al. and E. Kuranaga. *Nature Communications* | 6:10074 | DOI: 10.1038/ncomms10074

General conclusion

[Polarisation
Regionalisation + Cell Mechanics + Geometry & Boundary conditions = Tissue Morphogenesis]

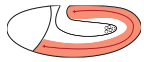


Division
Growth
Contractility
Adhesion
Motility

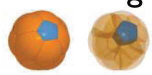
Constraints
Non-local coupling

Buckling/Looping

Flow/Extension



Sorting



General conclusion

Program

Information
(genetics/biochemistry)
↓
Mechanics

Self-Organisation

Information
(mechano-chemistry)
↻

General conclusion