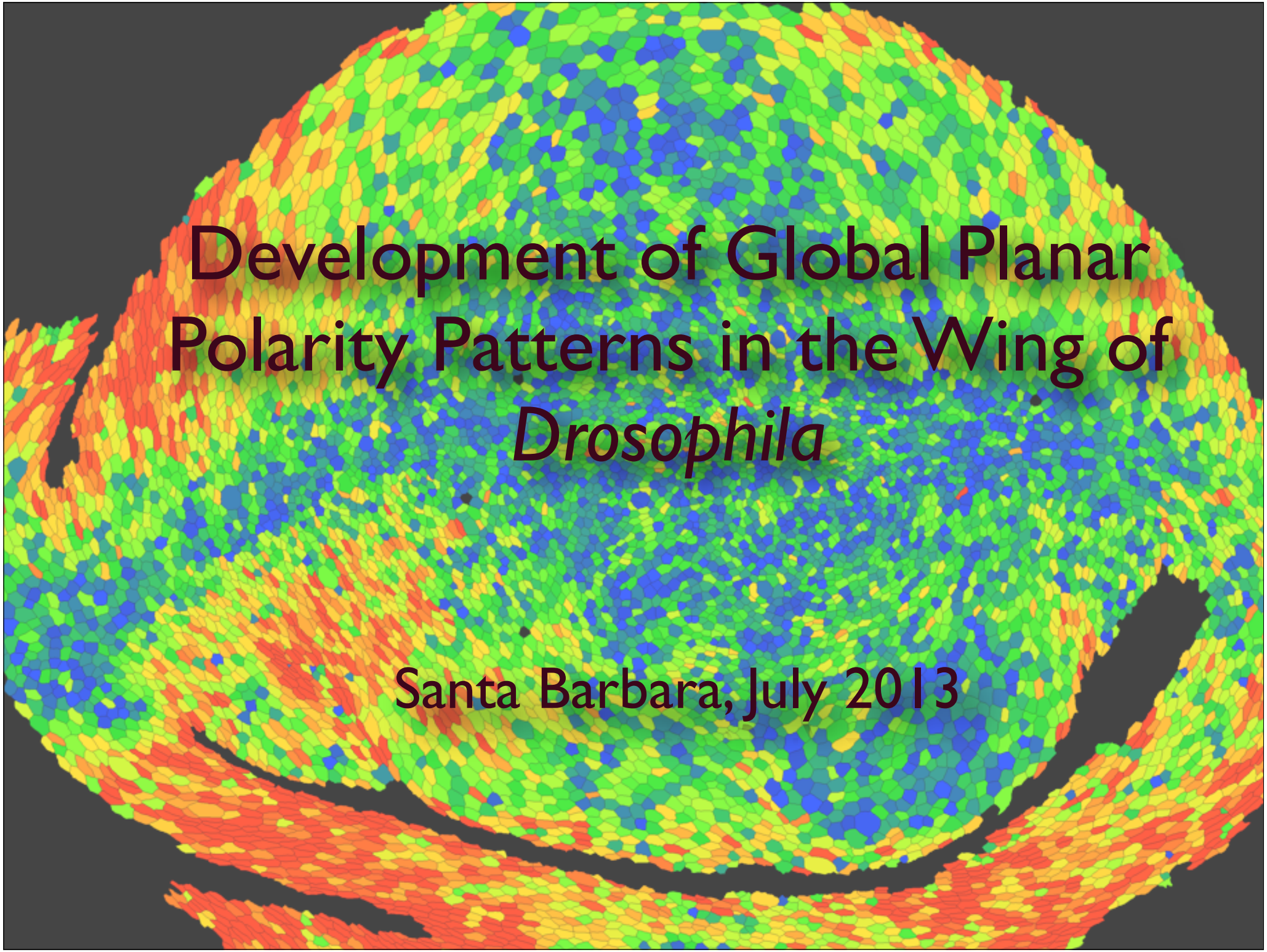
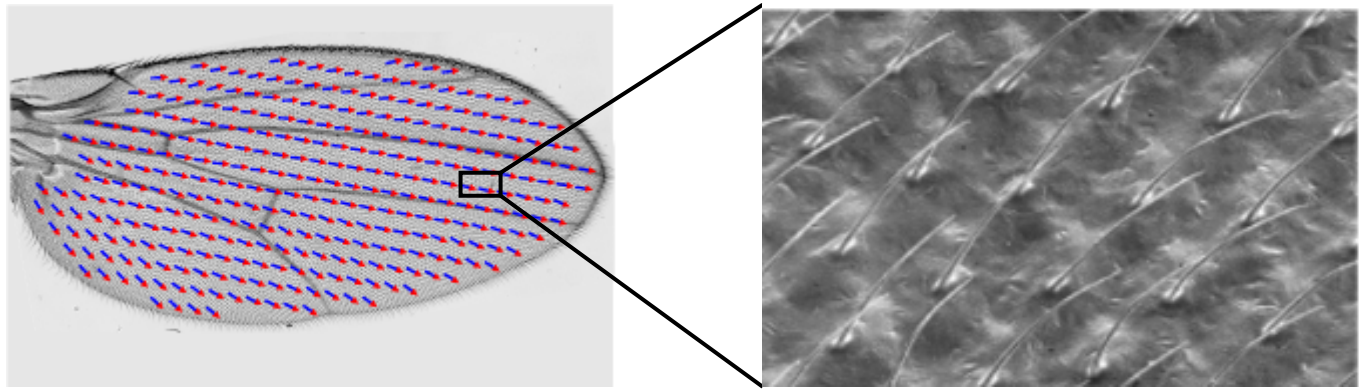
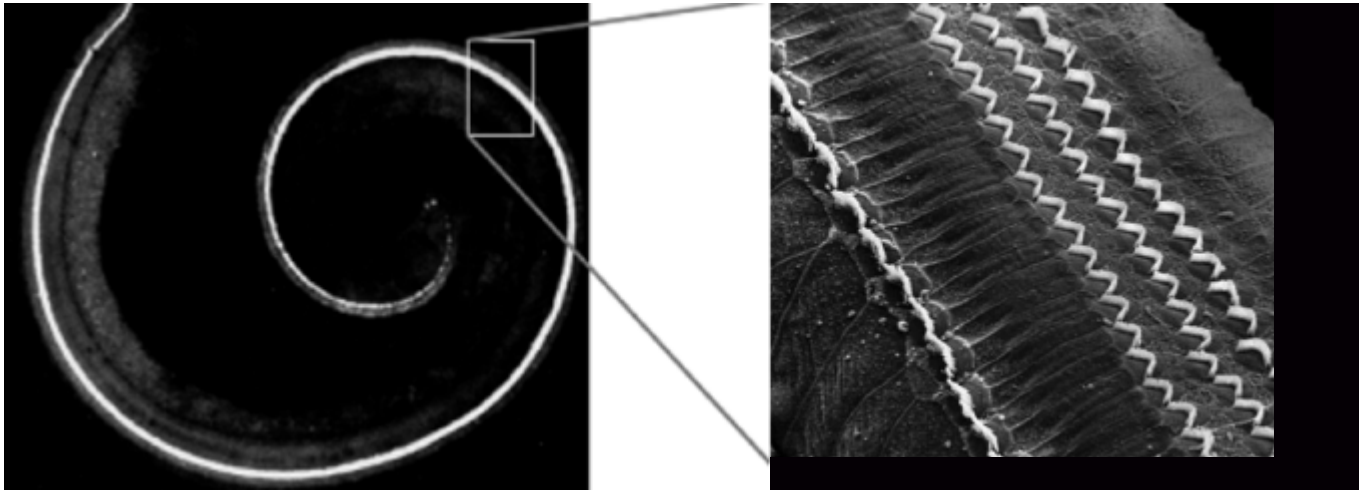


Development of Global Planar Polarity Patterns in the Wing of *Drosophila*

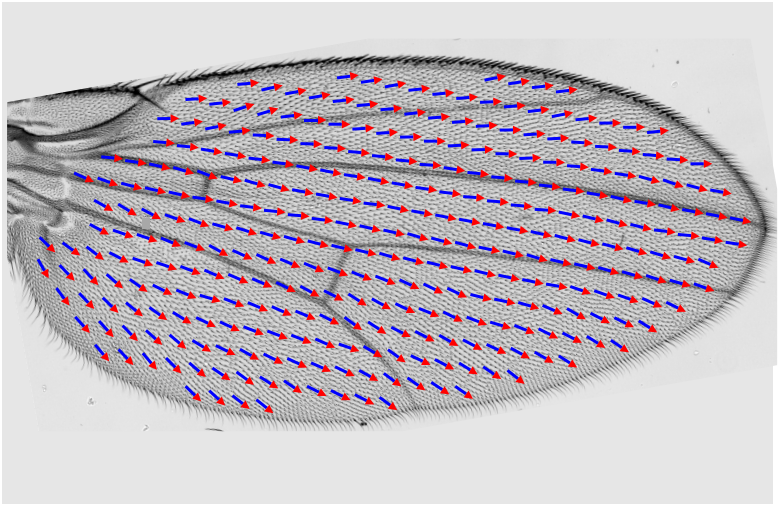
Santa Barbara, July 2013

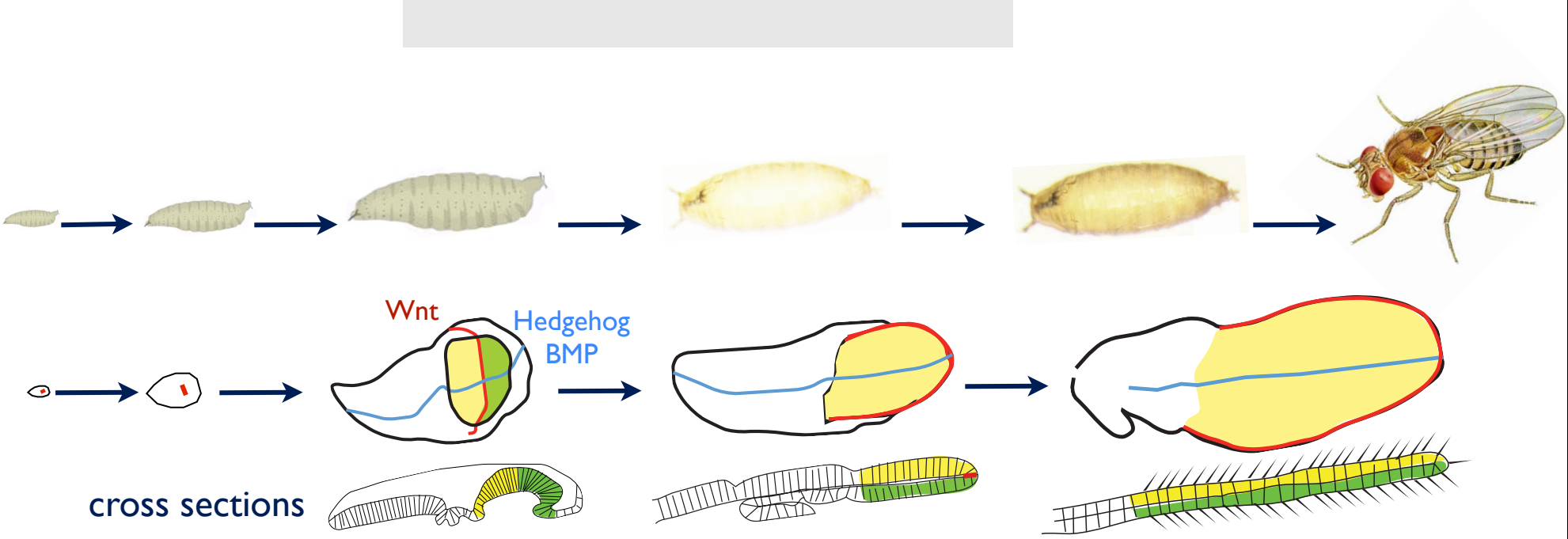
Planar polarity is coordinated with tissue shape





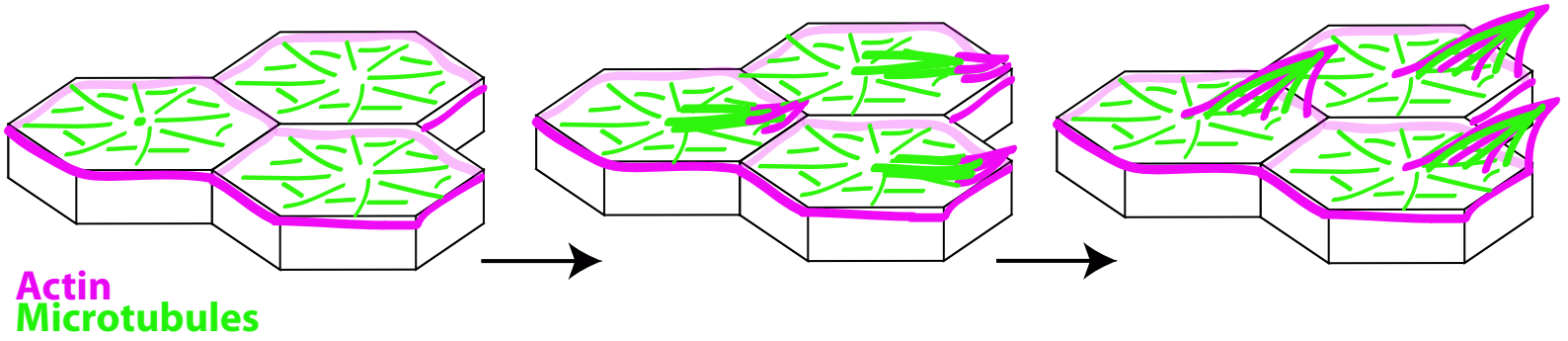
Planar polarized hairs emerge in pupal wings



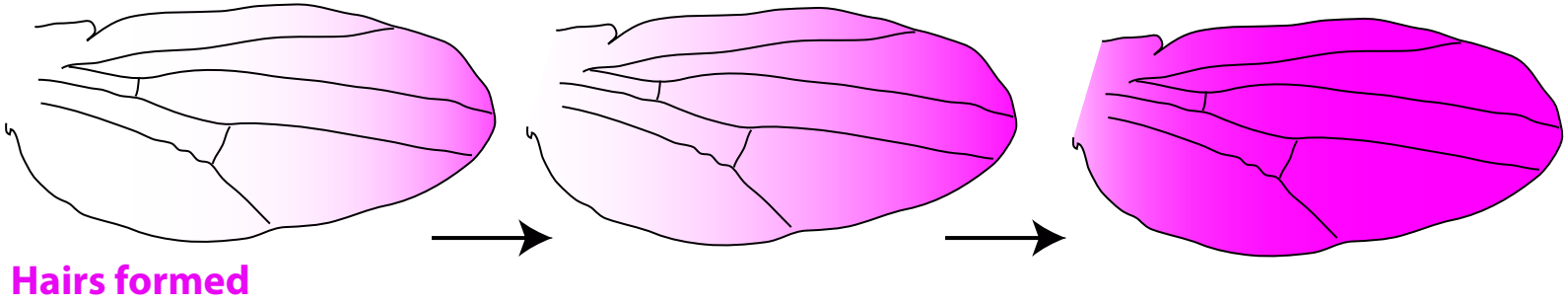


Hairs begin as actin and microtubule-filled outgrowths of the apical membrane

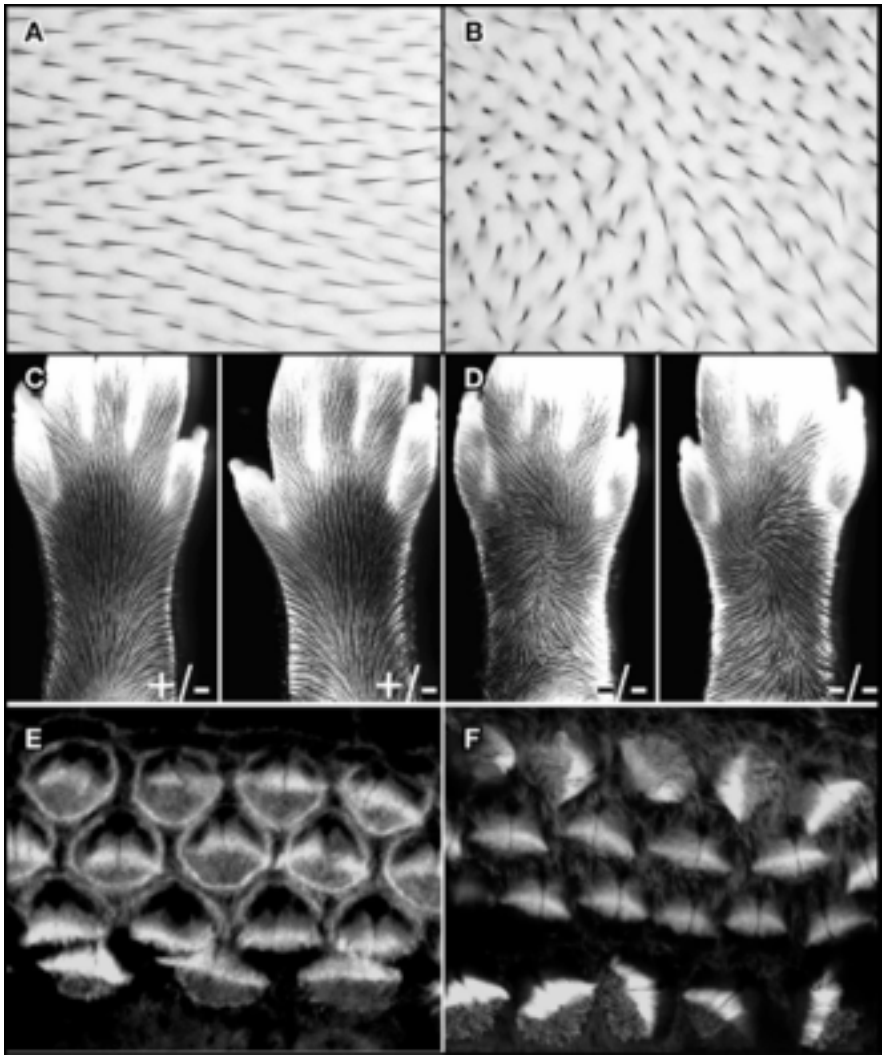
Actin polymerization initiates
at the distal edge of the cell



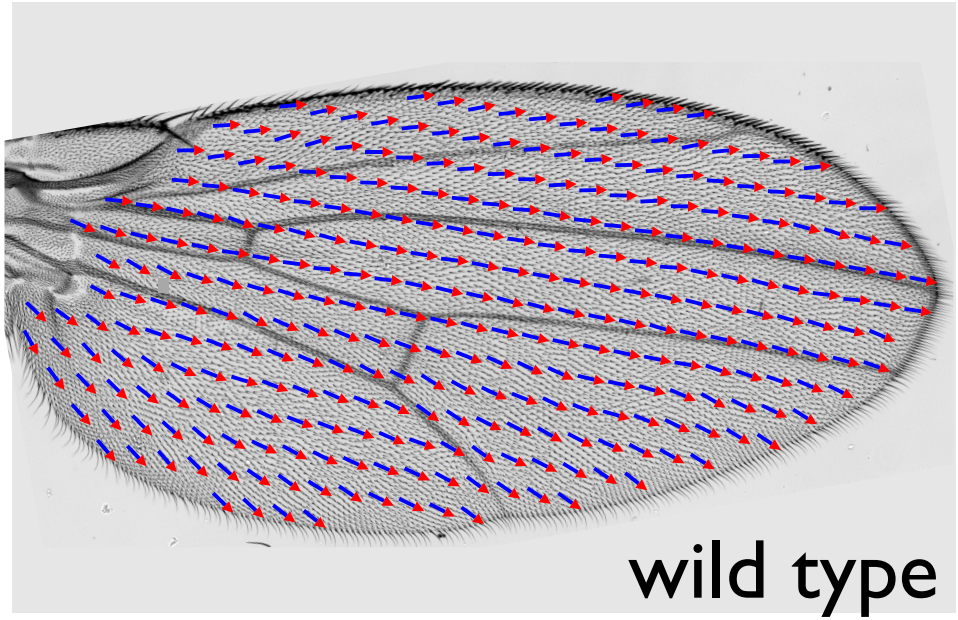
Hair formation starts distally and proceeds in a wave

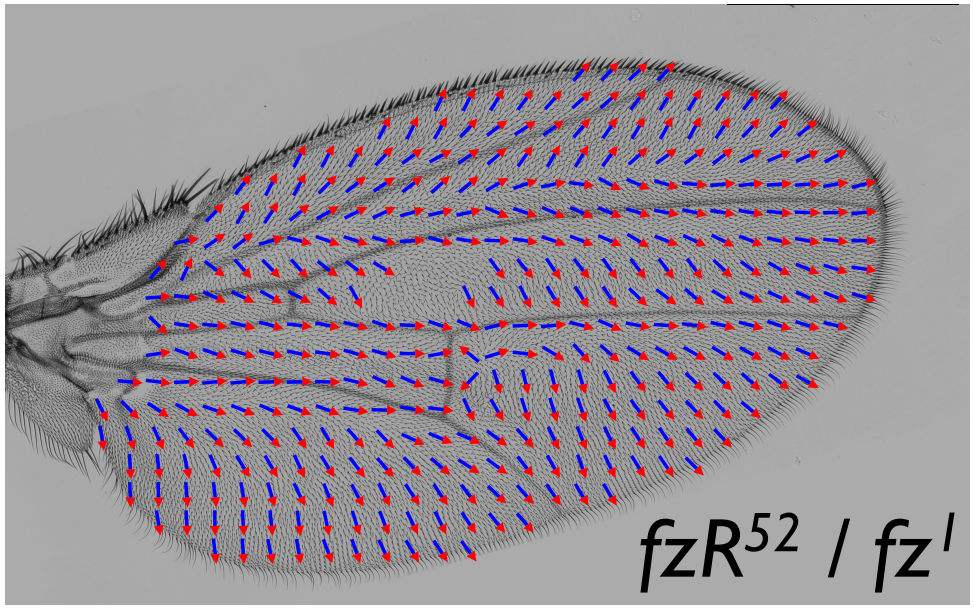


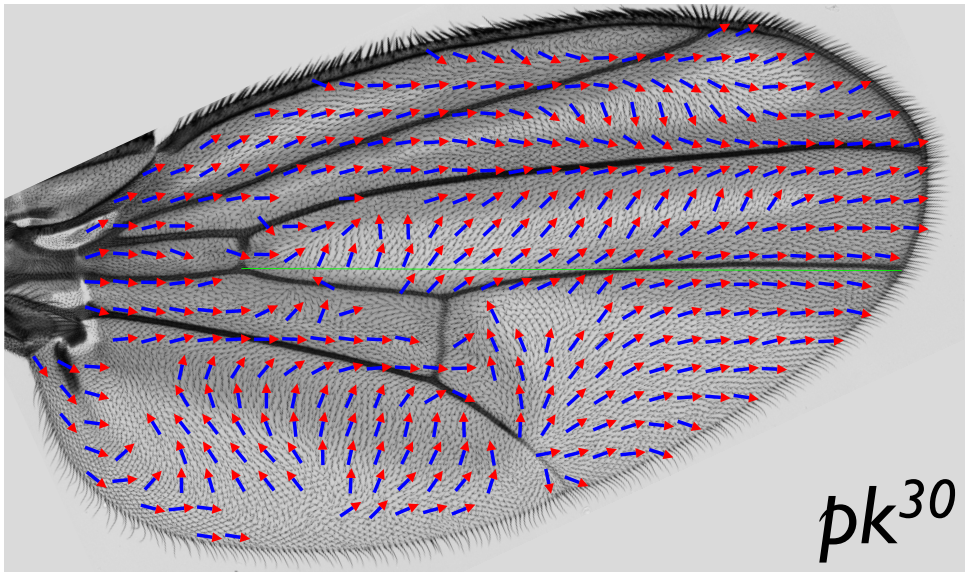
A conserved planar cell polarity (PCP) pathway orients tissue polarity from flies to vertebrates

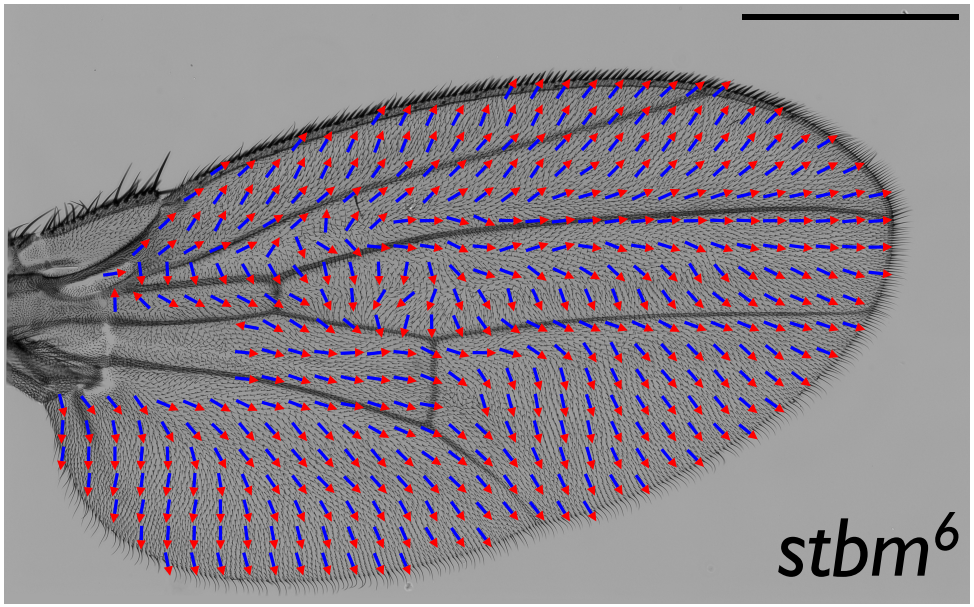


Different PCP mutants disturb polarity with distinct and reproducible patterns

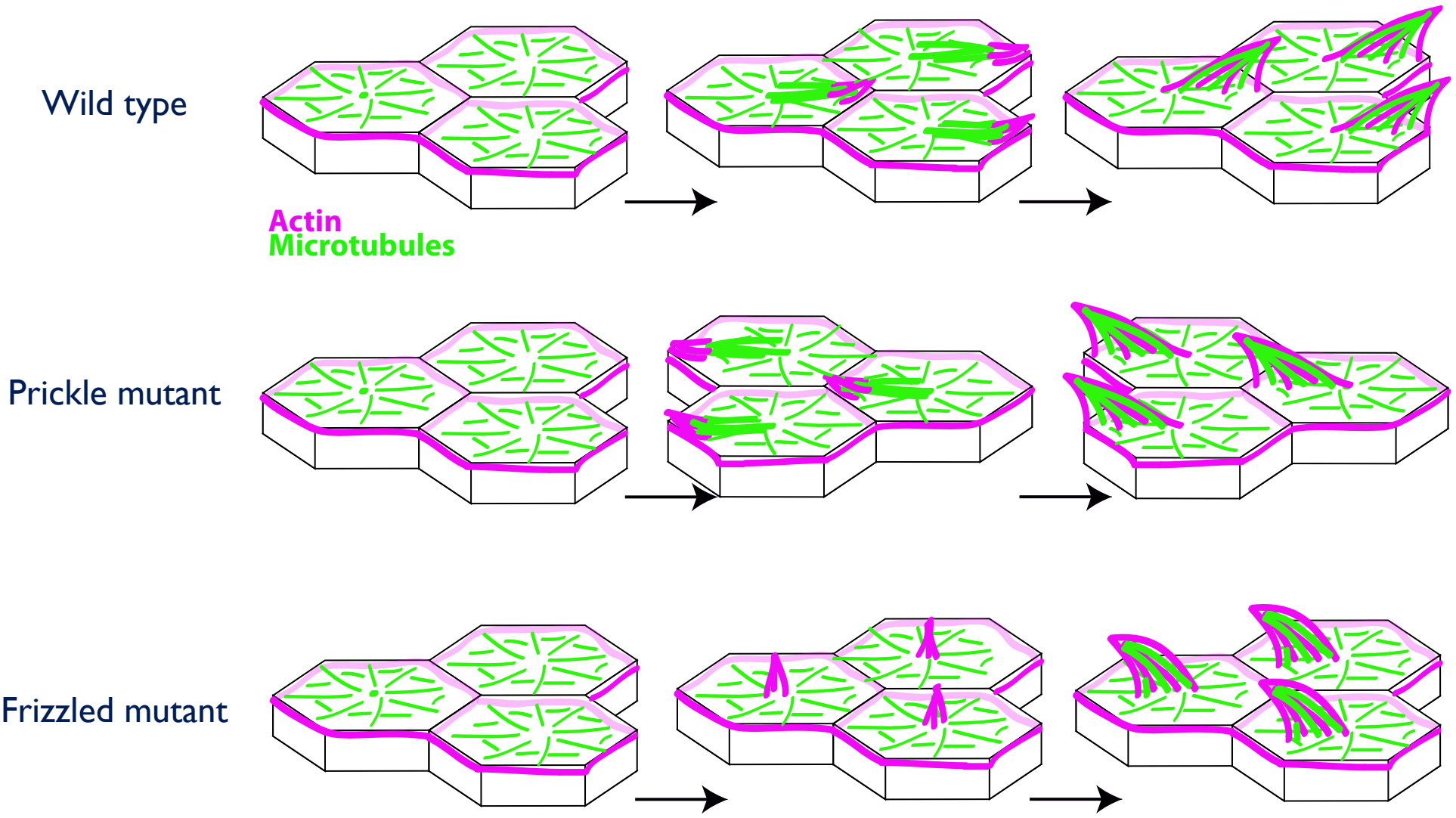




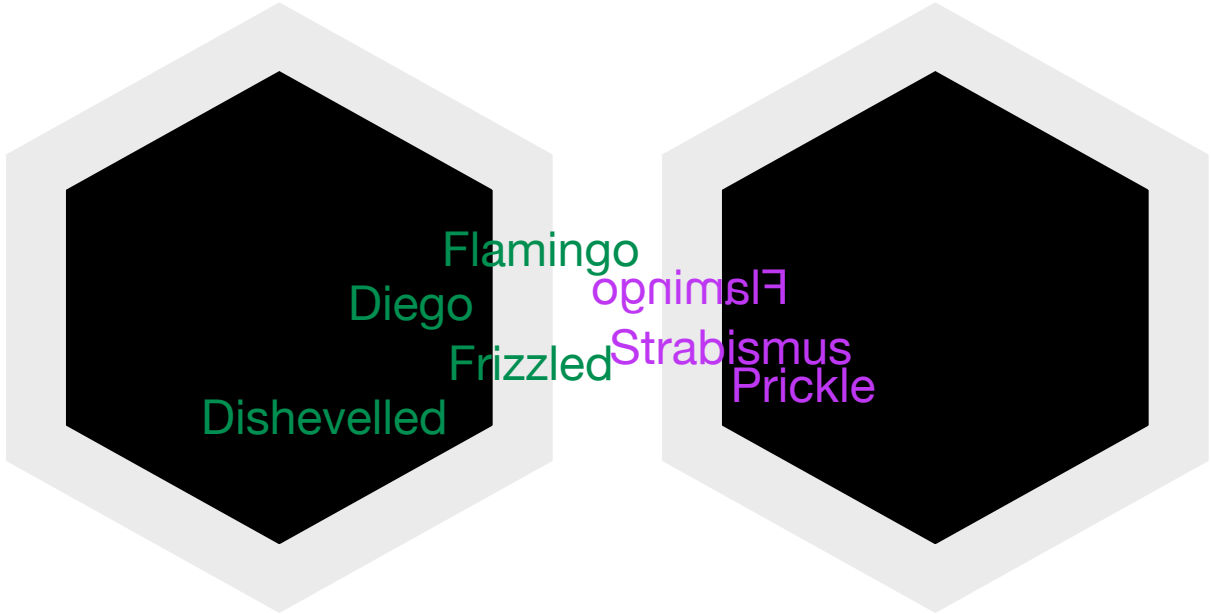


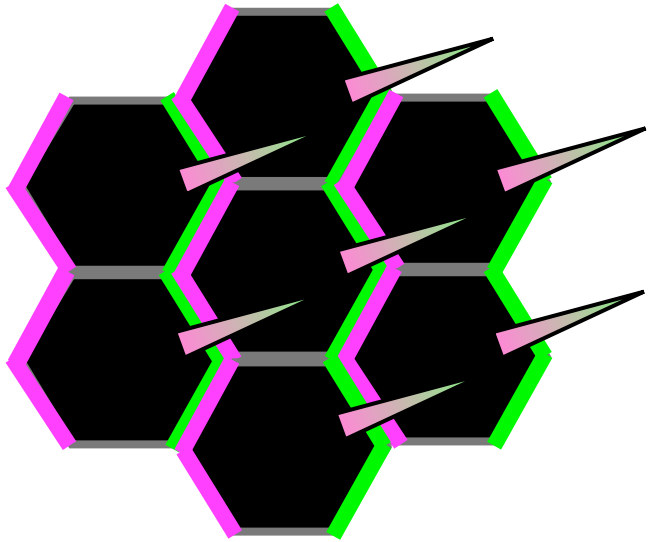


PCP mutants disturb hair outgrowth in different ways



PCP proteins form asymmetric cortical domains

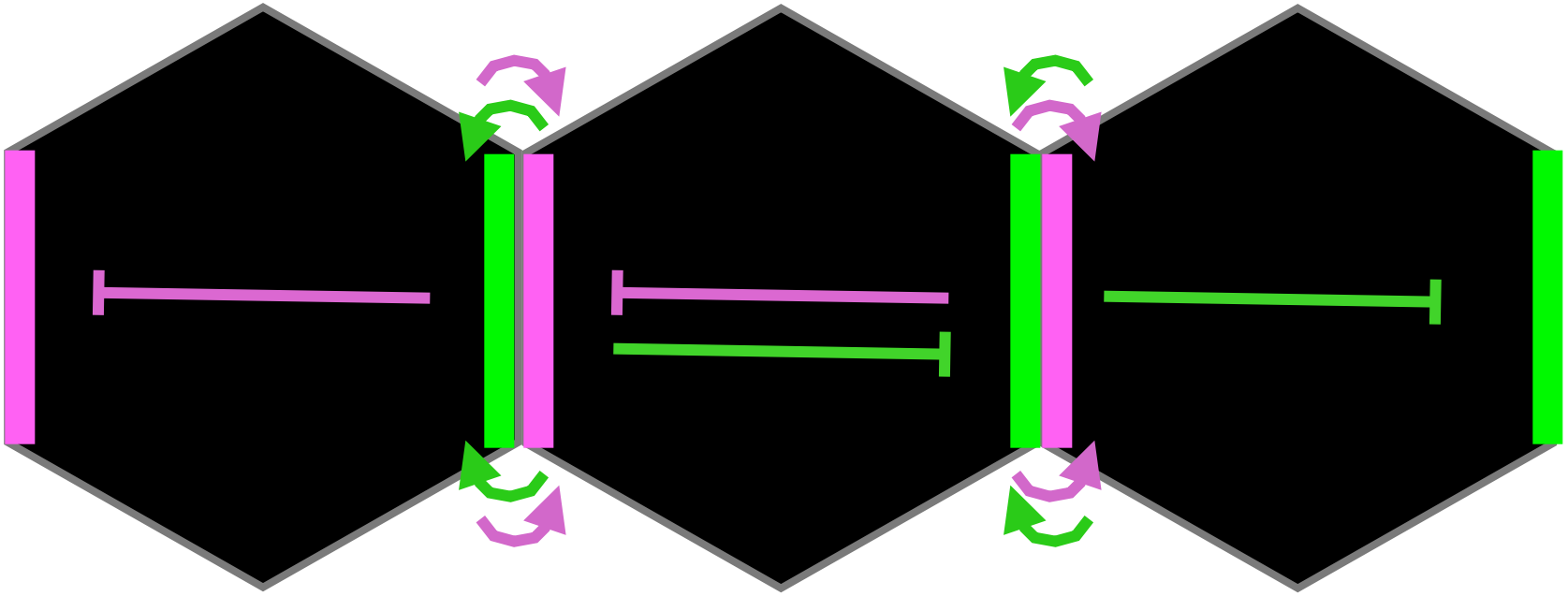




Proximal protein complexes

Distal protein complexes

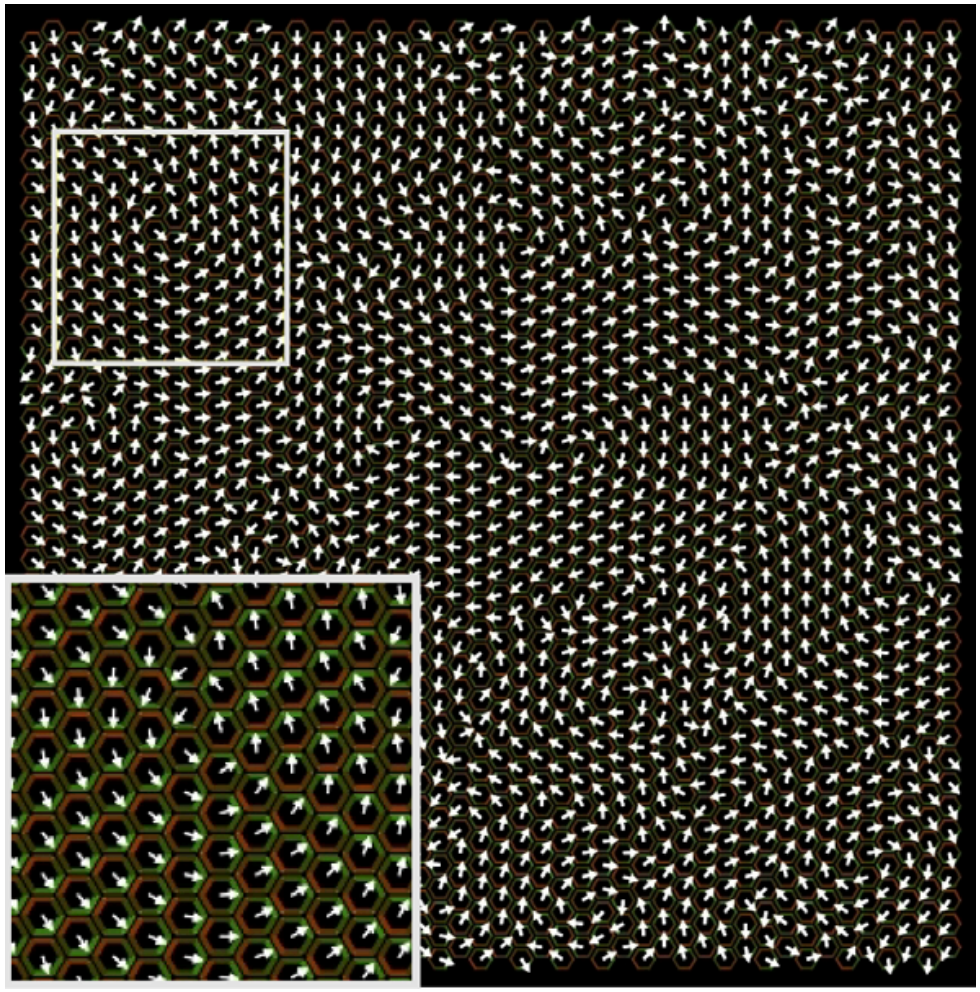
Local self-organization of planar polarity



Proximal protein complexes

Distal protein complexes

Local interactions cannot align polarity globally



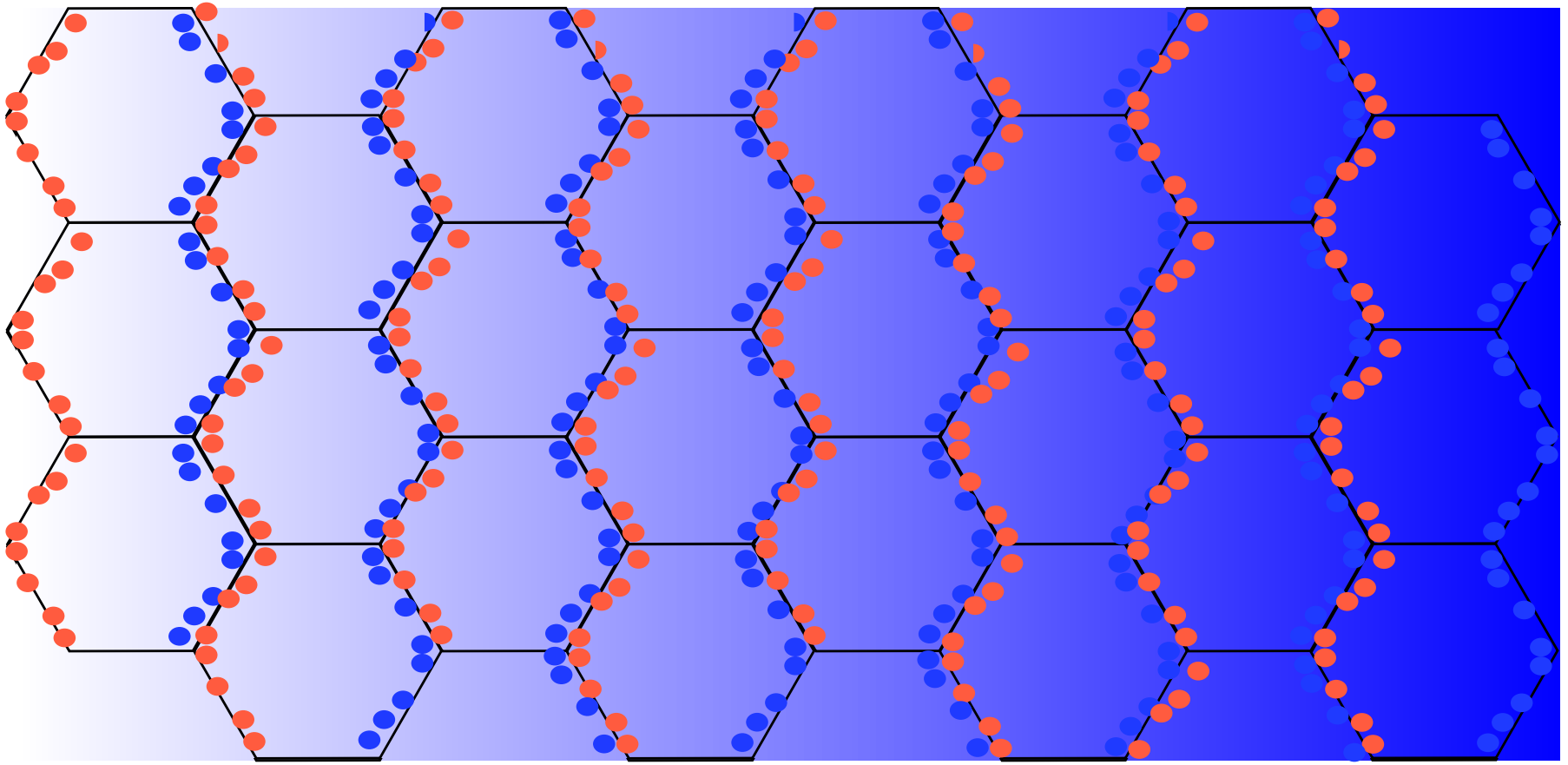
Almonlirdviman et al., 2005 (reaction-diffusion model)

Burak and Shraiman 2009 (Ising model)

Aigouy et al., 2010 (vertex model)

What orients global patterns of planar polarity?

Long-range gradients could help orient and maintain alignment of PCP



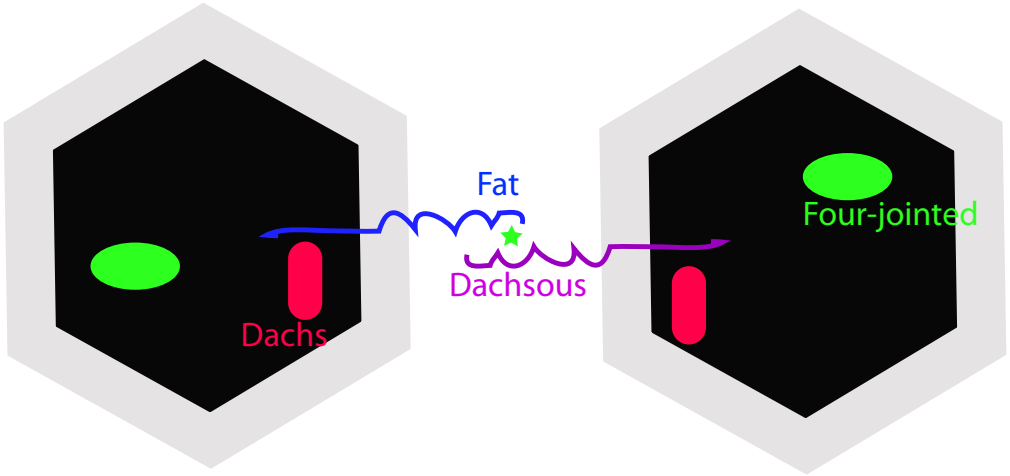
Secreted Factor X??

Atypical Cadherins Fat and Dachsous

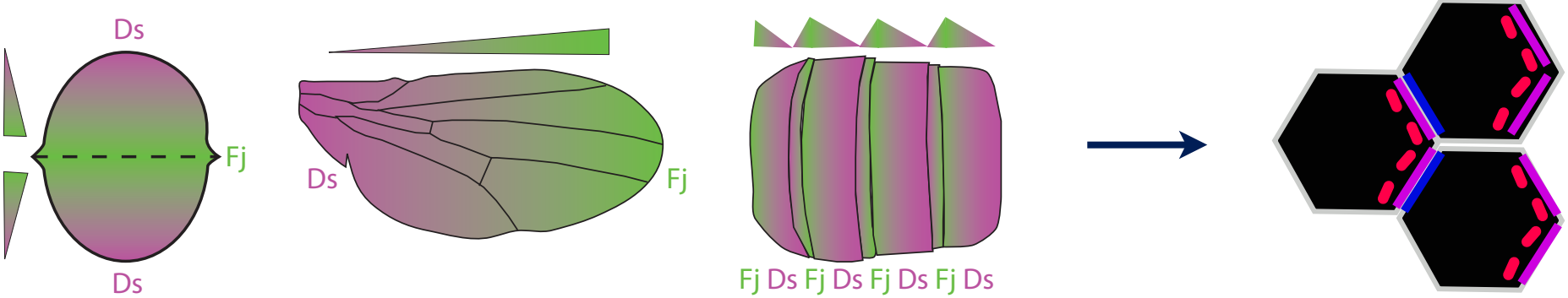
Fat/Dachsous/Four-jointed: an independent planar polarity system

Four-jointed = golgi kinase

Dachs = atypical myosin



Fat/Dachsous = atypical Cadherins



Planar Polarity Specification through Asymmetric Subcellular Localization of Fat and Dachsous

Amy Brittle,[1,2] Chloe Thomas,[1,2] and David Strutt[1,2]

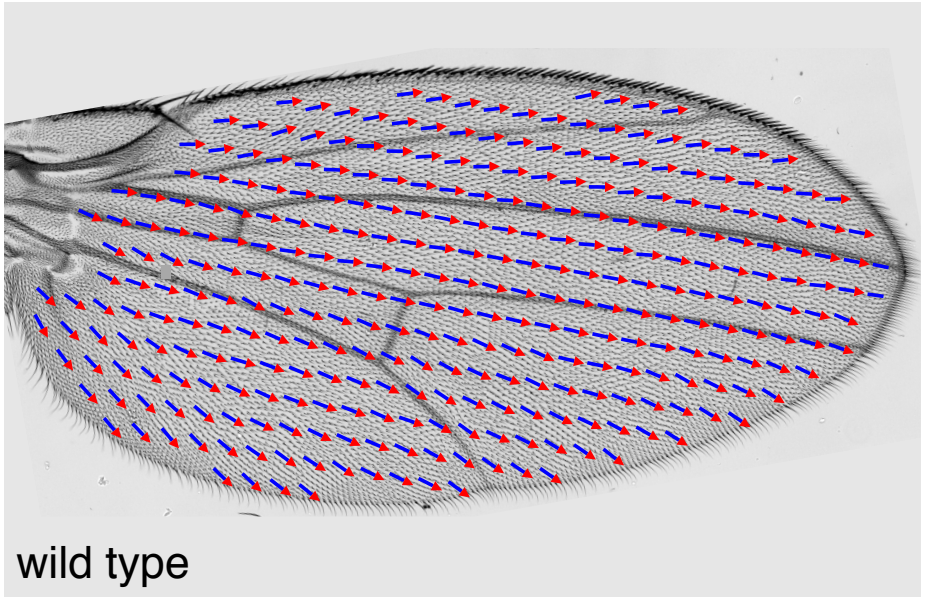
Propagation of Dachsous-Fat Planar Cell Polarity

Abhijit A. Ambegaonkar,[1] Guohui Pan,[1] Madhav Mani,[2] Yongqiang Feng,[1,3] and Kenneth D. Irvine[1,*]

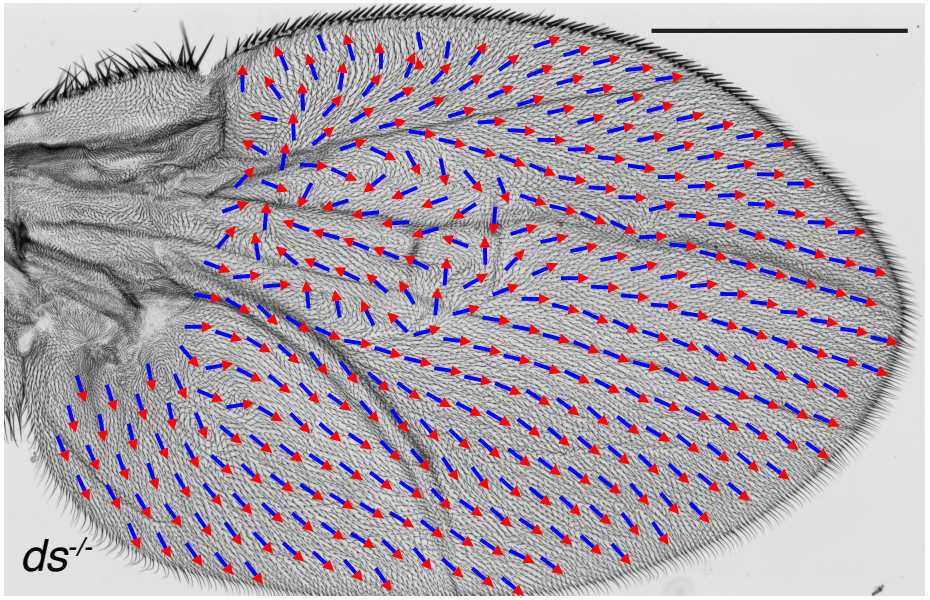
Planar polarization of the atypical myosin Dachs orients cell divisions in *Drosophila*

Yanlan Mao, Alexander L. Tournier, Paul A. Bates, et al.

The Fat/Dachsous pathway influences both planar polarity and growth



wild type



ds$^{-/-}$

Morphogen Control of Wing Growth through the Fat Signaling Pathway

Dragana Rogulja,[1,2] Cordelia Rauskolb,[1] and Kenneth D. Irvine[1,*]

Mutations in the cadherin superfamily member gene dachsous cause a tissue polarity phenotype by altering frizzled signaling

Paul N. Adler*, Jeannette Charlton and Jingchun Liu

Planar polarization of the atypical myosin Dachs orients cell divisions in *Drosophila*

Yanlan Mao, Alexander L. Tournier, Paul A. Bates, et al.

The Orientation of Cell Divisions Determines the Shape of *Drosophila* Organs

Luis Alberto Baena-López, Antonio Baonza, and Antonio García-Bellido*

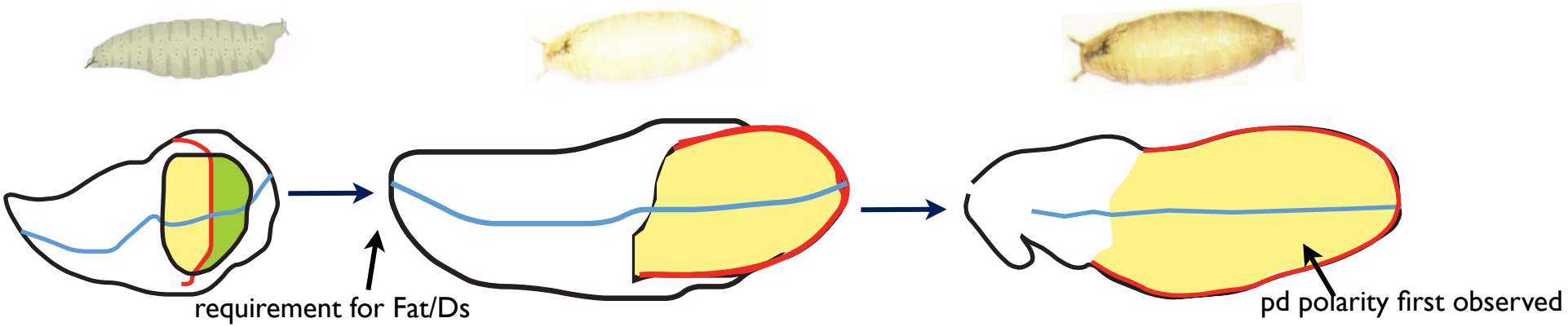
Fidelity in planar cell polarity signalling

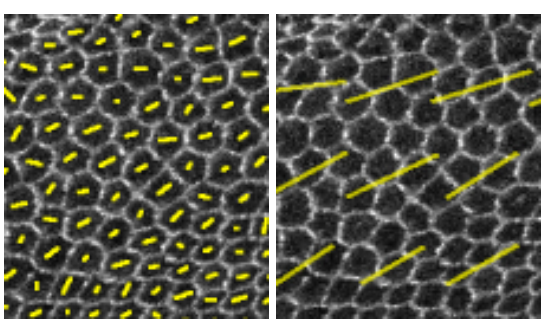
Dali Ma*, Chung-hui Yang†, Helen McNeill‡, Michael A. Simon† & Jeffrey D. Axelrod*

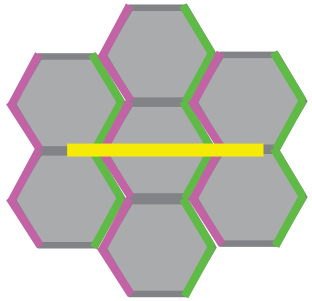
The Roles of the Cadherins Fat and Dachsous in Planar Polarity Specification in *Drosophila*

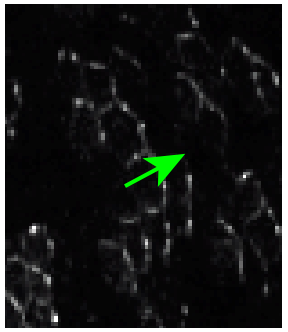
Chloe Thomas* and David Strutt*

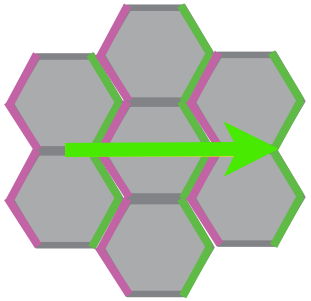
When does planar polarity first develop?







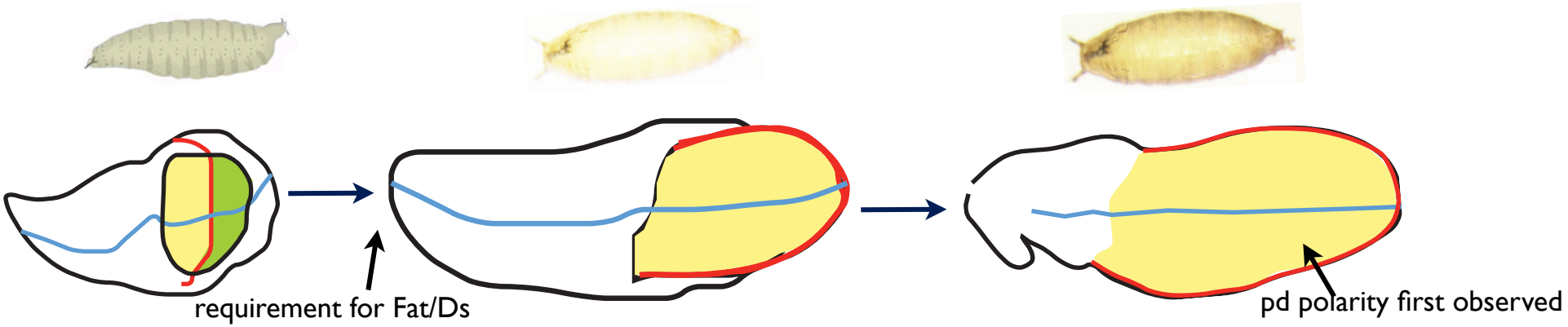


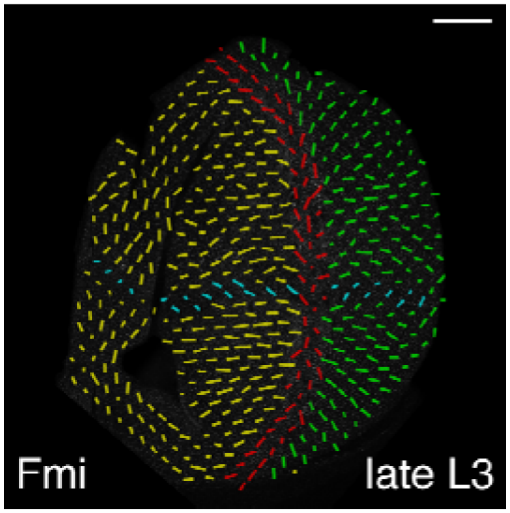


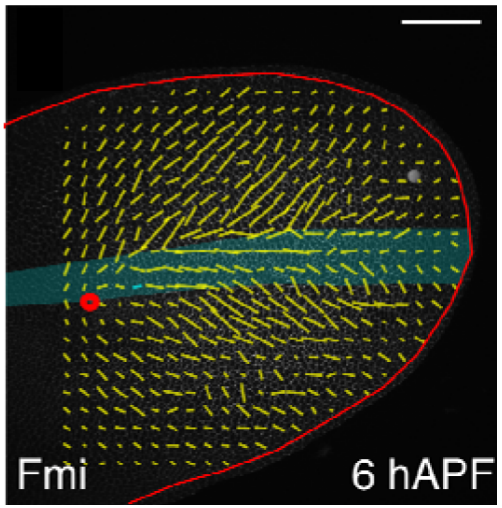
Sagner et al. (2012) Current Biology

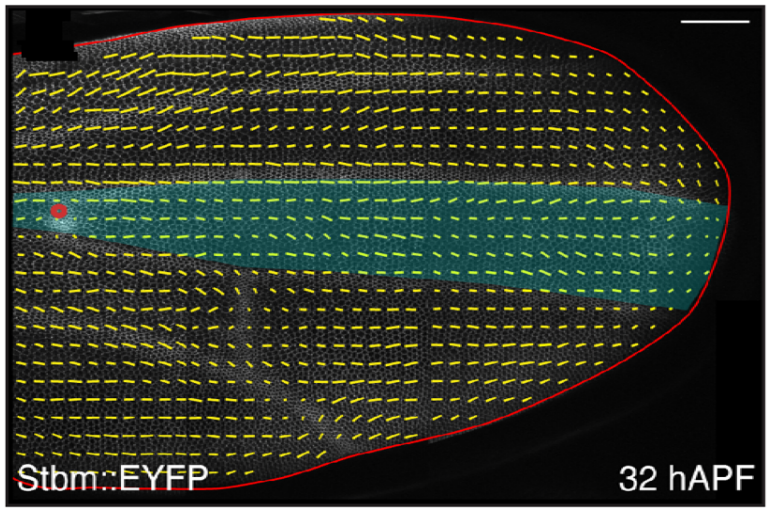
Aigouy et al. (2010) Cell

When does planar polarity first develop?









Global polarity patterns arise during growth and reorient during morphogenesis

Sagner et al. (2012) Current Biology

Aigouy et al. (2010) Cell

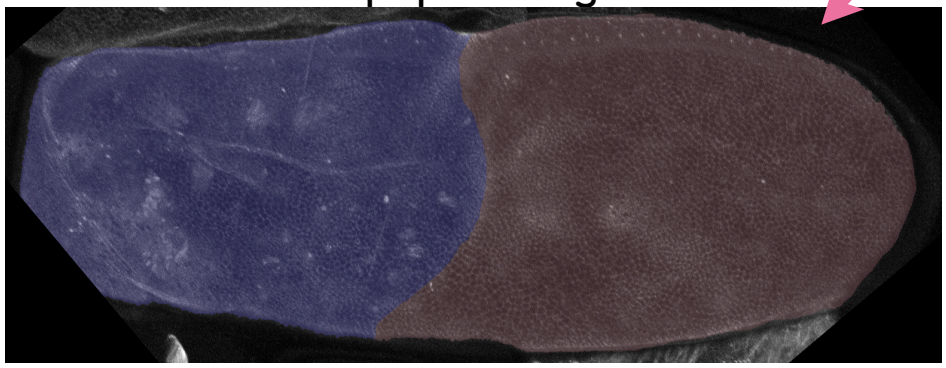
The shape of the wing is refined during pupal stages

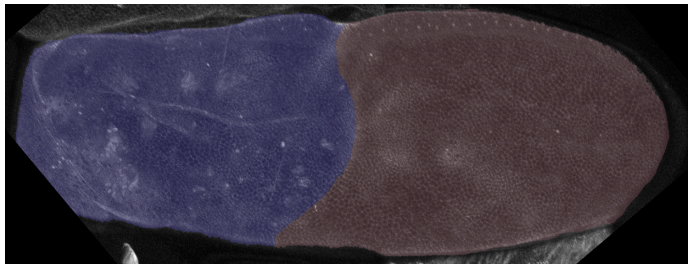
adult wing

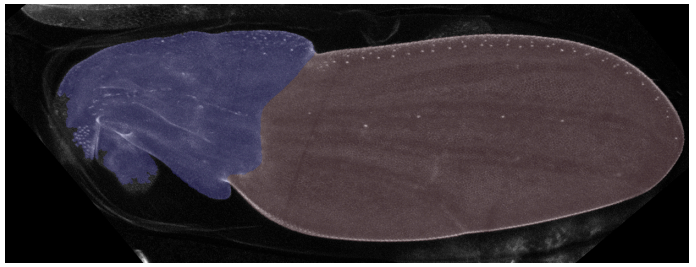
Wing hinge

Wing blade

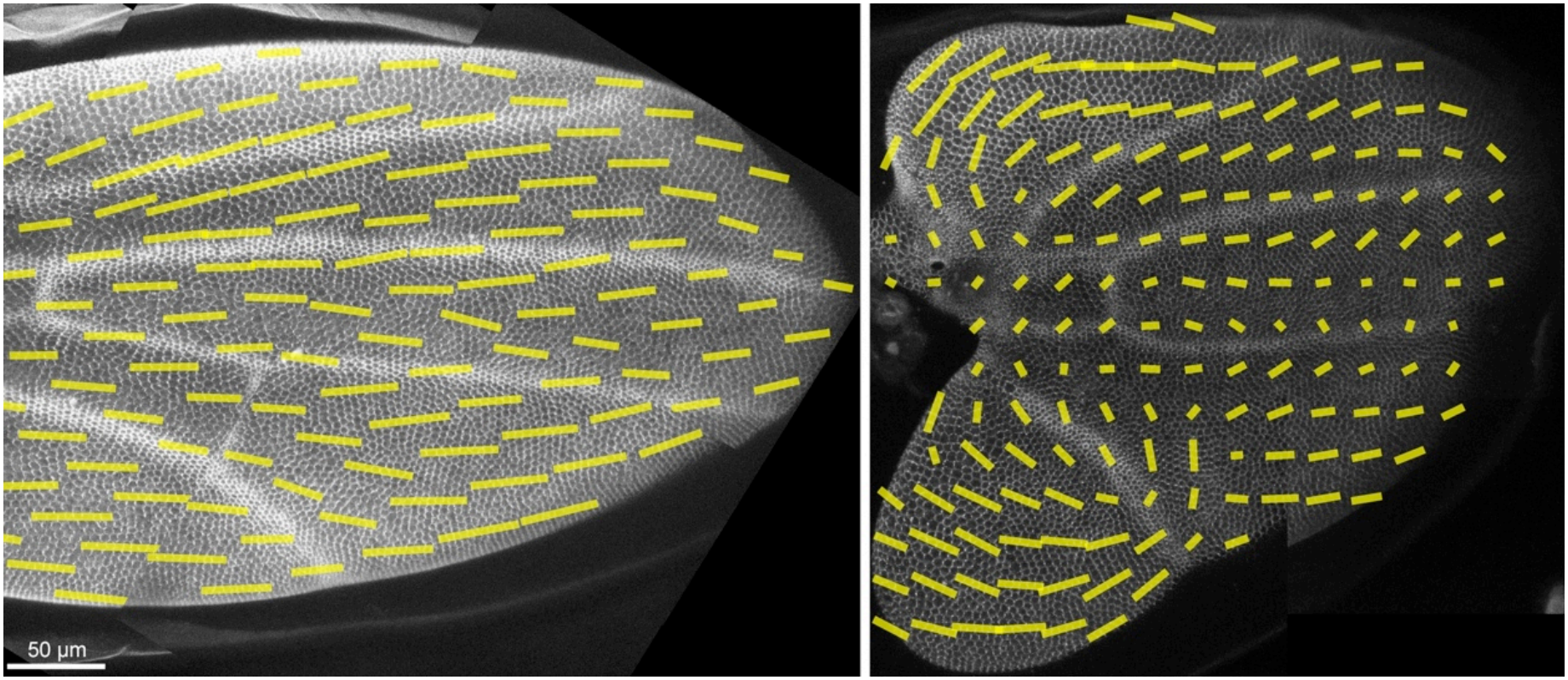
pupal wing





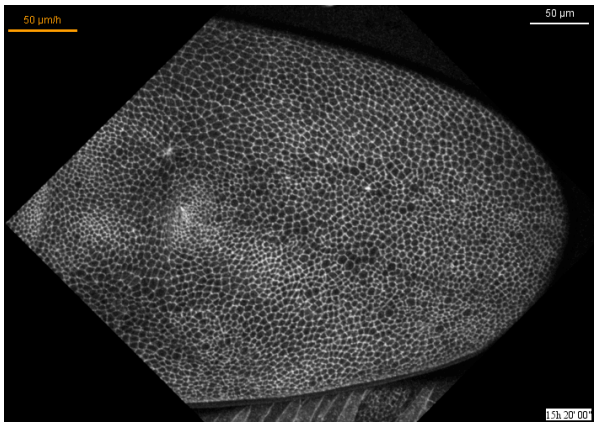


Wing remodeling guides reorientation of the planar polarity pattern

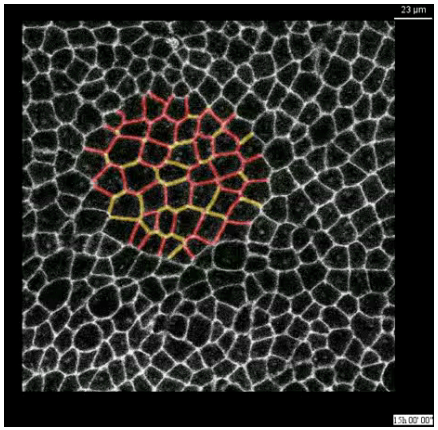


Aigouy et al. (2010) Cell

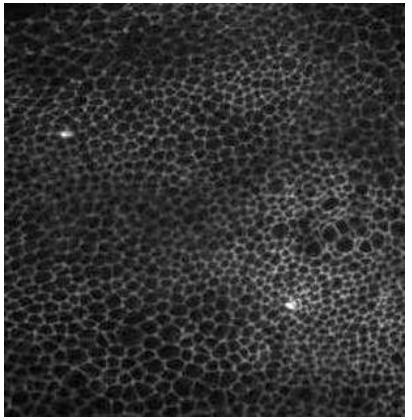
Anisotropic tissue stress orients cell elongation, cell divisions and rearrangements to remodel the wing blade



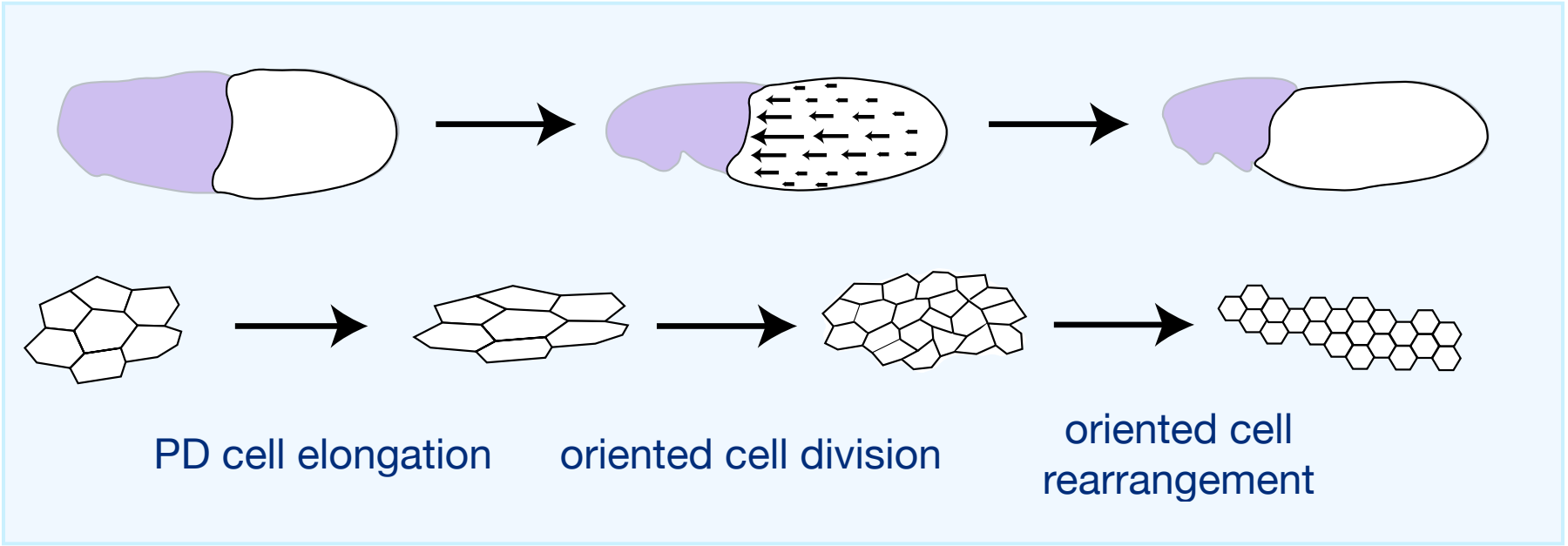
Quantify tissue flows



Track cells and cell boundaries



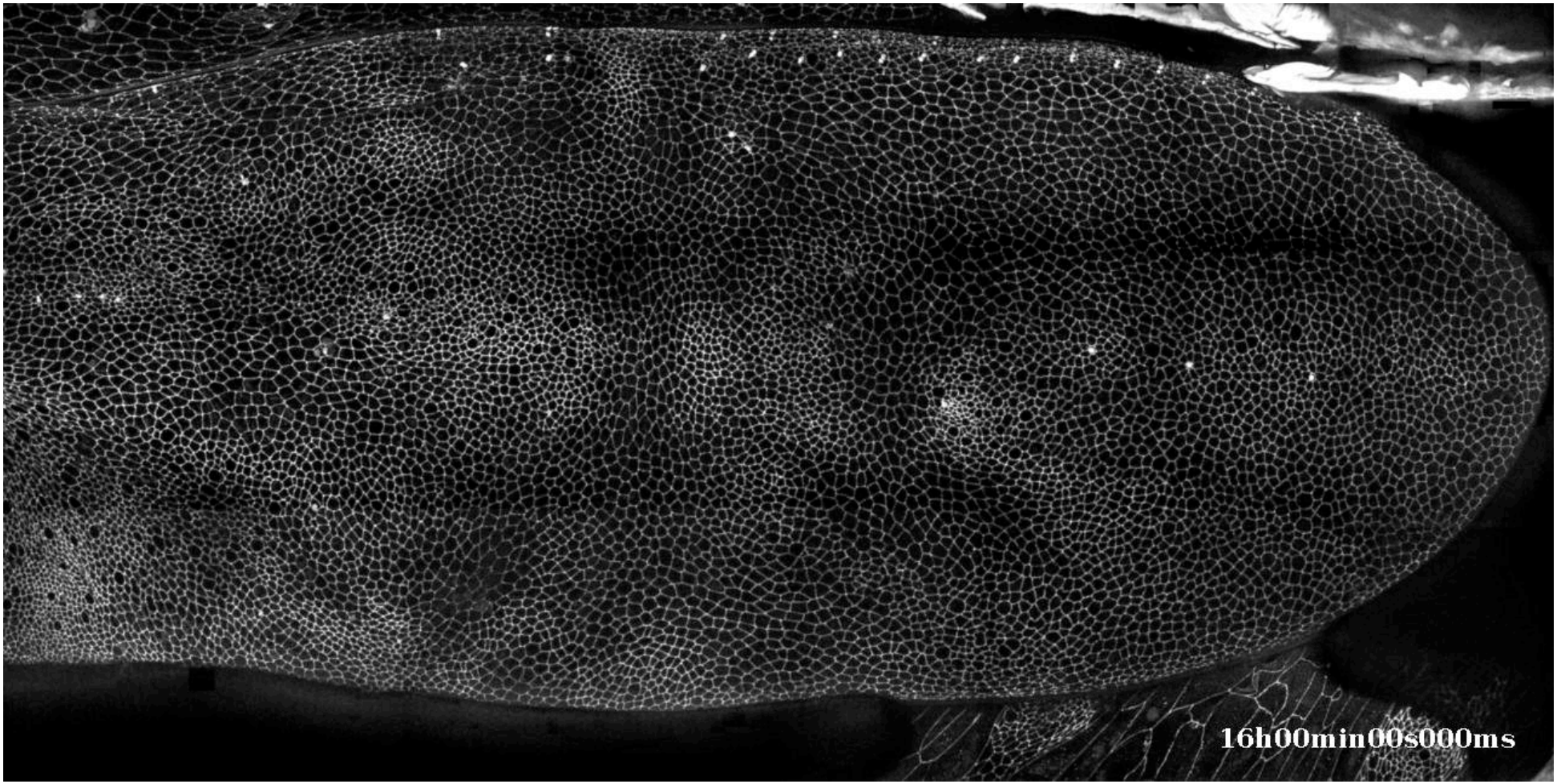
Measure and perturb tissue stress with laser ablation



Severing the blade from the hinge blocks cell elongation and misorients division and rearrangment

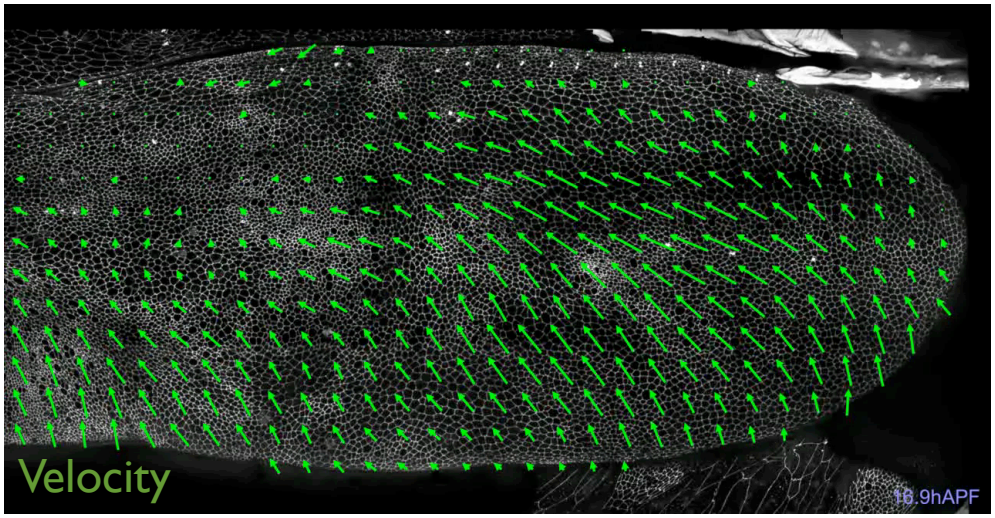
Aigouy et al. (2010) Cell

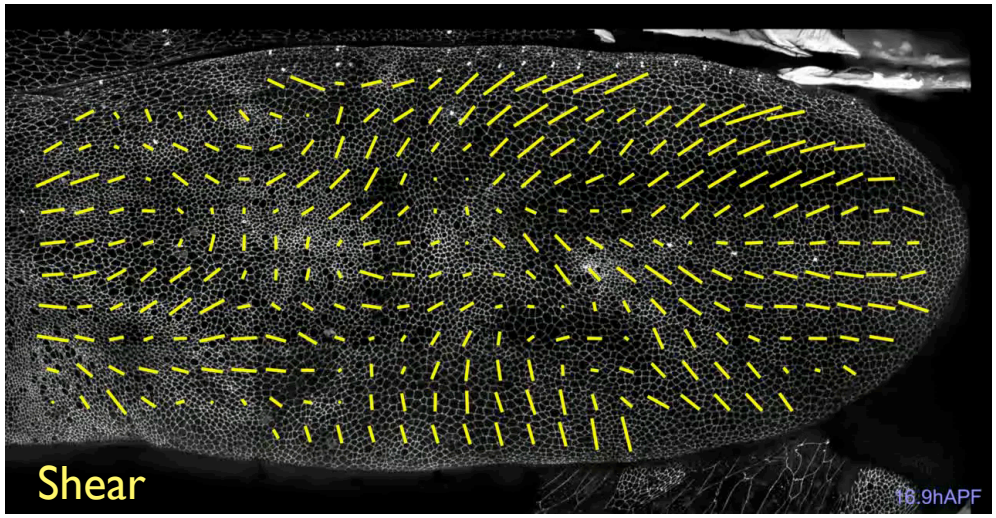
Imaging the entire wing at cellular resolution

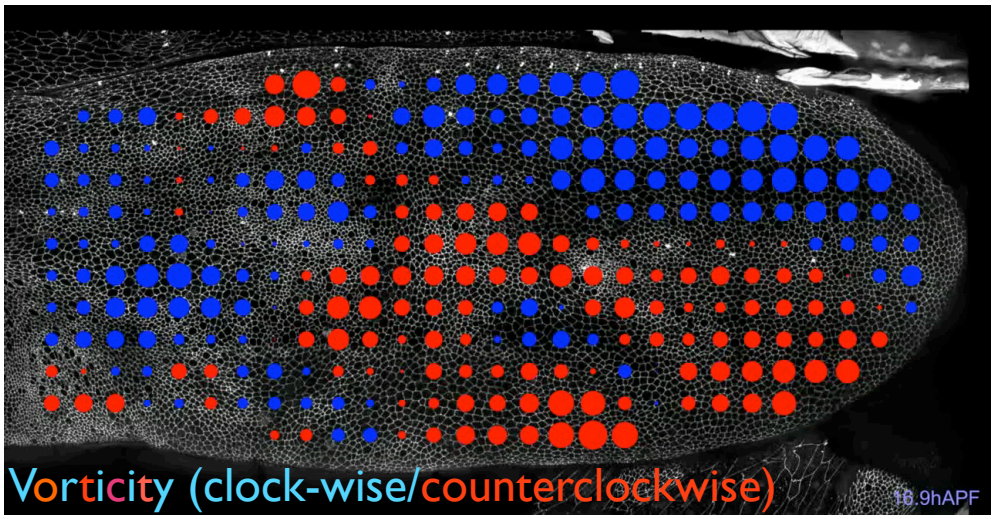


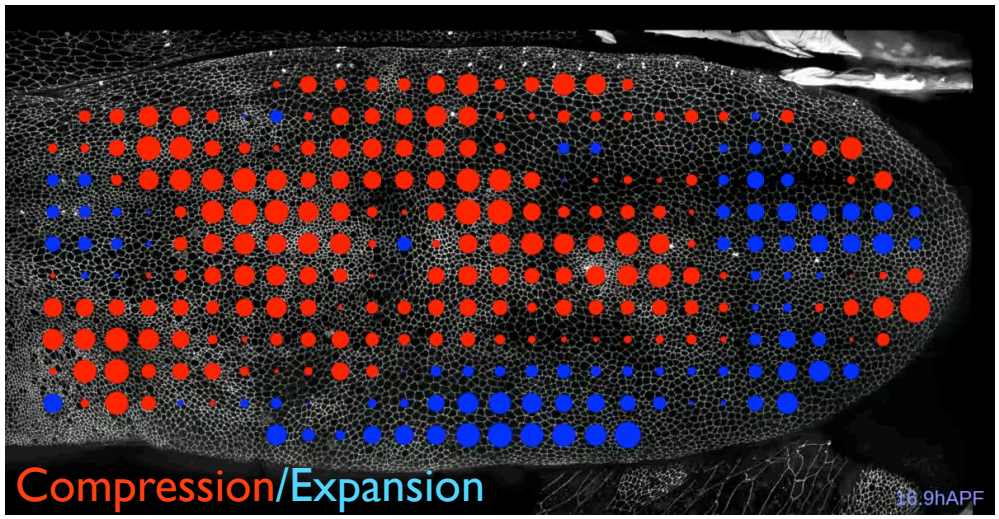
Raphael Etournay

Patterns of shear, vorticity and compression in the remodeling wing



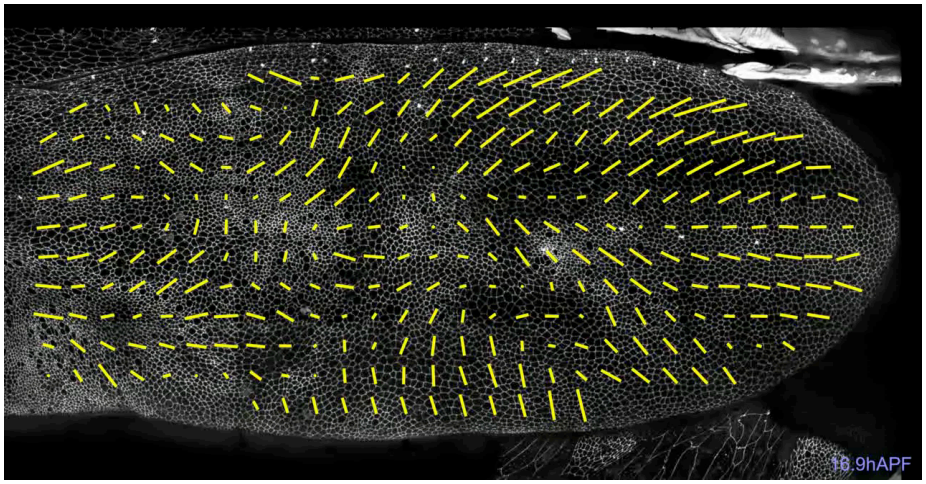


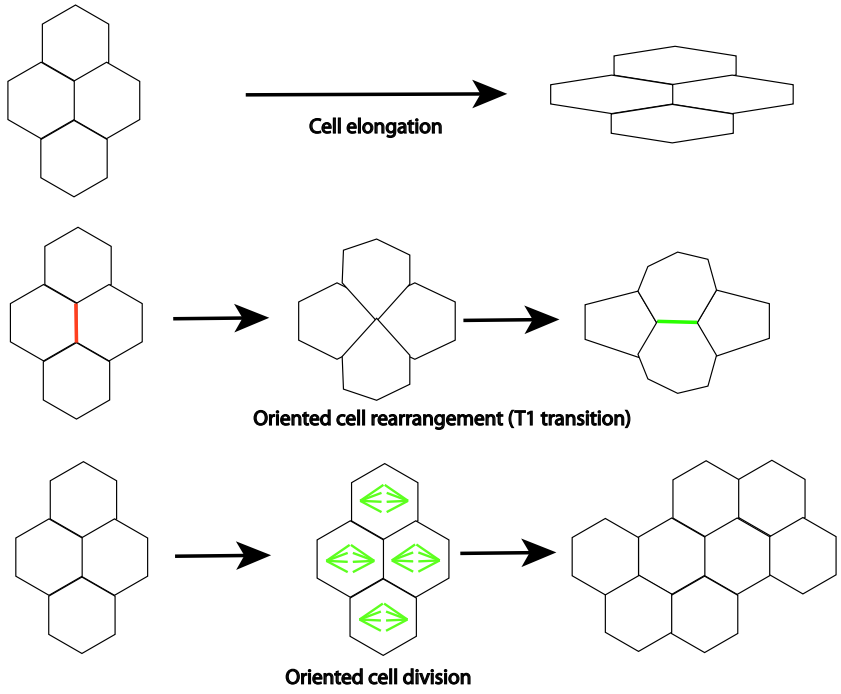




Matthias Merkel and
Raphael Etournay

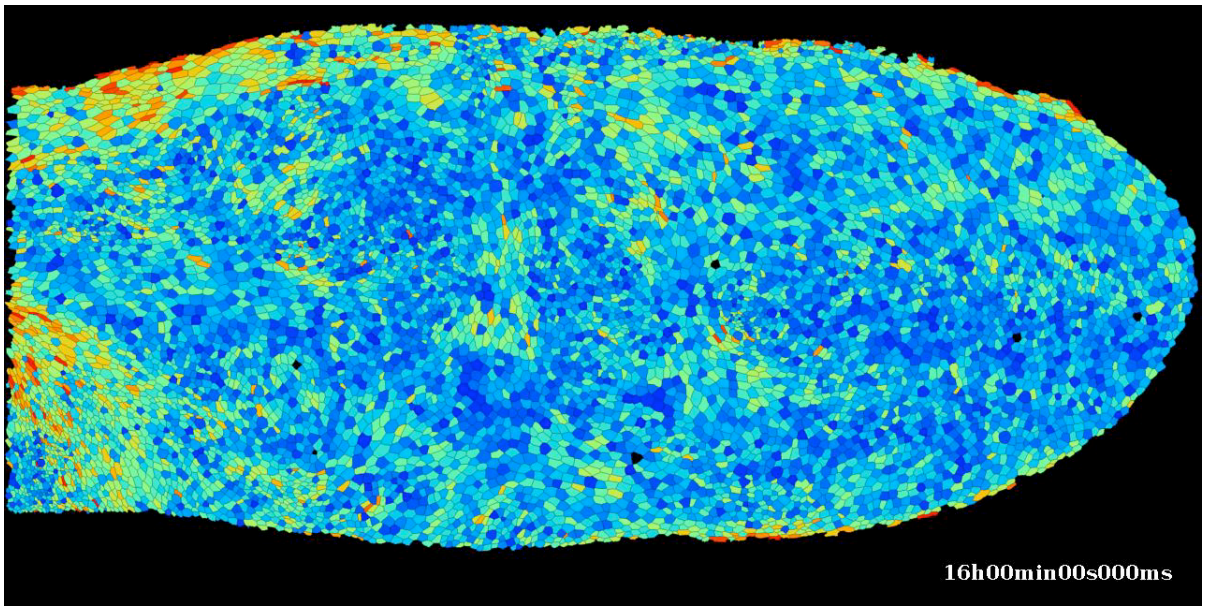
Are there different regional contributions of cell elongation division and rearrangment to the pattern of tissue shear?





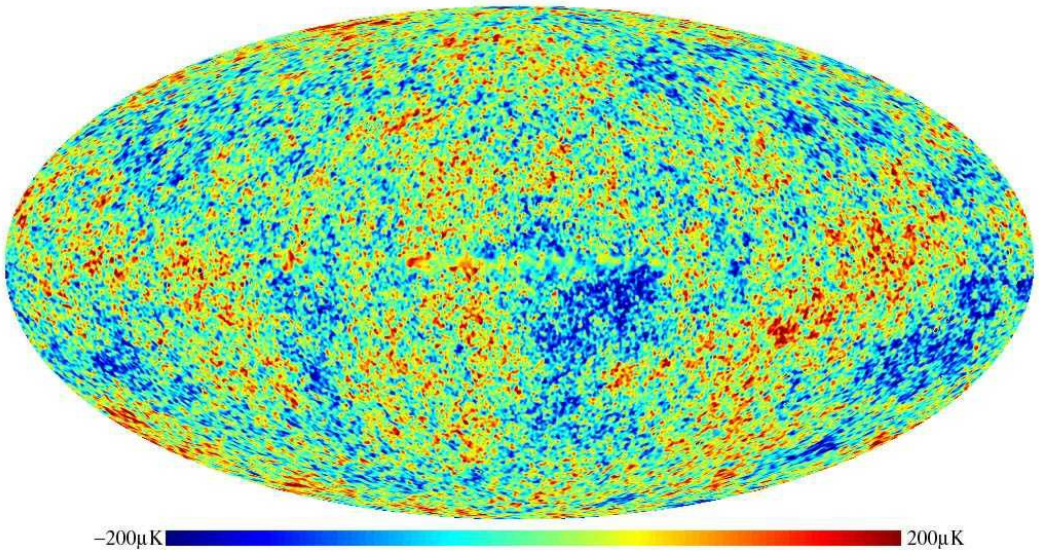
Matthias Merkel and Raphael Etournay

Dynamic patterns of cell elongation during wing remodeling



Matthias Merkel and Raphael Etournay

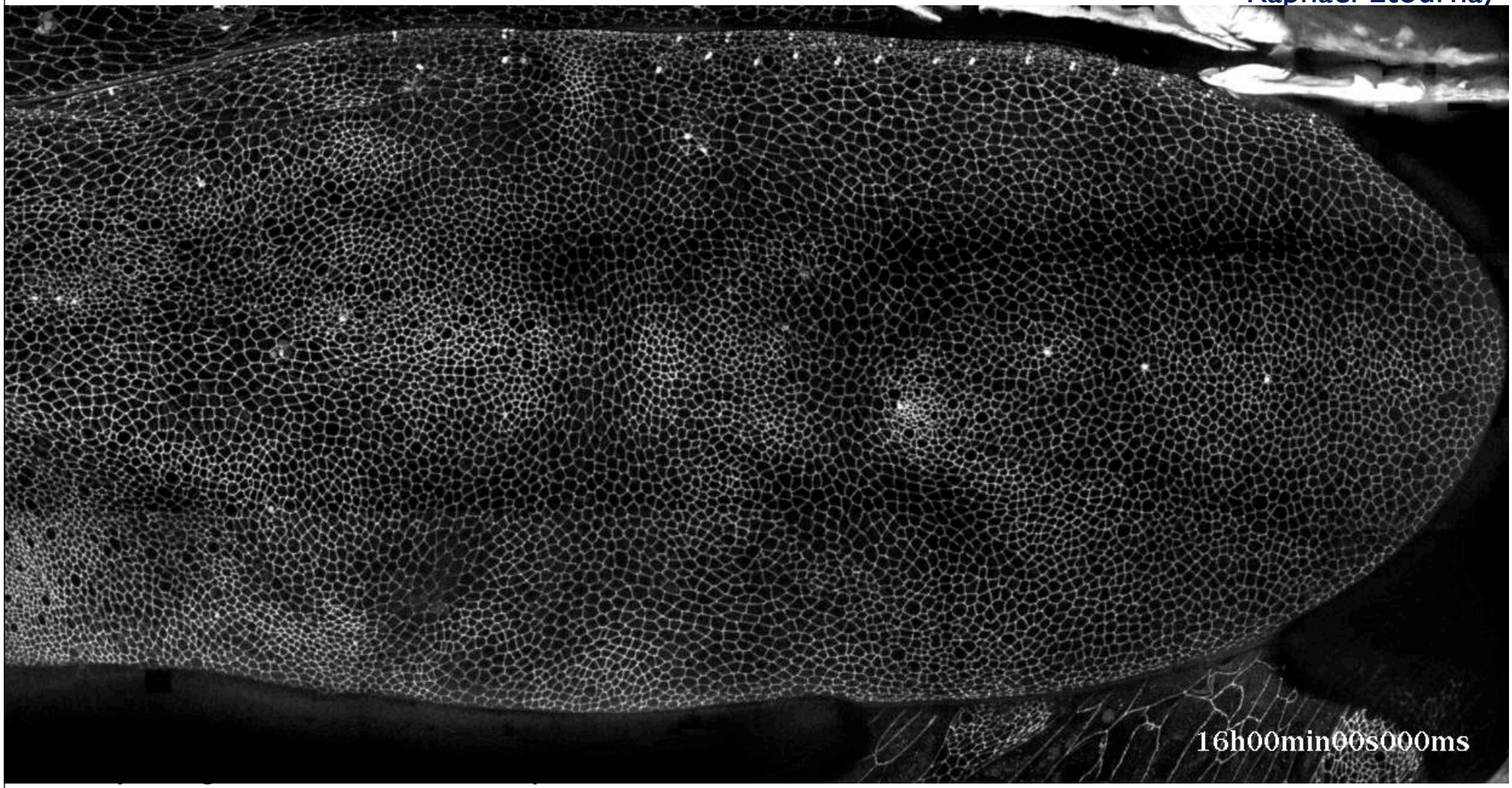
isotropic  elongated



Anisotropies in the Cosmic Microwave Background

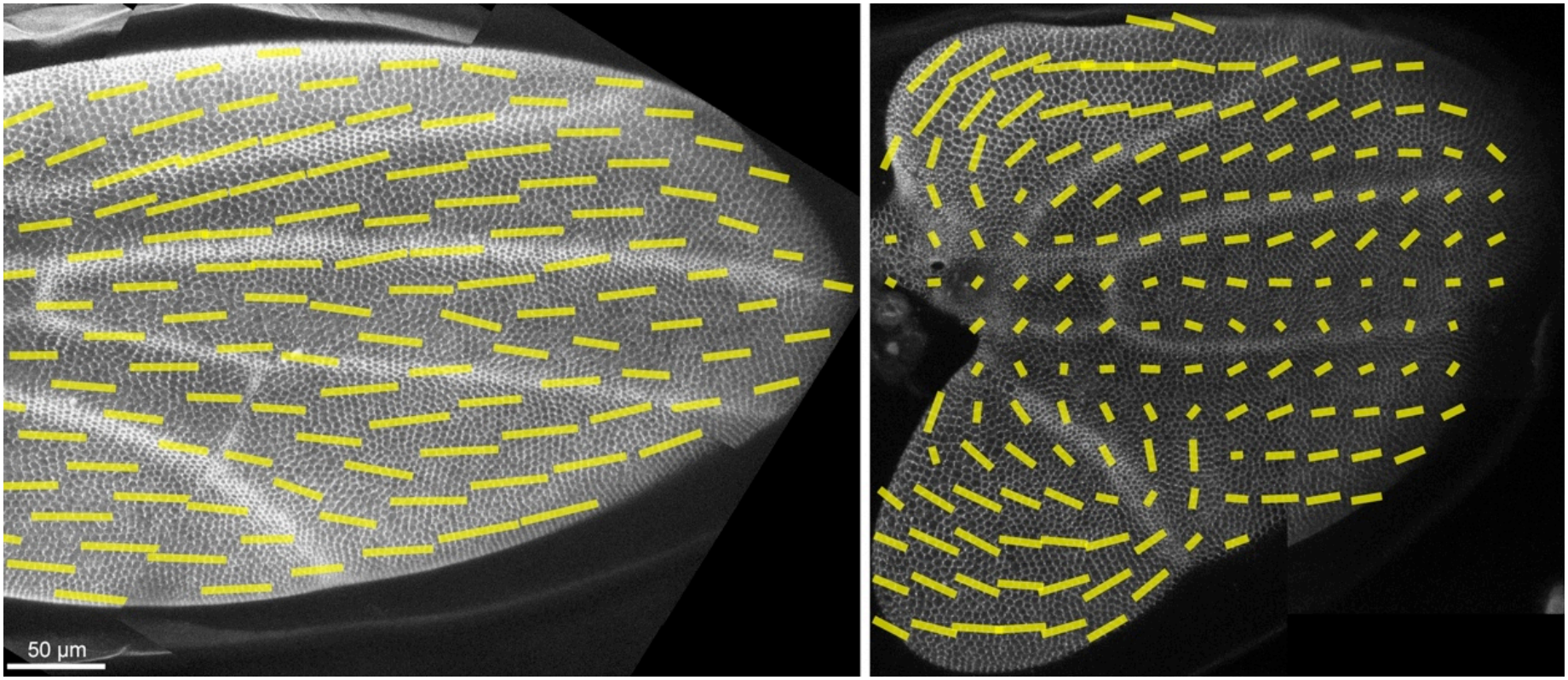
PD oriented divisions and rearrangements dominate at different places and times

Matthias Merkel and
Raphael Etournay



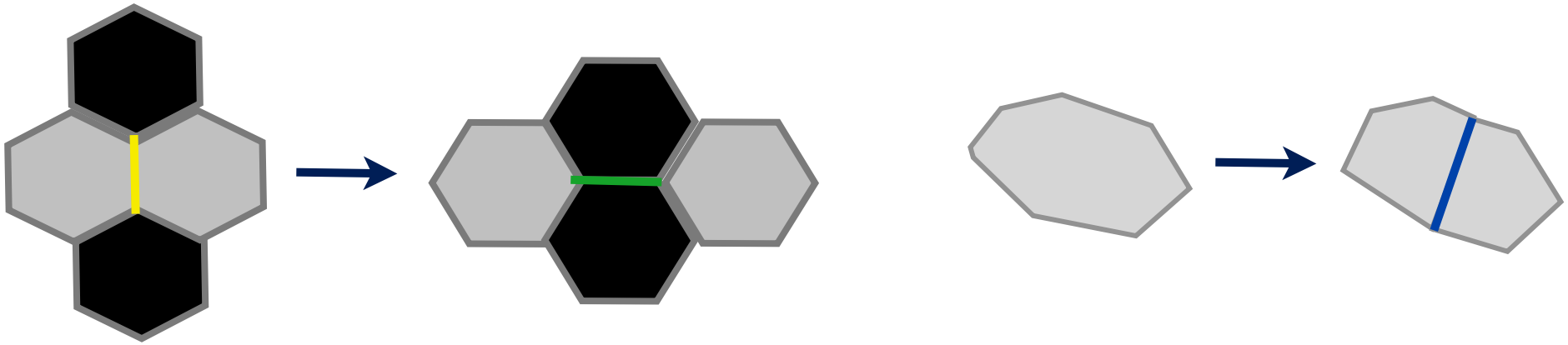
Matthias Merkel and Raphael Etournay

How does epithelial remodeling reorient the planar polarity pattern?

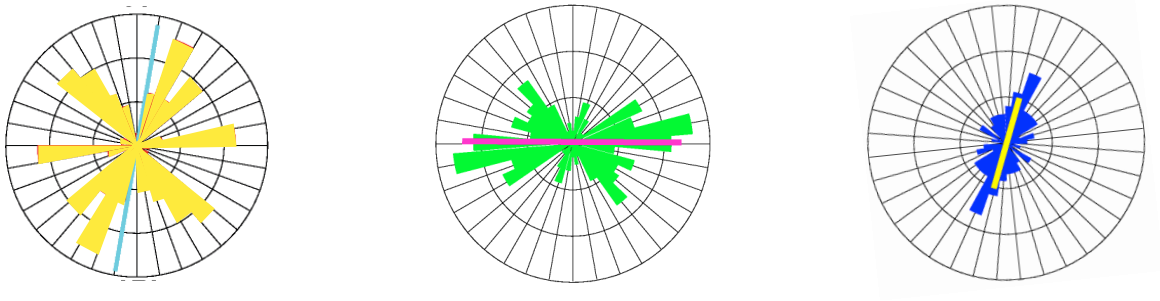


Aigouy et al. (2010) Cell

Oriented loss and formation of cell boundaries during remodeling



Proximal → Distal

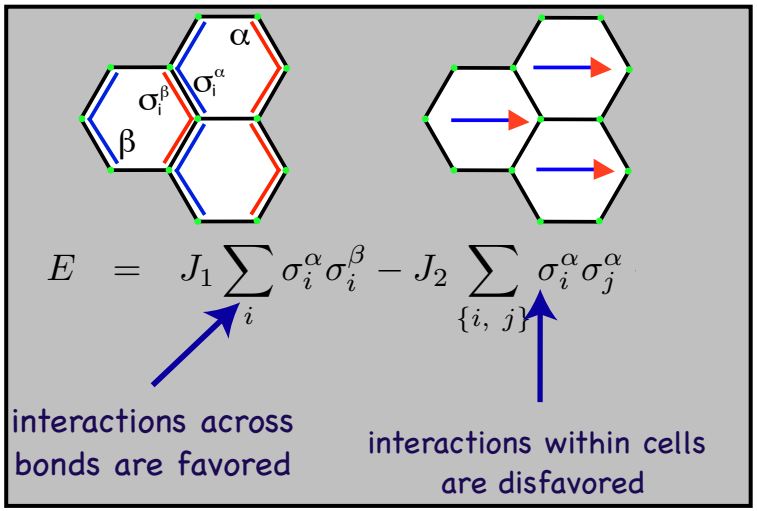


Could the oriented gain/loss of cell boundaries affect the global planar polarity pattern?

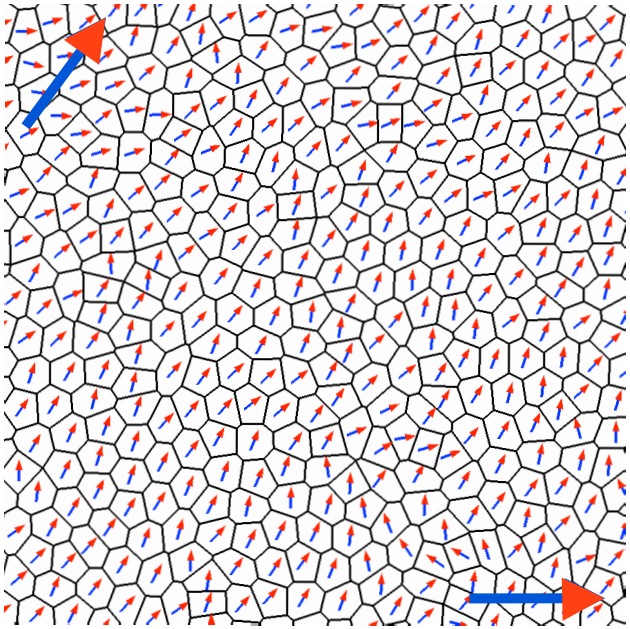
Aigouy et al. (2010) Cell

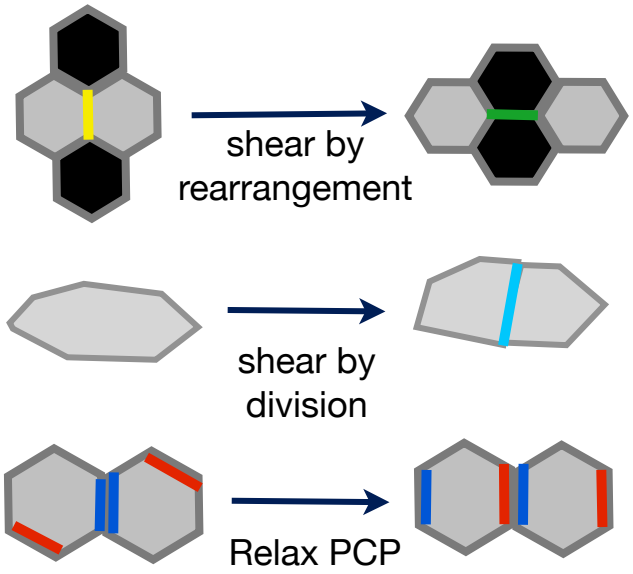
Oriented cell divisions/rearrangments shift the global PCP axis

Aigouy et al. (2010) Cell



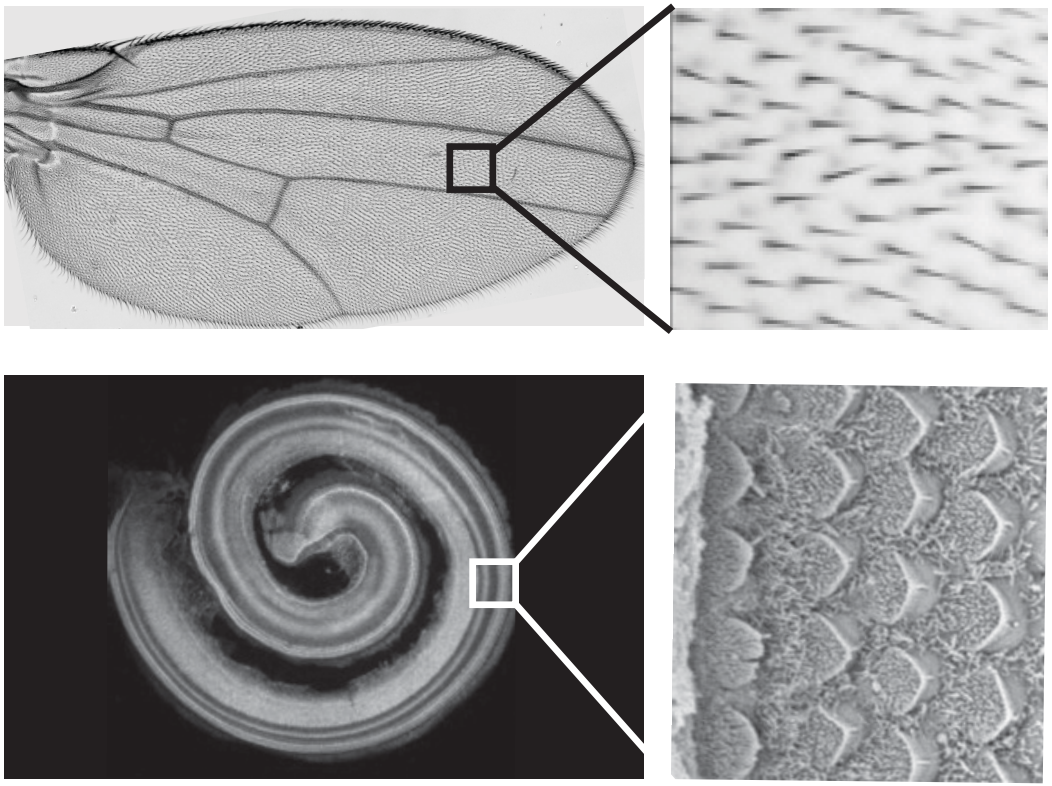
Frank Jülicher





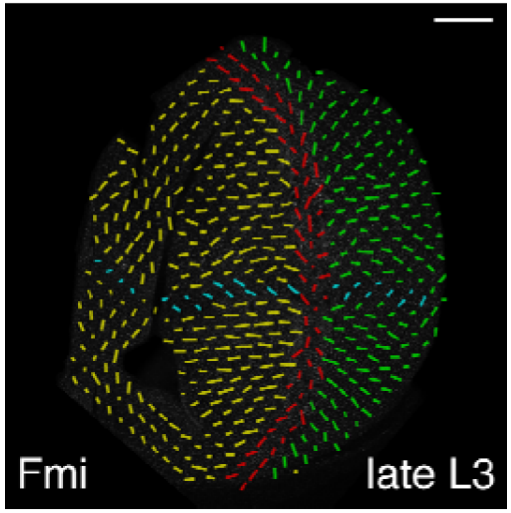
The global PCP axis rotates either parallel or perpendicular to the shear axis, depending on parameters

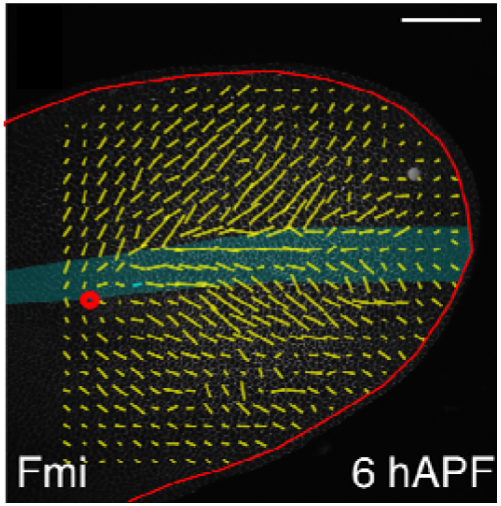
Oriented cell divisions and rearrangements can reorient the axis of planar polarity parallel or perpendicular to the shear axis

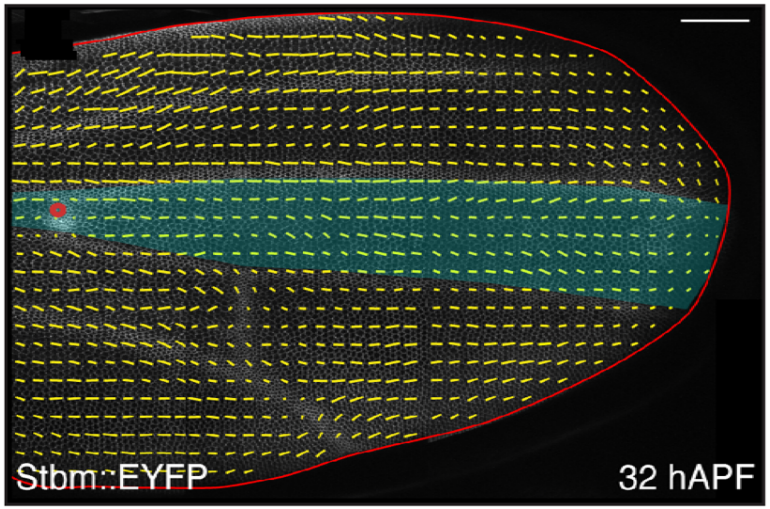


These versatile mechanisms may allow different orientations of PCP with respect to tissue axes

What mechanisms establish the earlier PCP pattern?

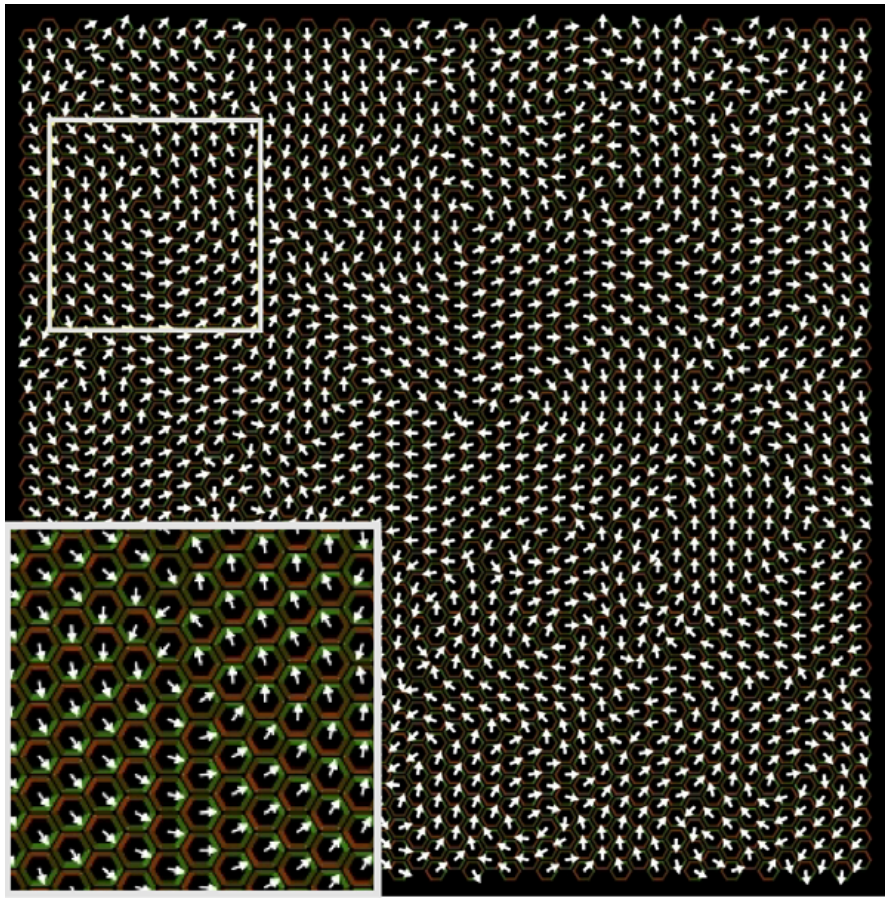


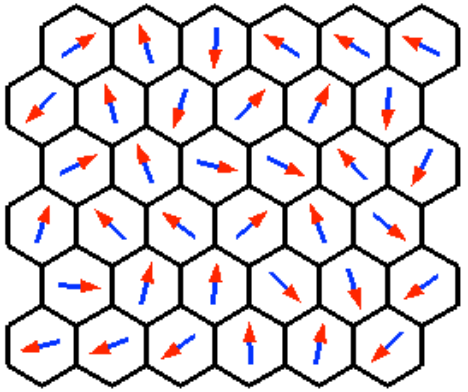




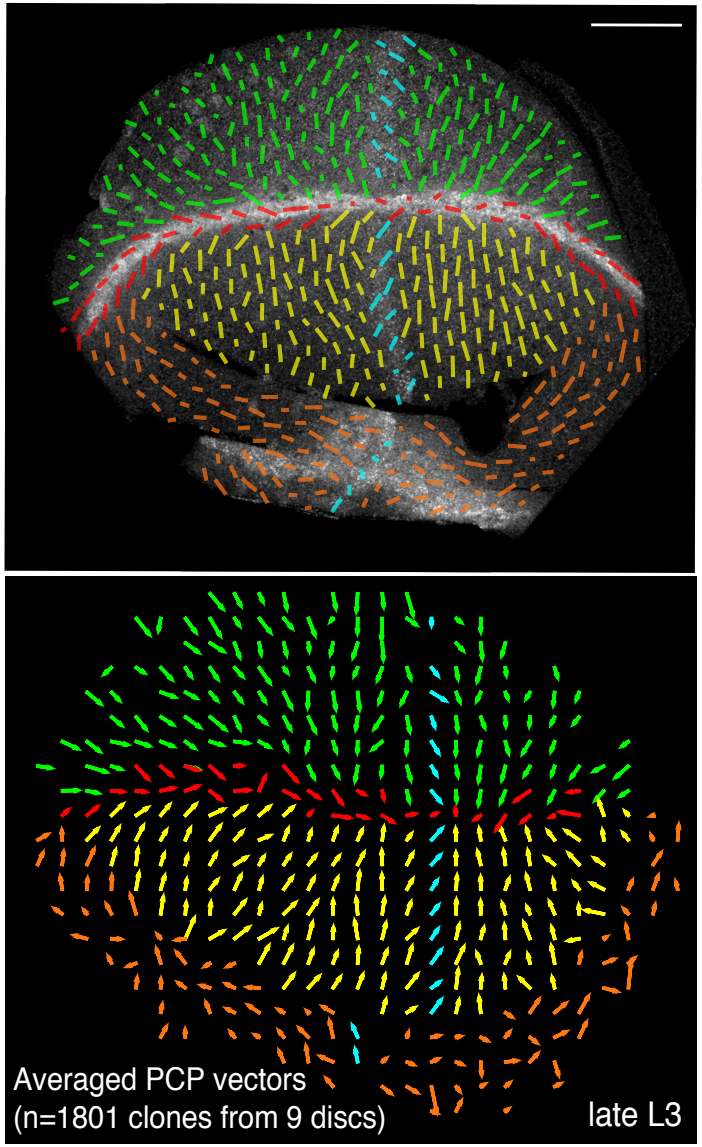
?????

Global alignment of PCP in the absence of gradients

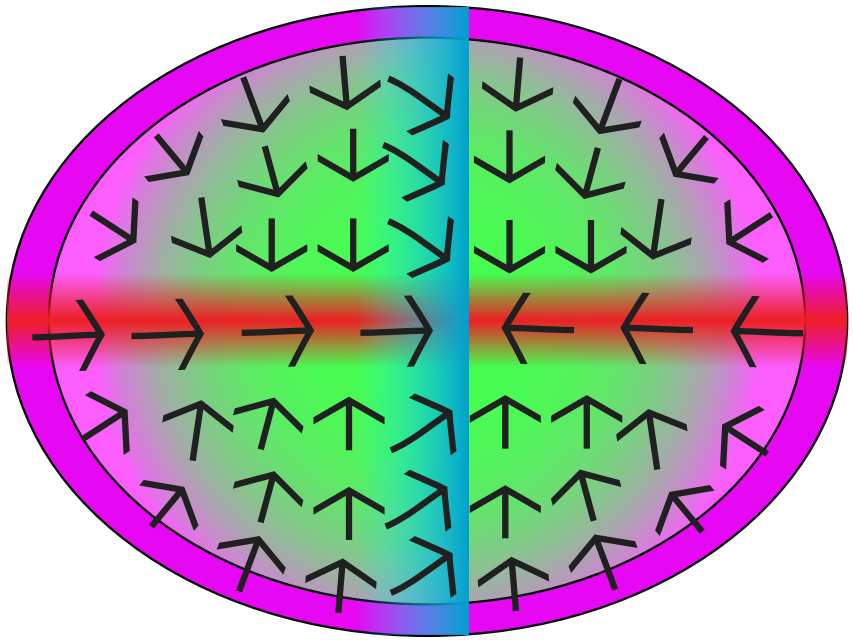




The planar polarity pattern is oriented with respect to organizer regions



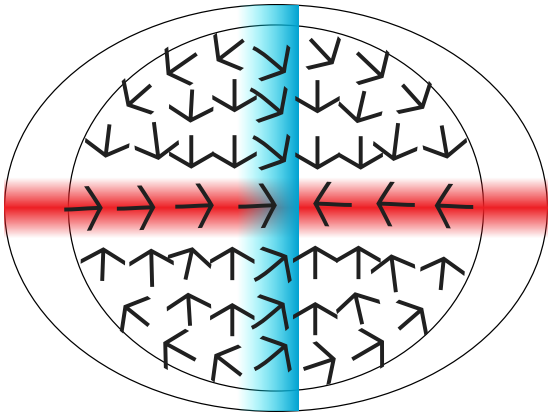
Hedgehog signaling



Wingless/
Notch

Dachsous/Four-jointed

Perturbing each signaling center alters both growth and the polarity pattern

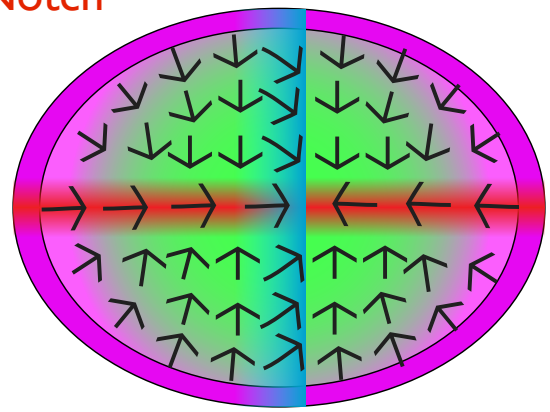


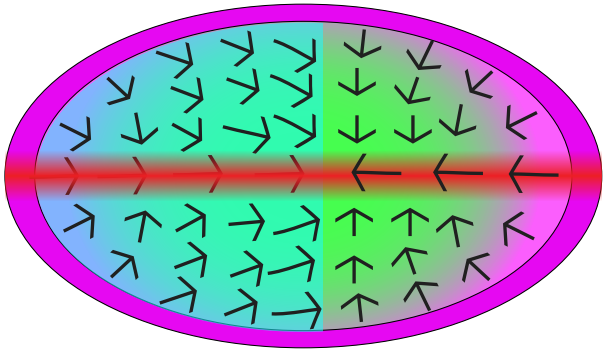
Fat mutant

Hedgehog

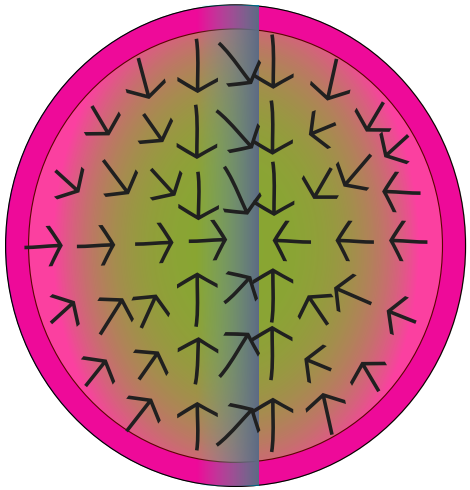
Wingless/
Notch

Dachsous

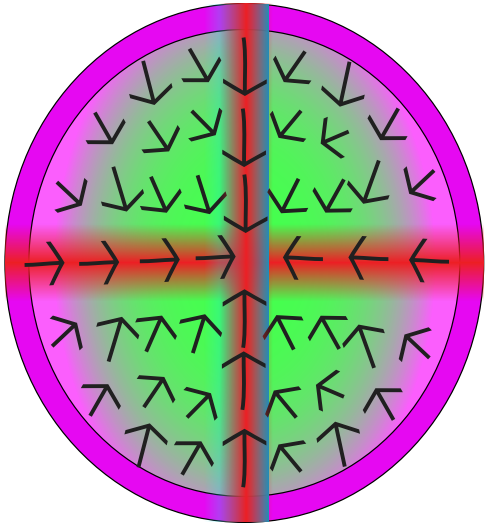




Uniform Hh expression

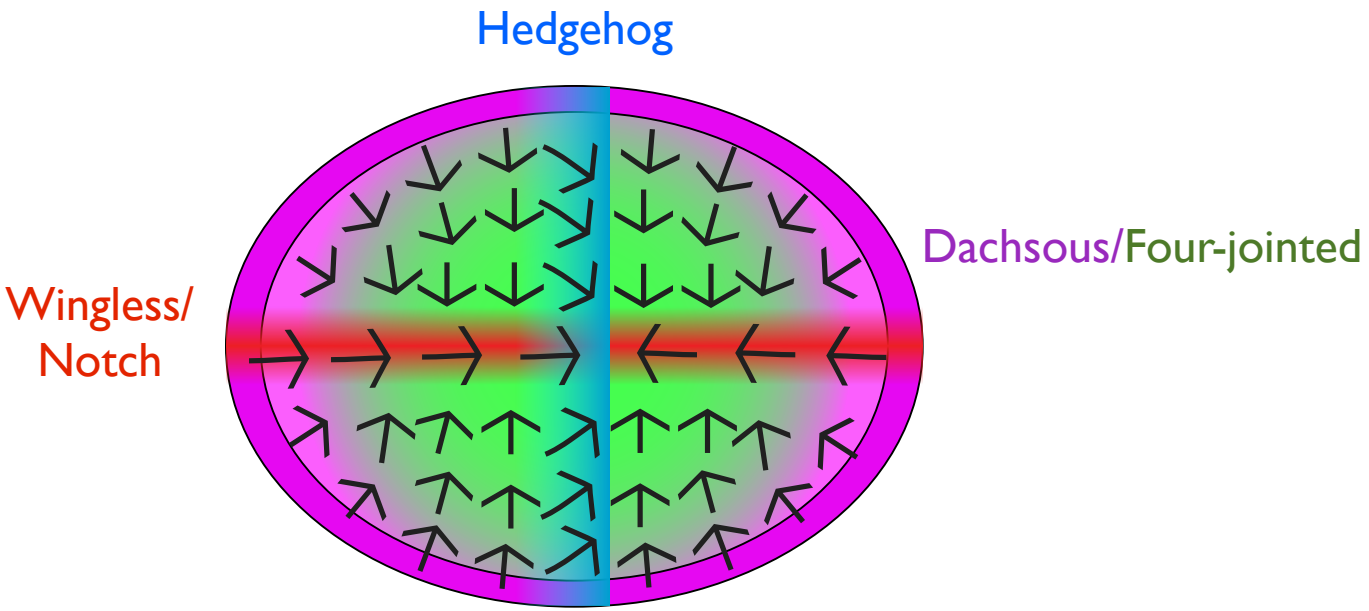


Uniform Wg expression



Wg expression at the AP boundary

Summary 1

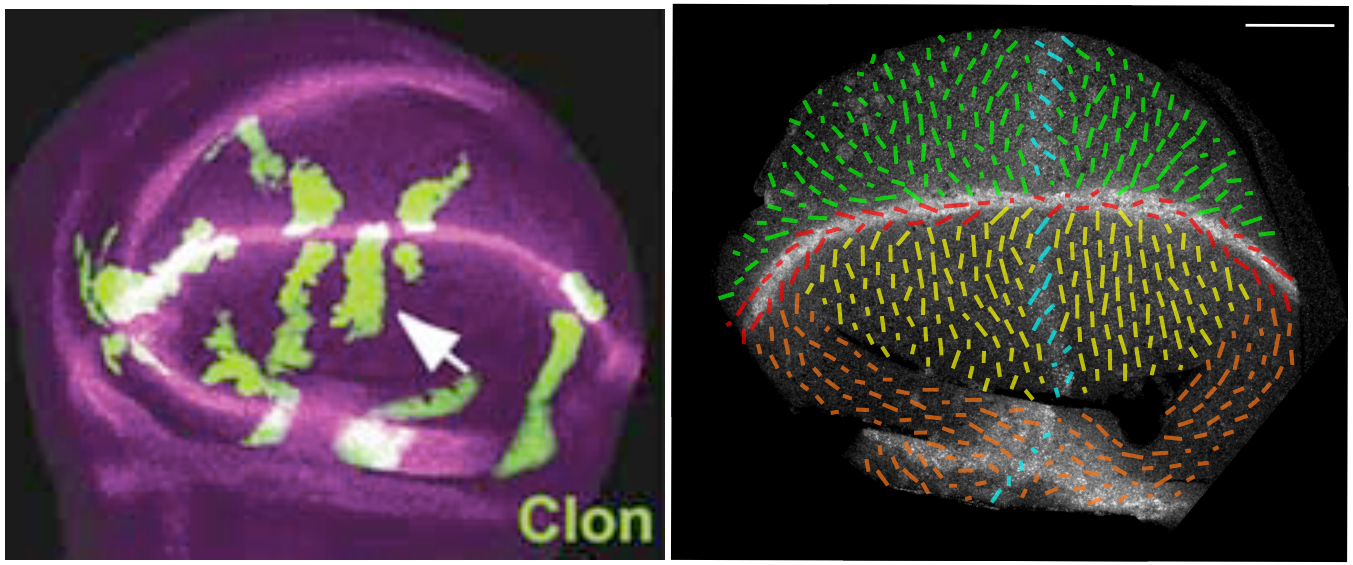


The global PCP pattern is oriented by 3 signaling systems that control growth

These three cues generally reinforce each other

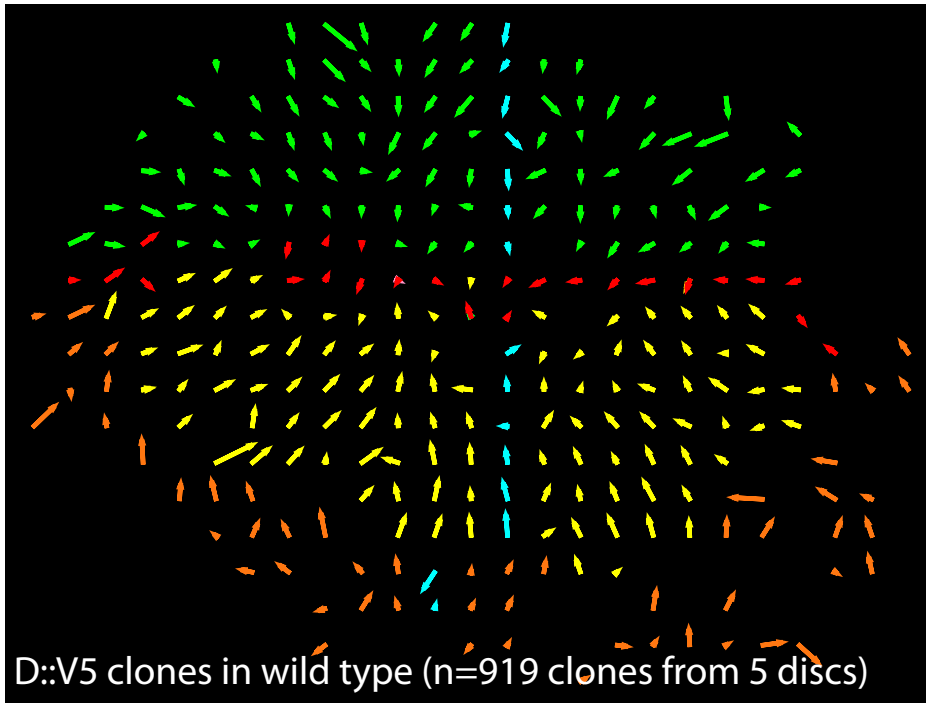
Uniform high level expression of Wg or Hh does not interfere with the ability of cells to polarize - it just produces a new PCP *pattern*. These molecules are unlikely to directly influence PCP through gradients

The PCP pattern resembles the growth pattern

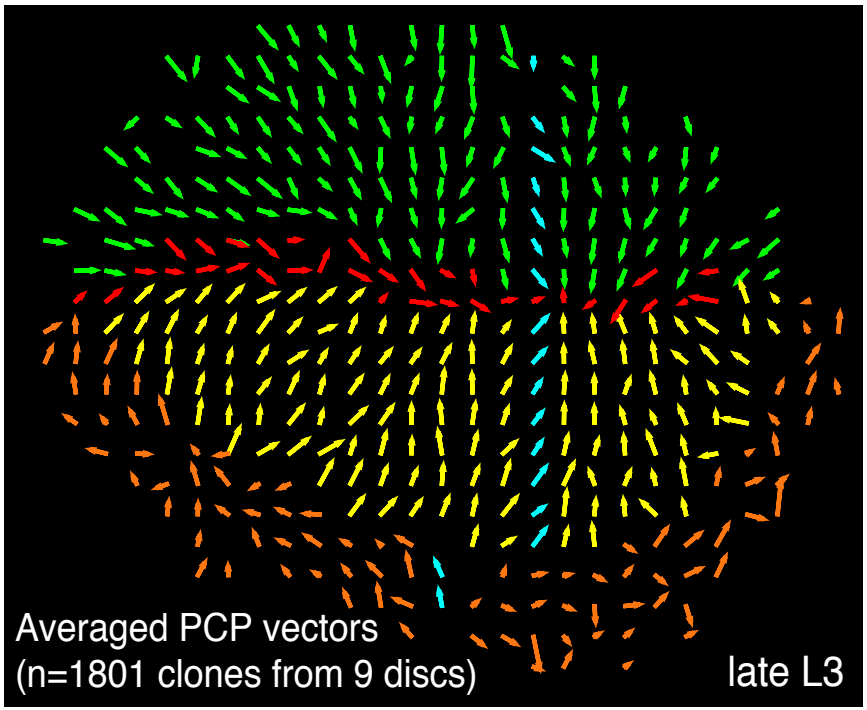


Could the PCP pattern in discs result from growth orientation?

Dachs polarity resembles core PCP polarity in the disc

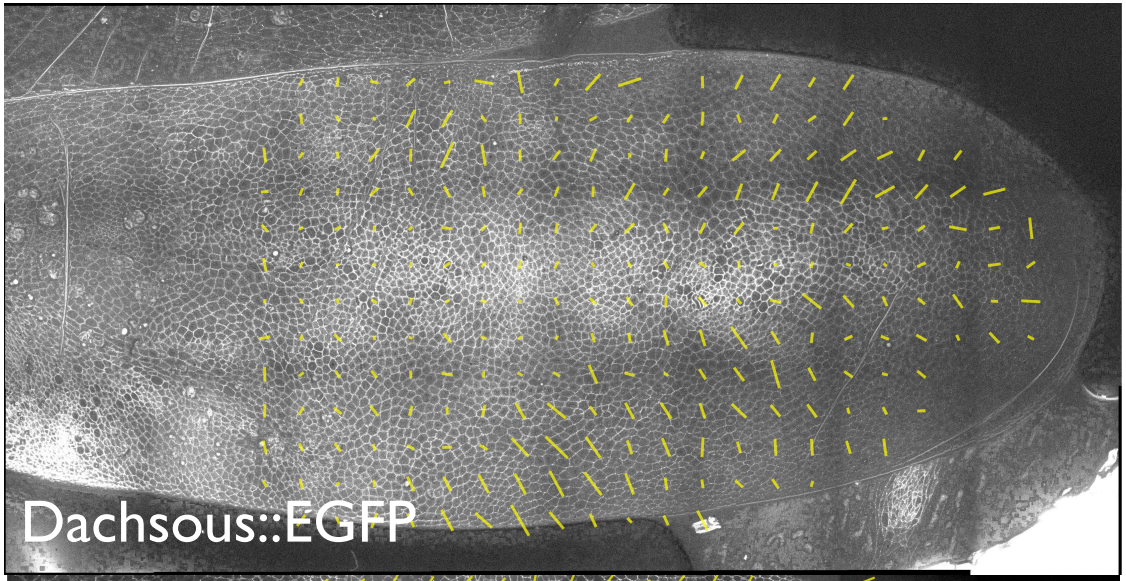


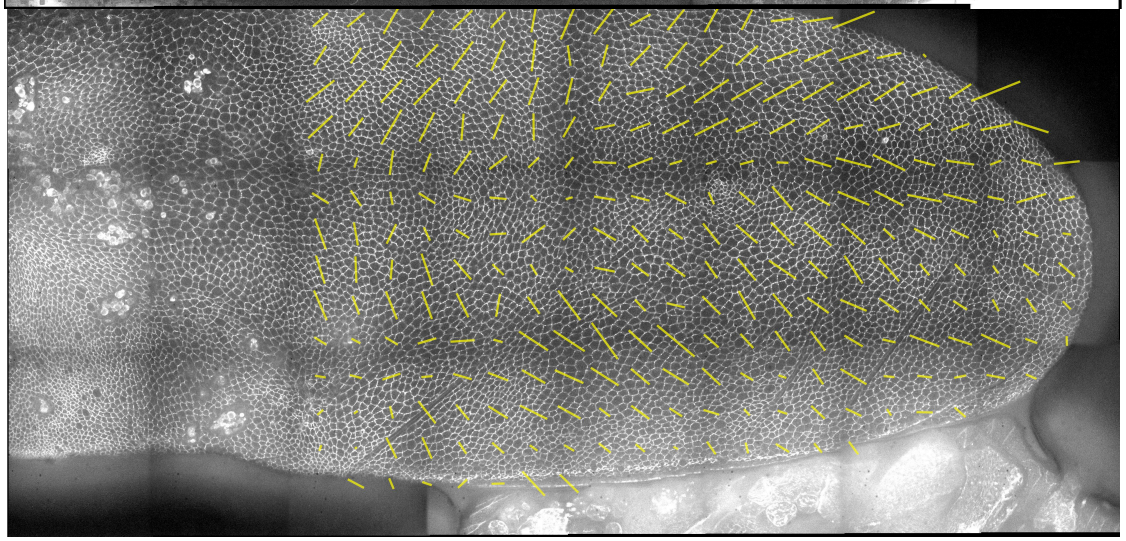
Dachs polarity vectors

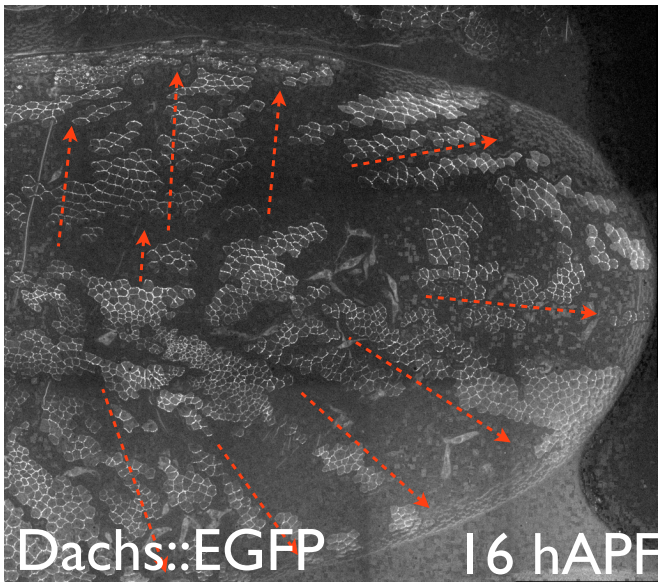


Core PCP vectors

Dachs and Ds are oriented towards the wing margin at 16 hours APF - similar to core PCP



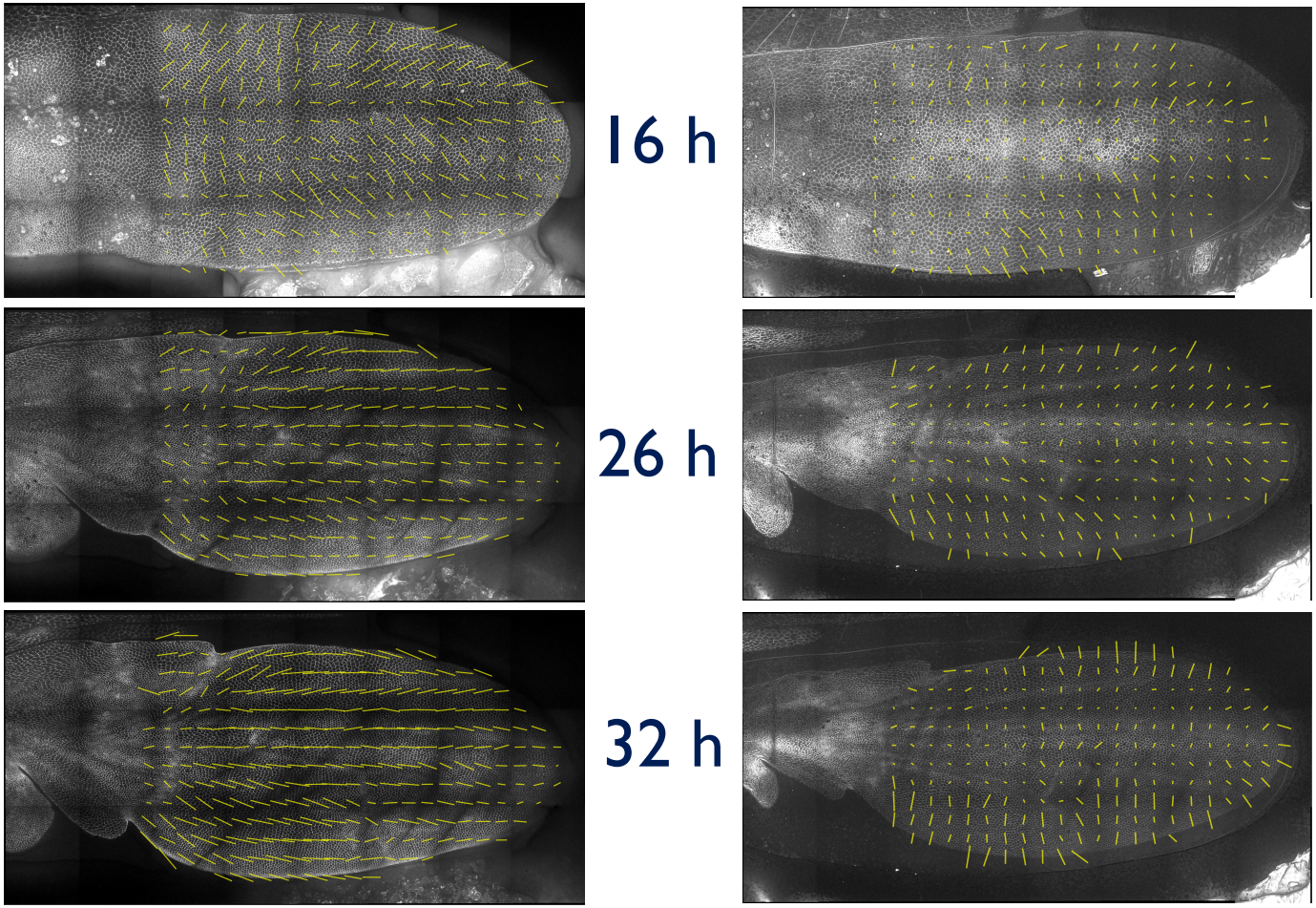




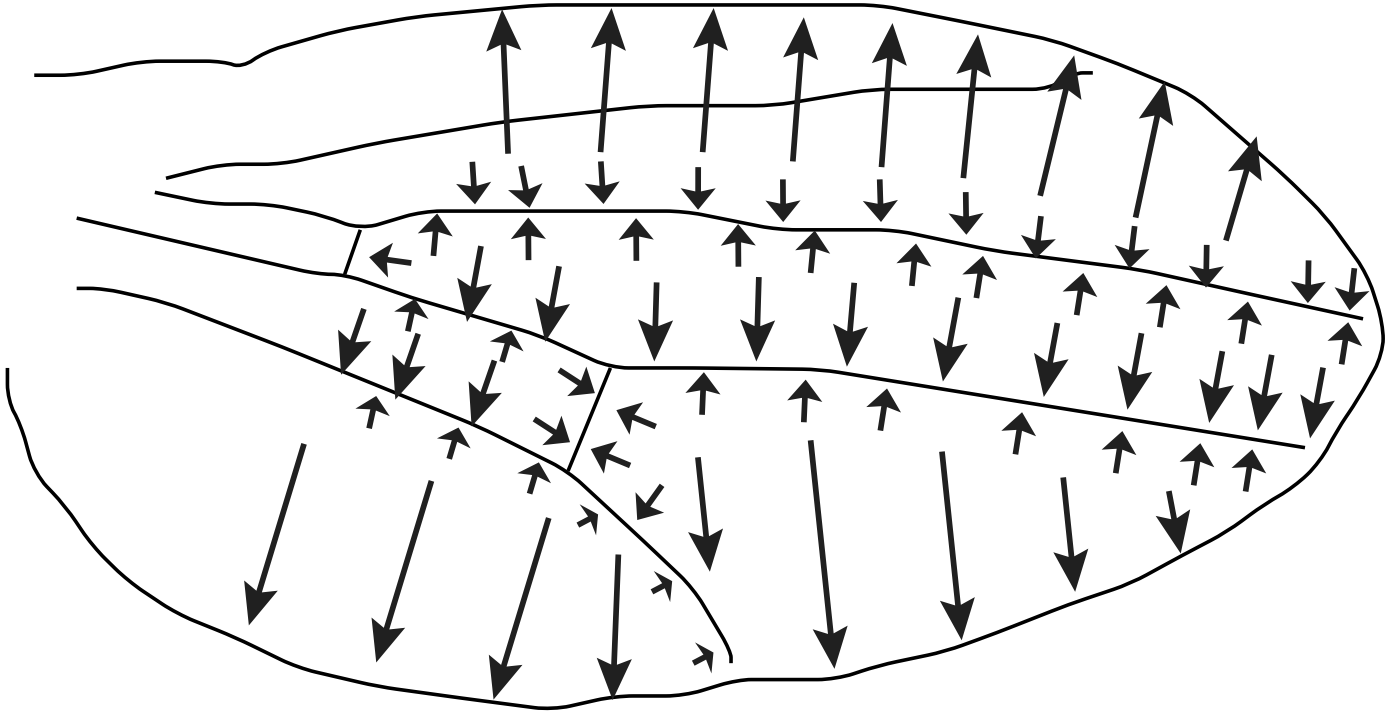
Dachsous polarity is not reoriented during flow

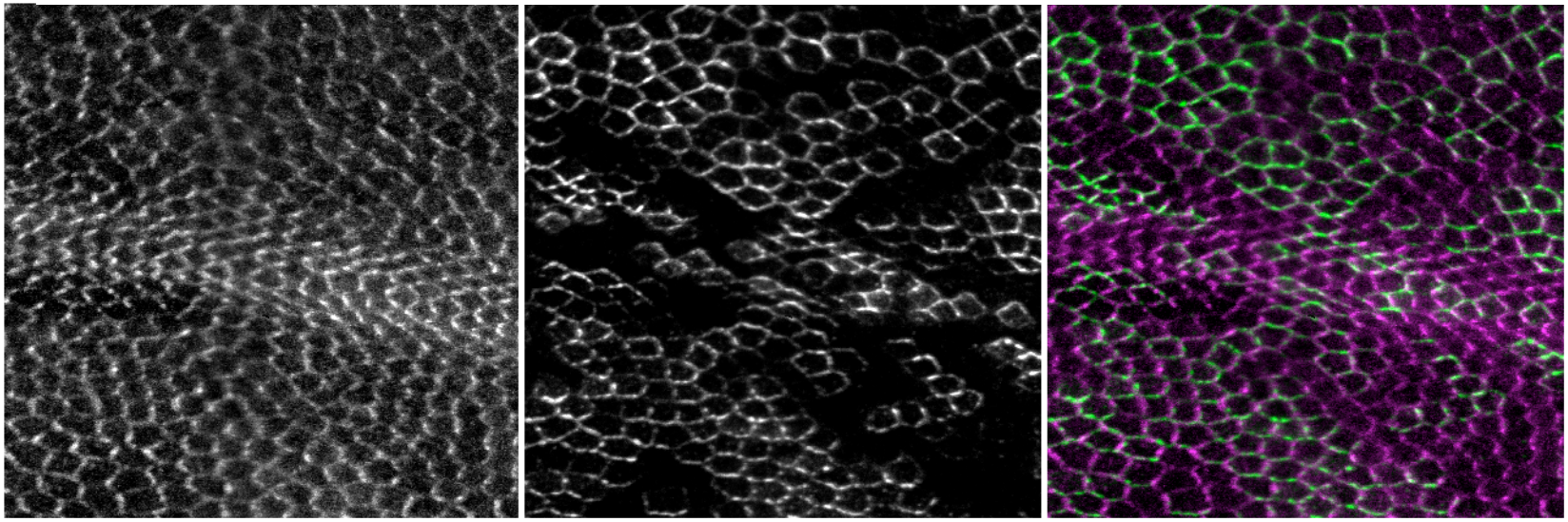
Strabismus

Dachsous



Dachs orients towards veins as they differentiate





Summary 2

Unlike Core PCP, Fat/Dachsous/Dachs PCP is not reoriented by tissue flows

Core PCP and Fat/Dachsous/Dachs PCP polarity patterns diverge during pupal morphogenesis

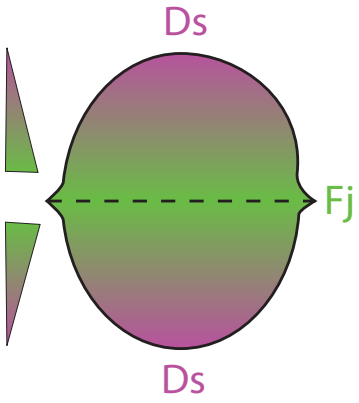
When the two PCP systems specify different polarity patterns, hair outgrowth follows core PCP

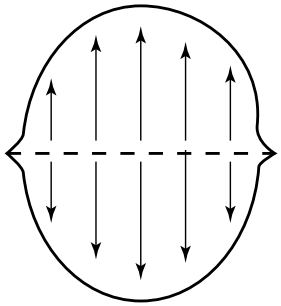
Signals emanating from veins locally reorient Fat/Dachsous/Dachs PCP at late stages

The influence of the Fat/Dachsous polarity system on core PCP patterns in the wing is likely indirect - possibly through growth orientation

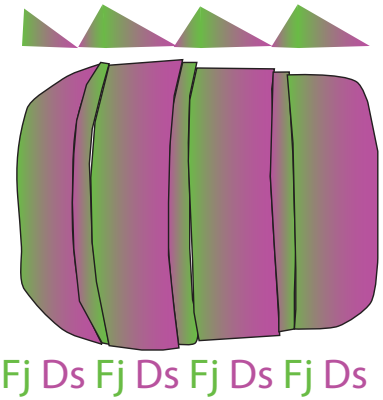
Core PCP and Fat/Ds PCP vectors have different relationships in different tissues

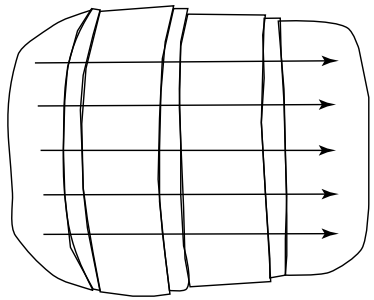
eye



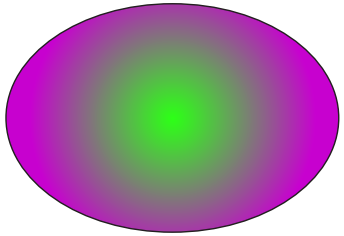


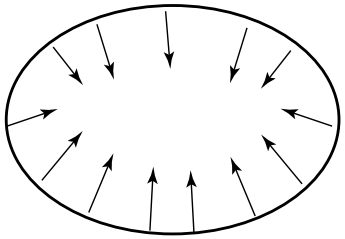
abdomen



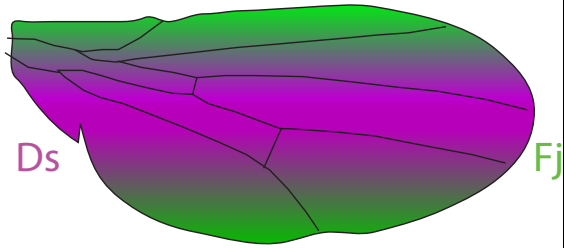


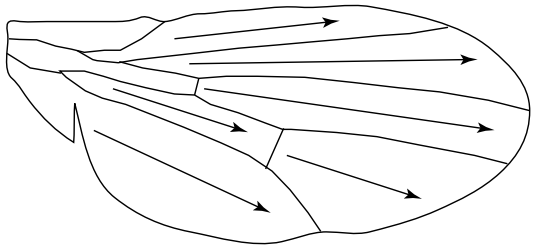
3rd instar wing



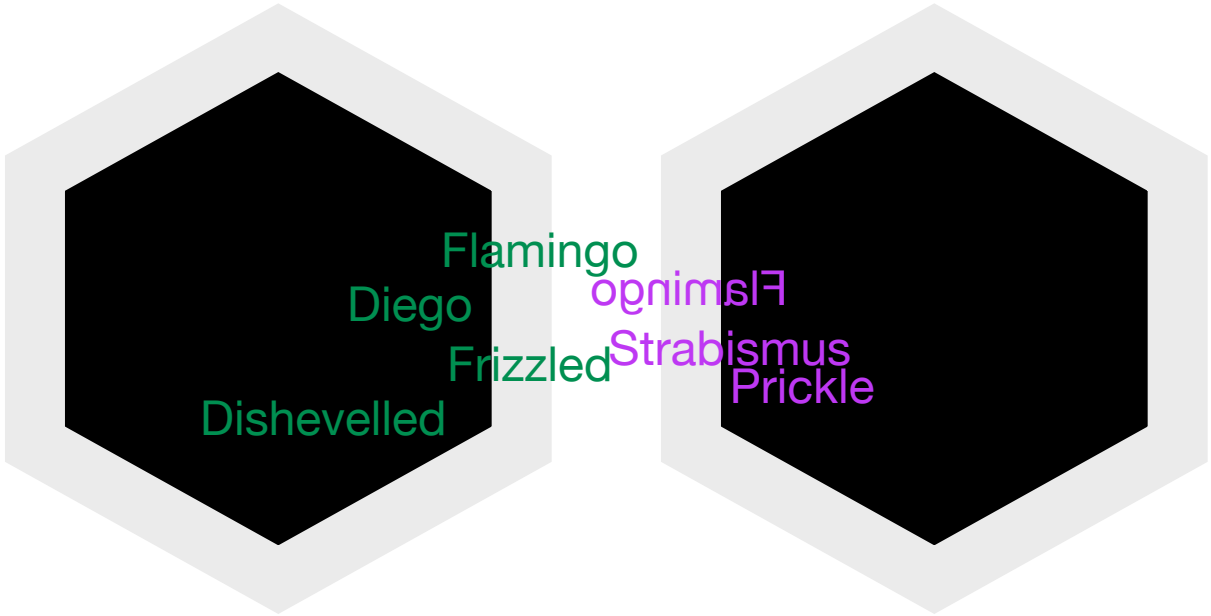


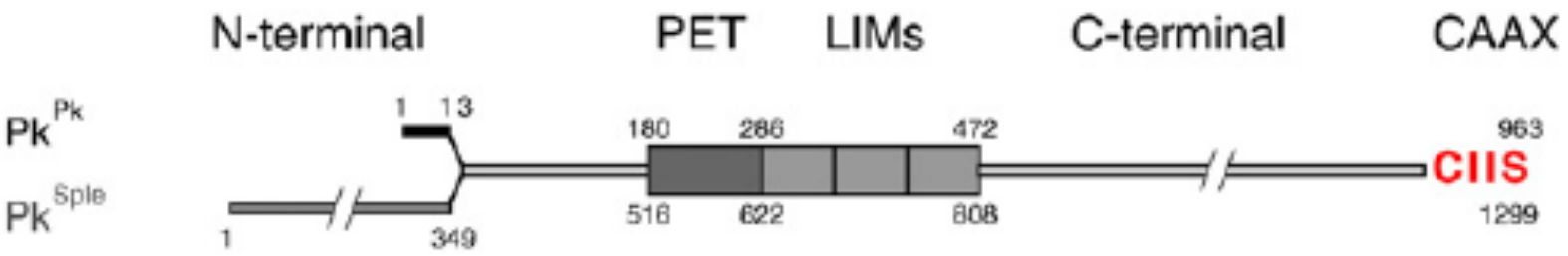
pupal wing





The Prickle locus produces two proteins: Prickle and Spiney leg

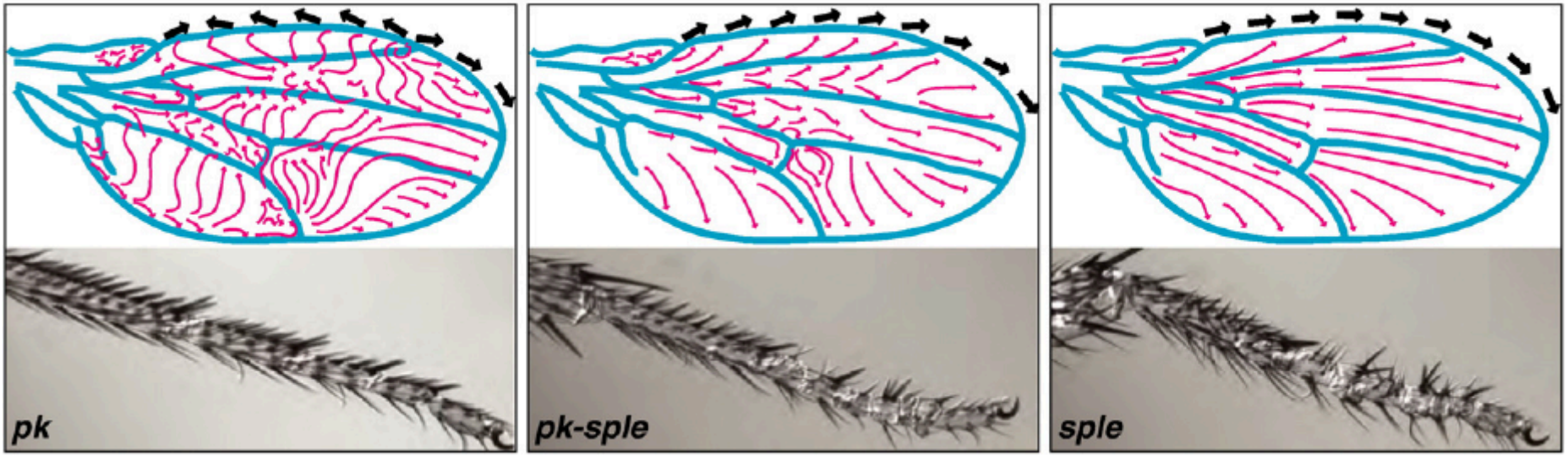




The balance between isoforms of the Prickle LIM domain protein is critical for planar polarity in Drosophila imaginal discs

David Gubb,1 Clare Green, David Huen, Darin Coulson, Glynnis Johnson, David Tree, Simon Collier, and John Roote

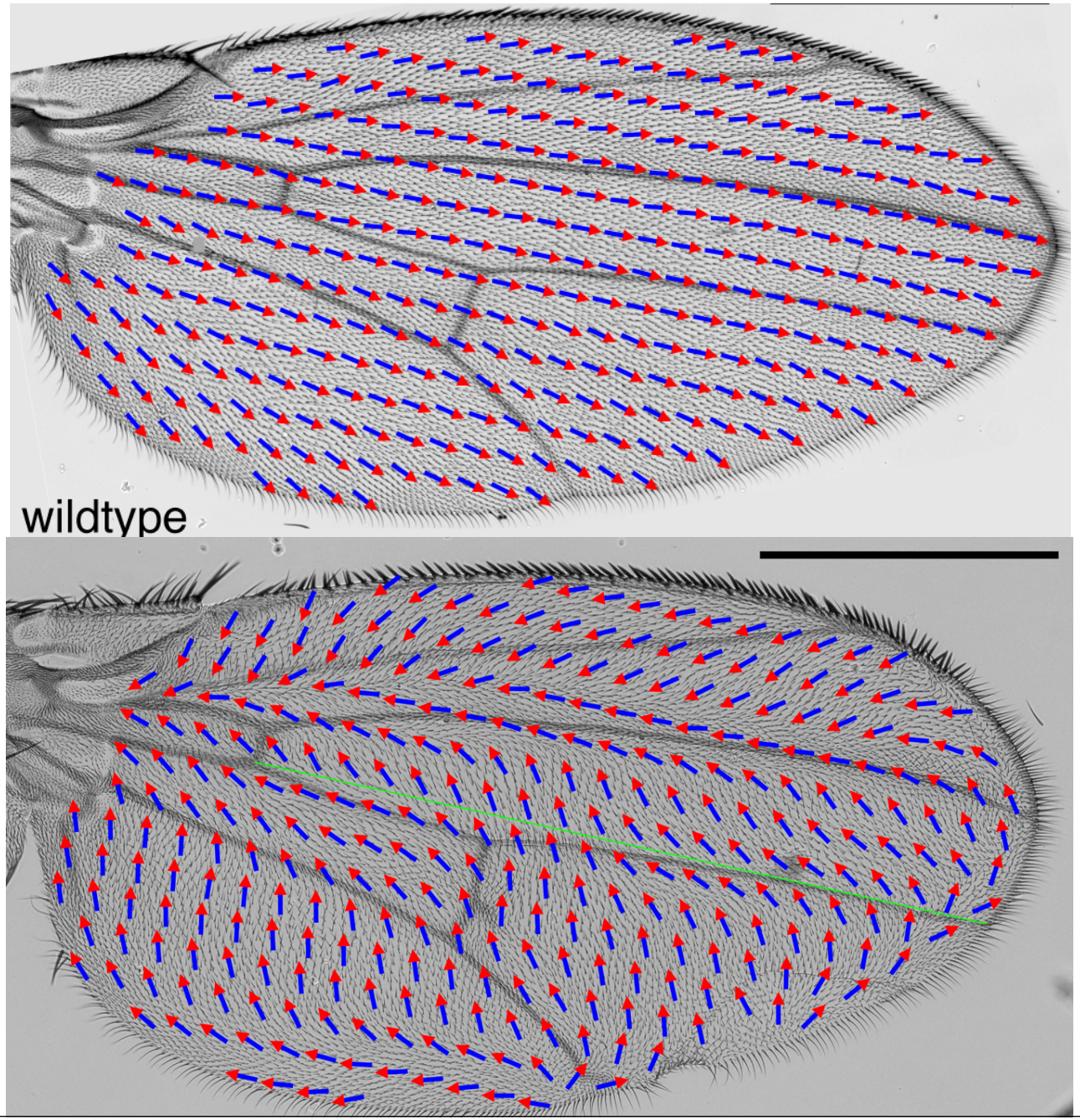
Pk and Sple are required in different tissues and have antagonistic activities



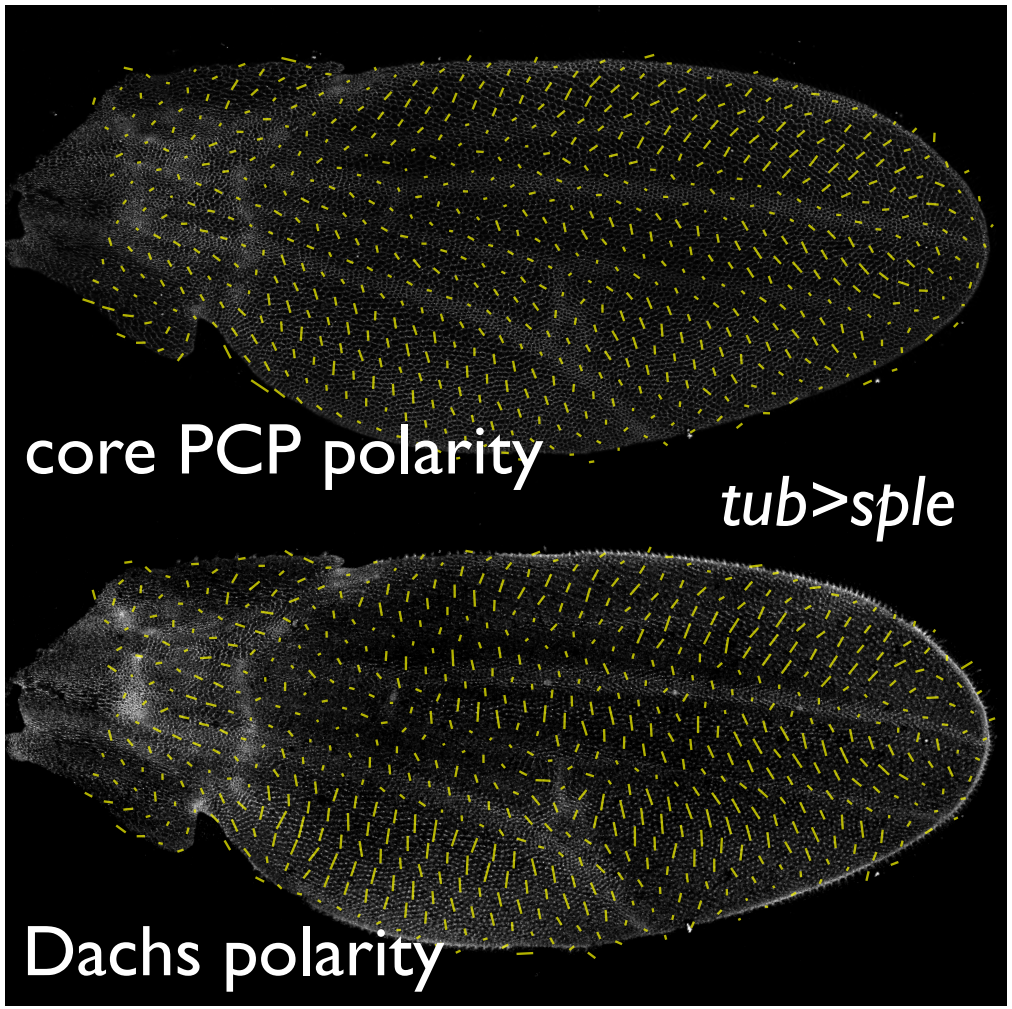
Strong phenotypes of *pk*$^{-}$ or *sple*$^{-}$ are due to dominant effects of the other isoform

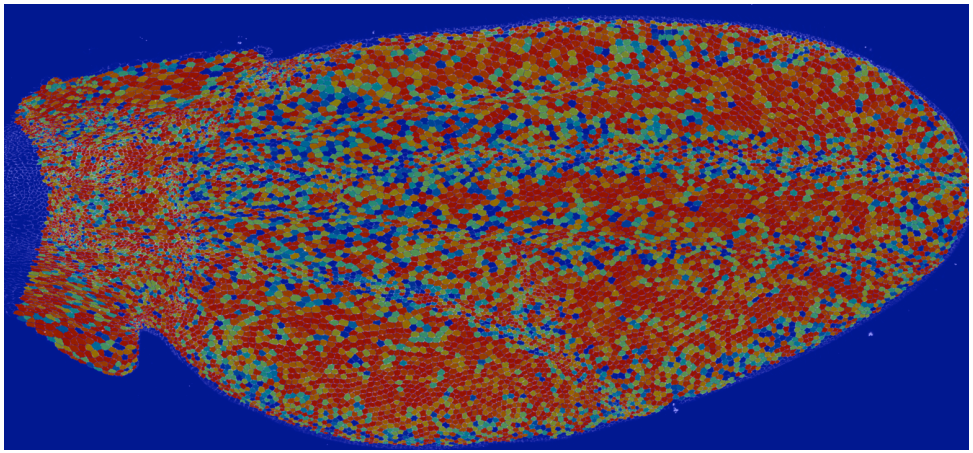
Could Prickle and Spiney leg specify different coupling of core PCP domains to the Fat/Ds polarity system?

Does ectopic Sple expression in the wing couple core PCP domains to the Fat/Ds system?

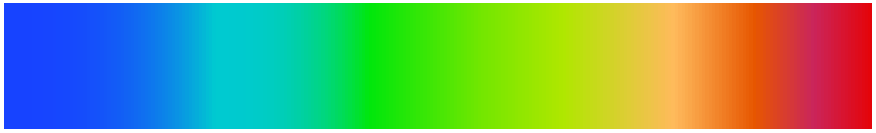


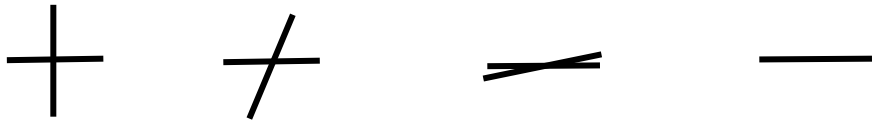
Spiney leg expression in the wing aligns the axes of core PCP with Fat/Ds PCP

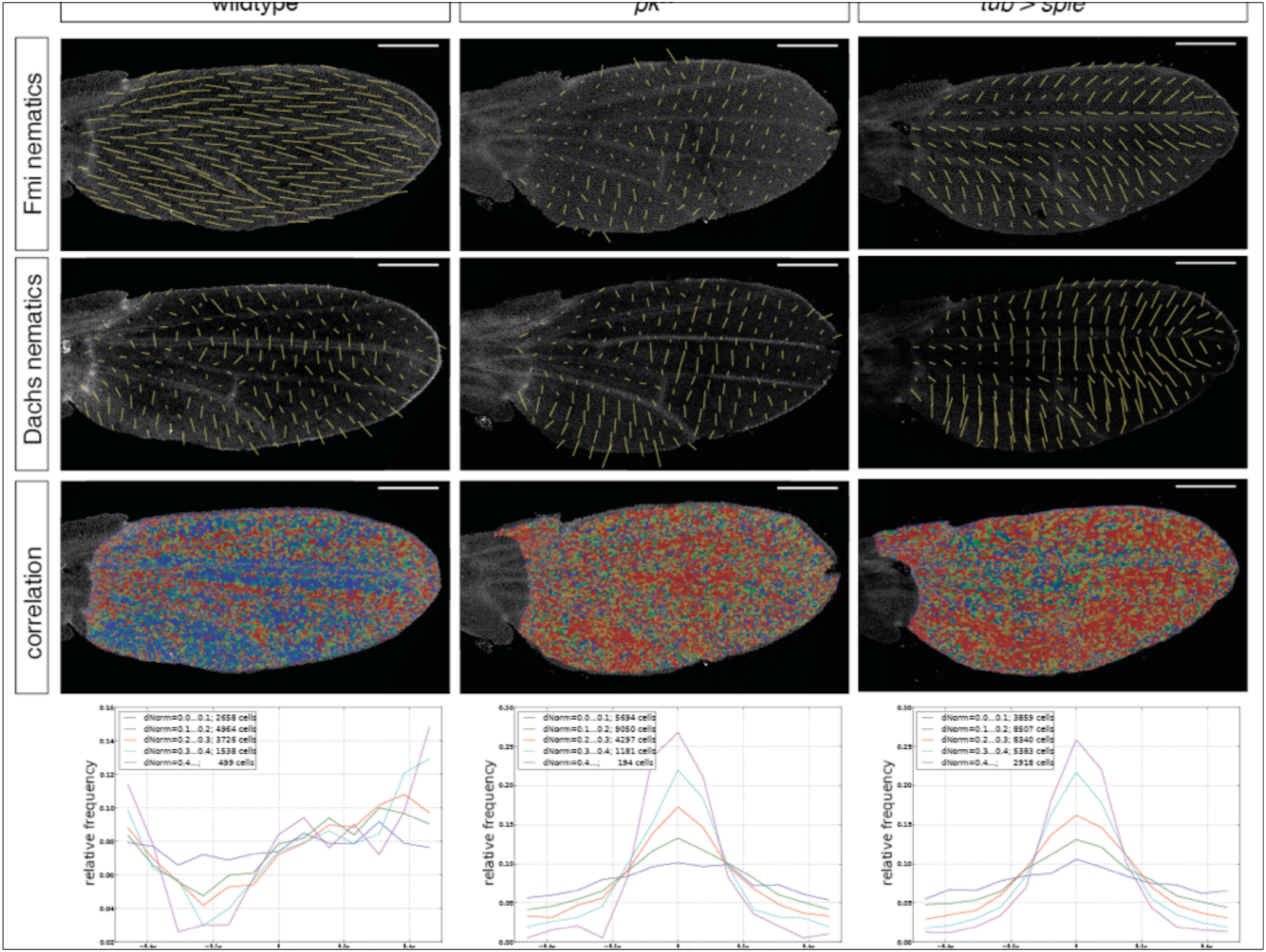




Correlation of polarity axes in individual cells






wildtype
pk
tub > sple
Fmi nematics
Dachs nematics
correlation
relative frequency
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dNorm=0.1...0.2; 4964 cells
dNorm=0.2...0.3; 3726 cells
dNorm=0.3...0.4; 1538 cells
dNorm=0.4...; 499 cells
dNorm=0.0...0.1; 5694 cells
dNorm=0.1...0.2; 9050 cells
dNorm=0.2...0.3; 4297 cells
dNorm=0.3...0.4; 1181 cells
dNorm=0.4...; 194 cells
dNorm=0.0...0.1; 3859 cells
dNorm=0.1...0.2; 8507 cells
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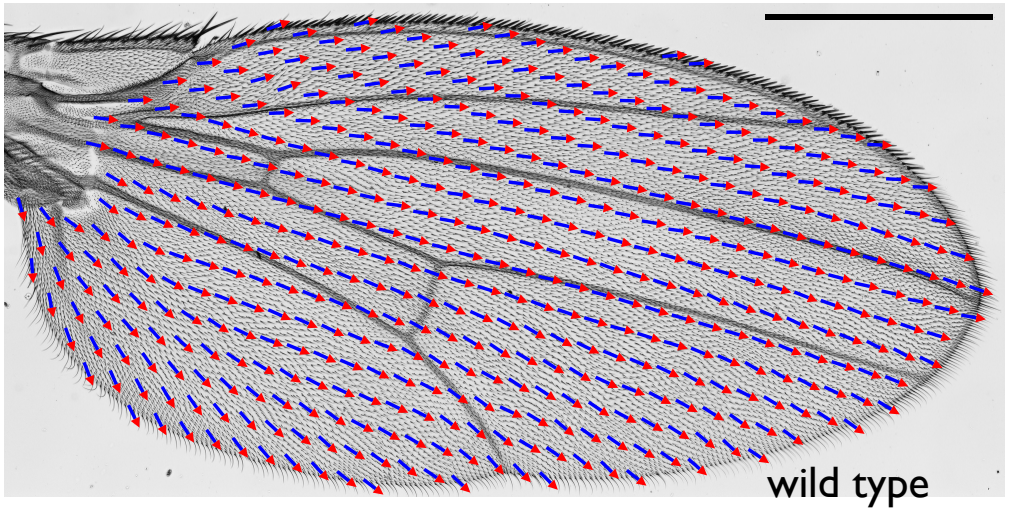
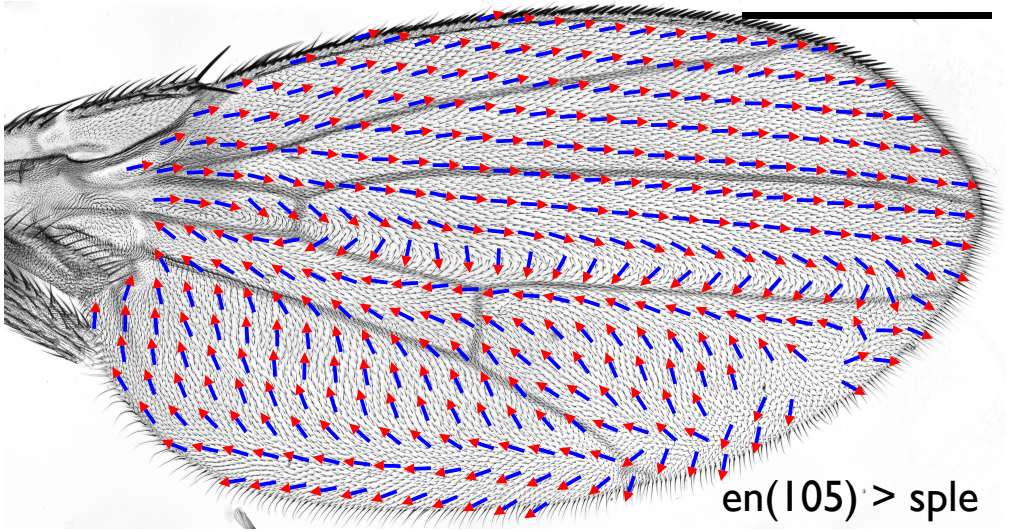
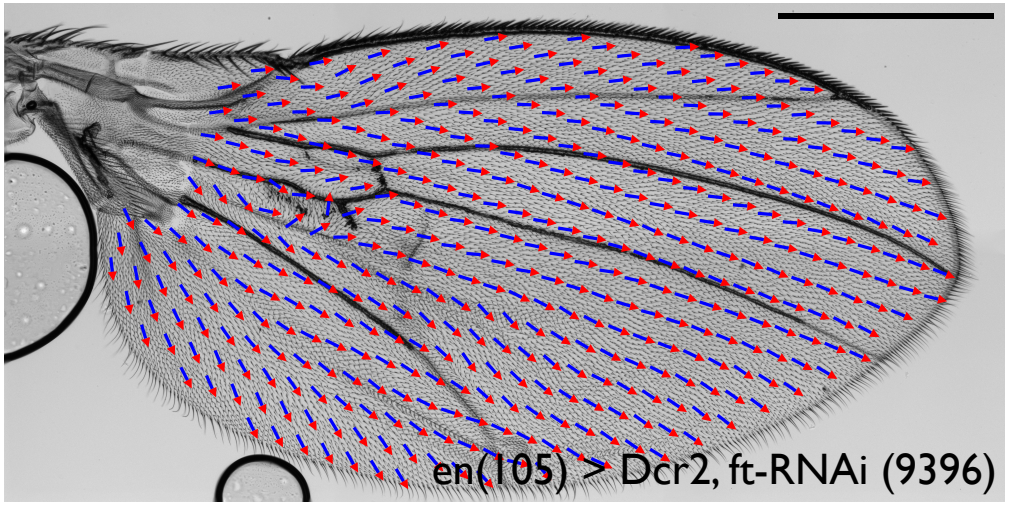
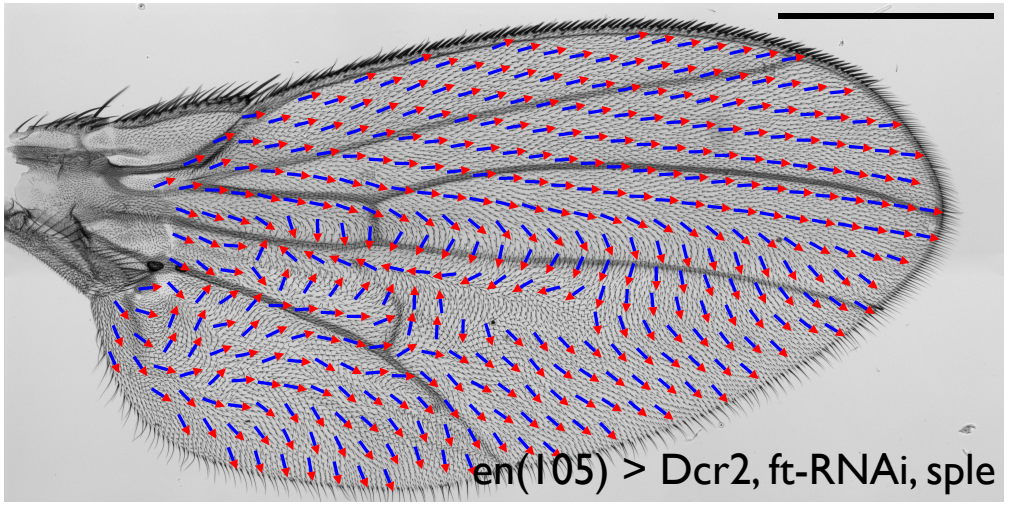
Reducing Fat levels supresses polarity defects caused by Sple expression









Polarity reorientation in Sple-expressing wings depends on the Fat/Dachsous system

Some things to remember...

Global patterns of PCP can be oriented by morphogenesis

The Sple isoform directly couples core PCP to Fat/Dachsous polarity with the orientation seen in the eye and abdomen

The Prickle isoform allows uncoupling of the core PCP pattern from that of the Fat/Dachsous system in the wing, allowing PCP to respond to morphogenesis.

A wide variety of polarity patterns in different tissues can be produced by selective coupling to Fat/Dachsous polarity and by different cellular mechanisms underlying growth and morphogenesis.

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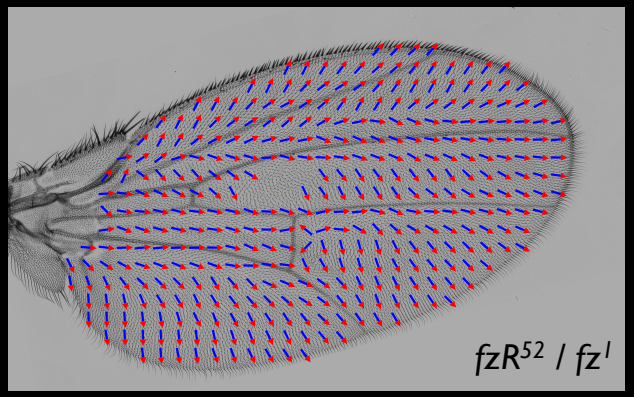
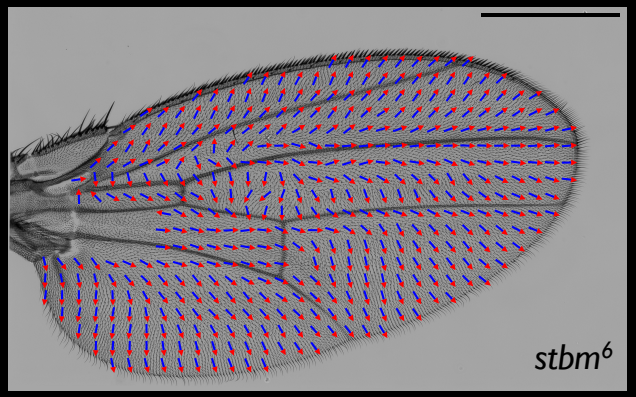
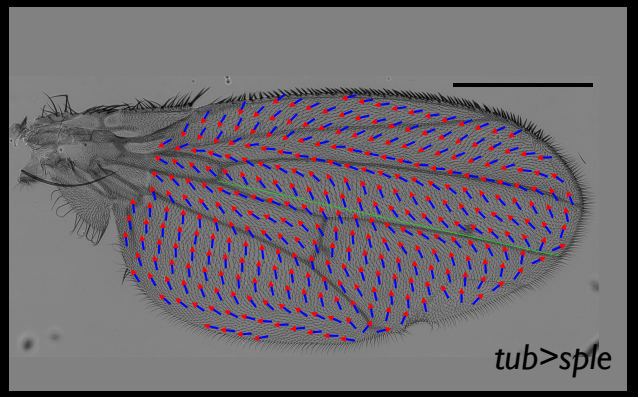
erc
Deutsche Forschungsgemeinschaft DFG
Federal Ministry of Education and Research
EMBO

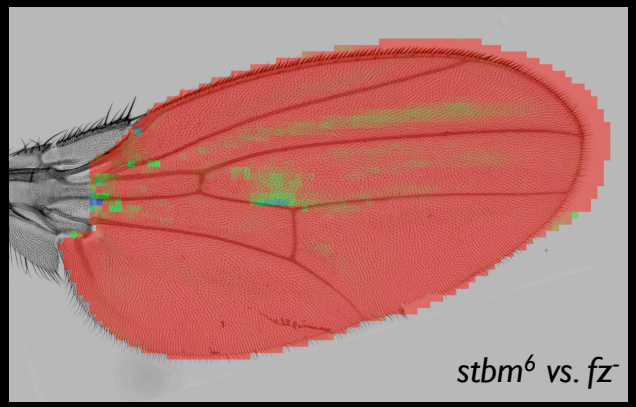
Quantitative comparison of hair polarity patterns in wings with perturbed core PCP systems

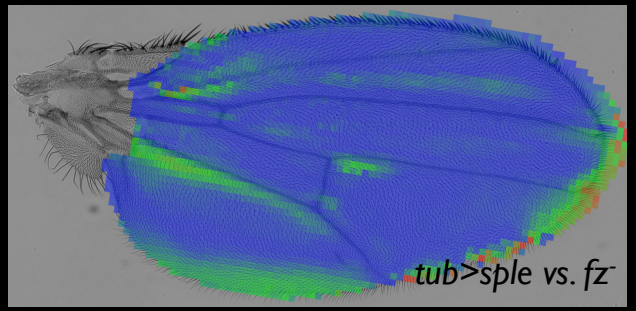


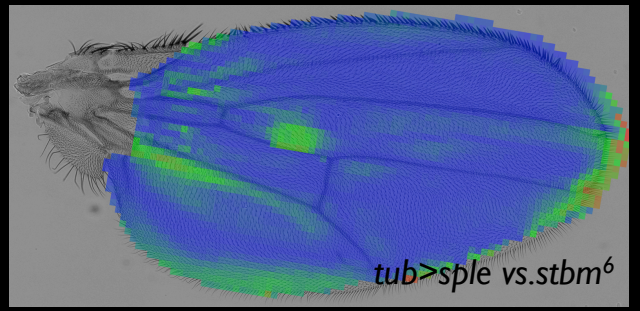




averages of min. 8 wings each
comparison of the average patterns

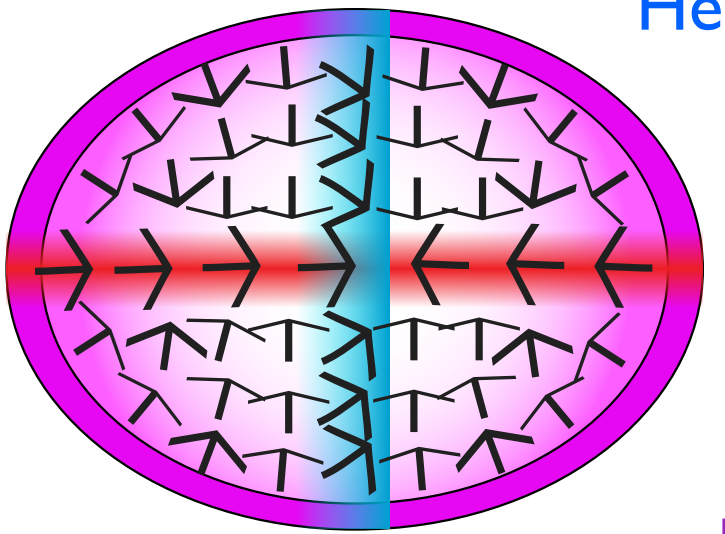




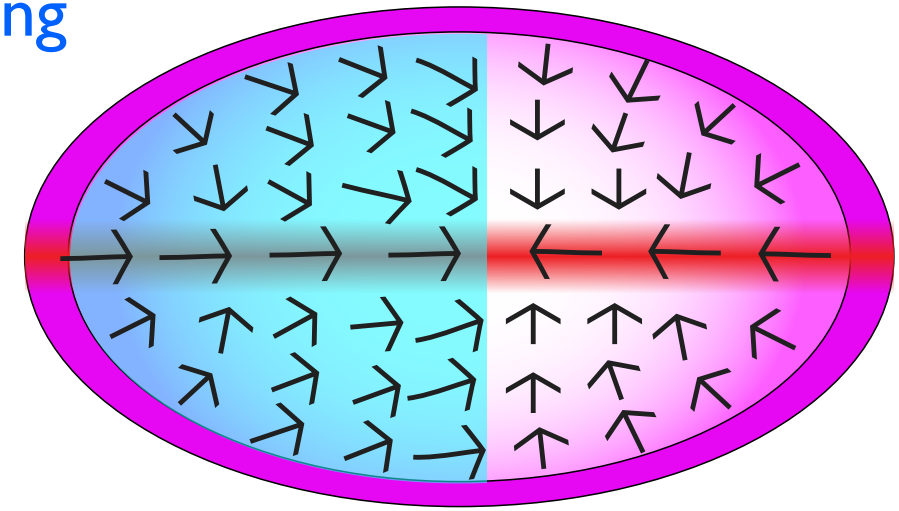


Hedgehog signaling organizes the PCP pattern near the AP boundary

Hedgehog signaling



Wingless/
Notch



Fat/Dachsous

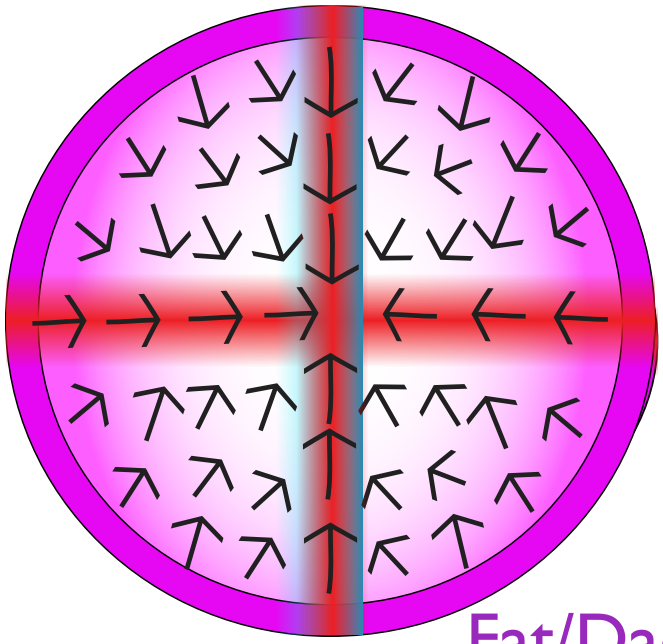
wild type

uniform Hedgehog expression

...and promotes growth parallel to the DV boundary

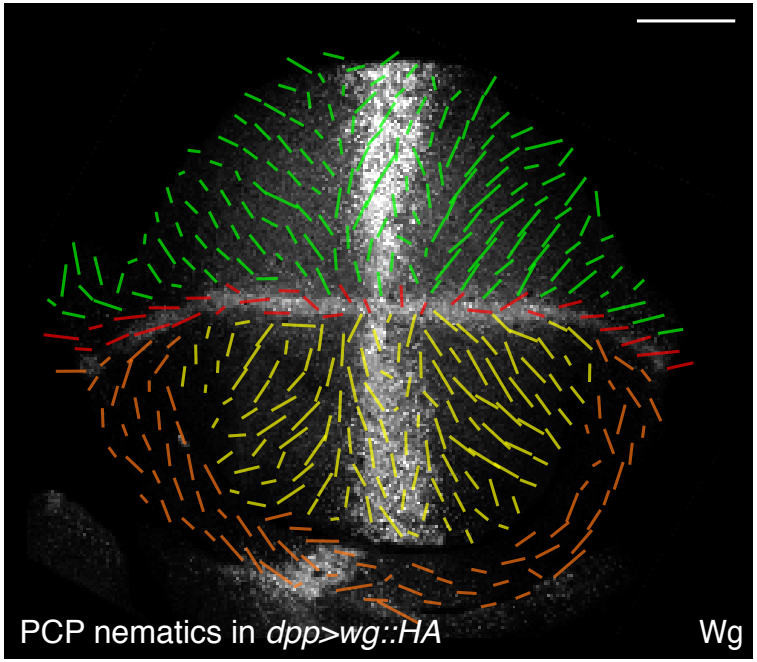
Wingless/Notch signaling organizes the PCP pattern near the DV boundary

Hedgehog signaling



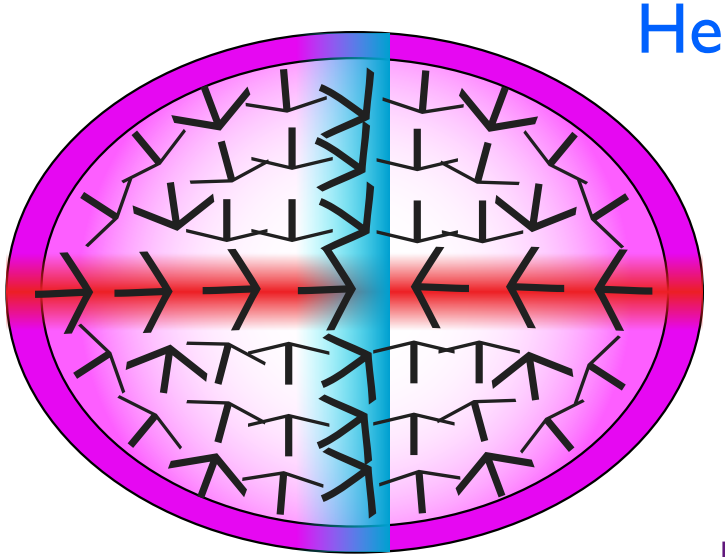
Wingless/
Notch

Fat/Dachsous



...and orients growth parallel to the DV boundary

Fat/Dachsous signaling organizes the PCP pattern near the hinge

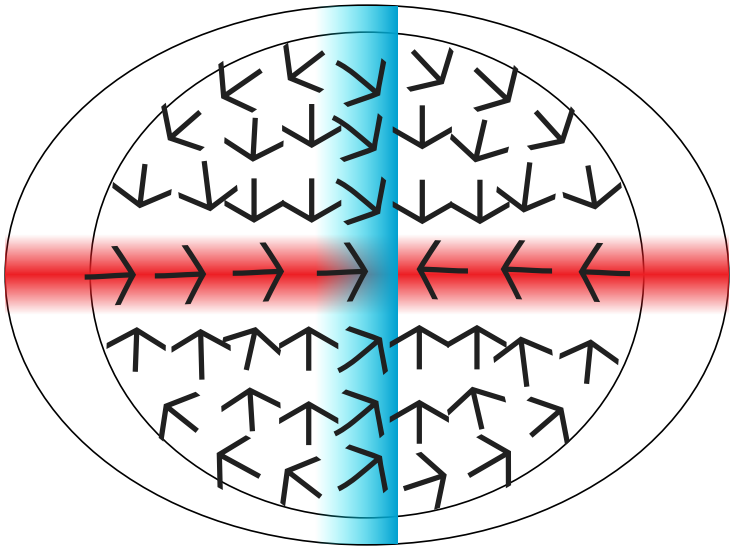


wild type

Hedgehog signaling

Wingless/
Notch

Fat/Dachsous



dachsous mutant

...and limits growth near the hinge