From egg to embryo to organism…

Positional information

Size and shape of organs and tissues

Physiological connections

Improvised use of basic cellular mechanisms

Complex regulatory circuits controlling cell division

Spatio-temporal regulation of gene expression

One cell to multiple cells; The genome remains the same in all cells

Conferring identity means, activating different sets of genes in different cells.

Spatio-temporal regulation of gene expression

Cytoskeletal dynamics

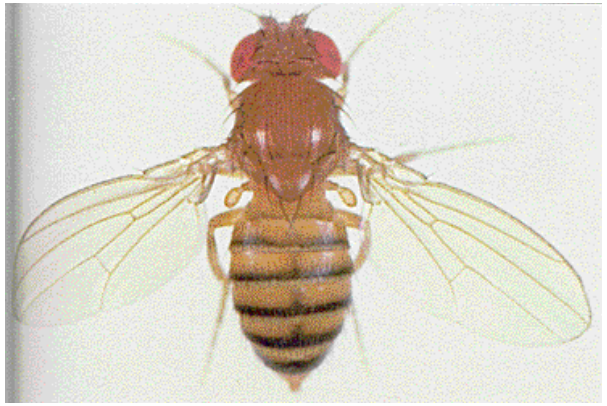
Is that all?

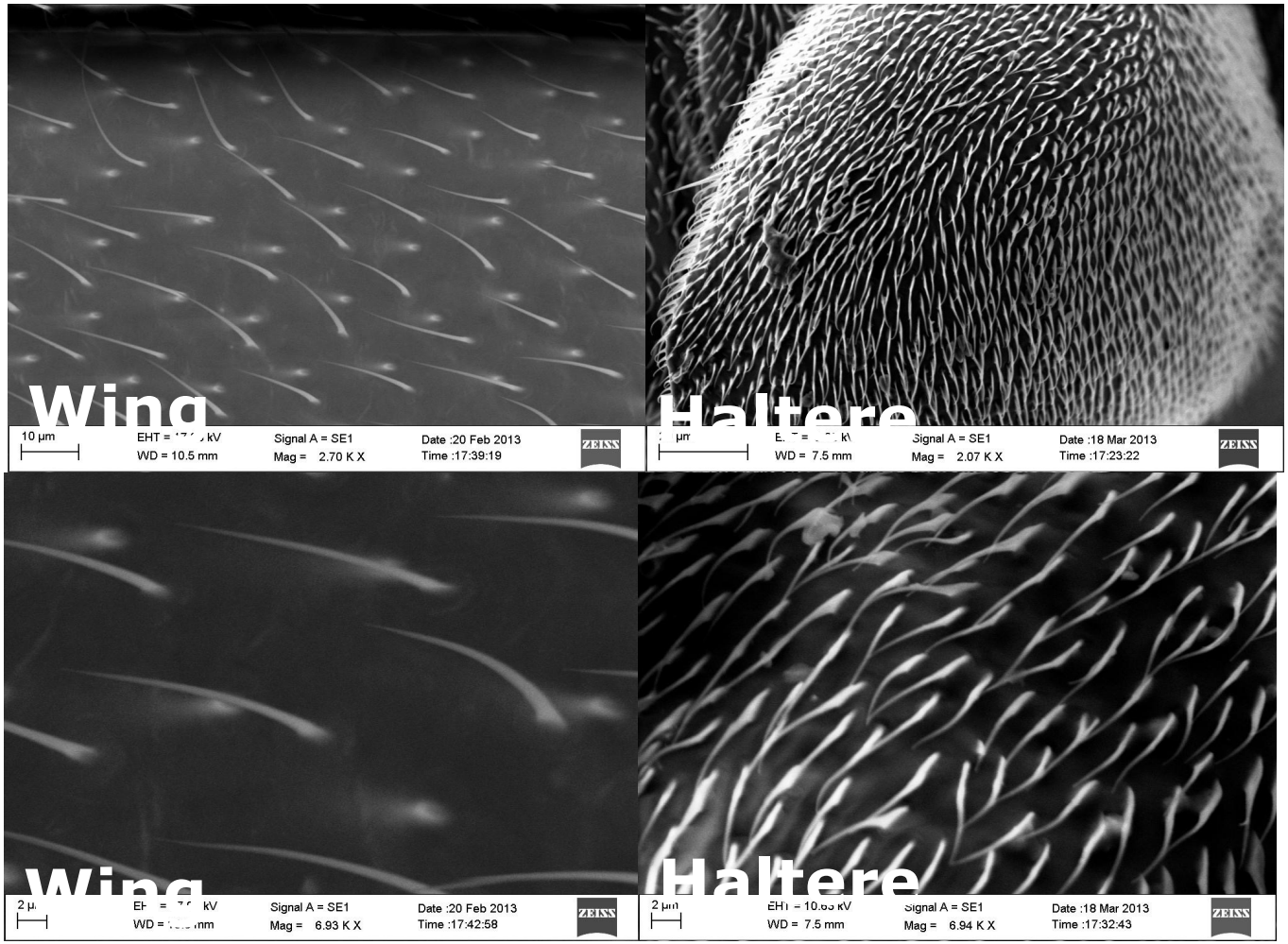
What about internal and external forces that change the mechanical properties of cells?

Are these shape as per the unravelling developmental programs? Example, cell-cell interactions between two cells vs hundreds-thousands of cells at different developmental stages?

Passive role or lack of it vs active role of cortical actin, microtubular cytoskeleton, membranes, extra-cellular matrix…in shaping size/shape/interactions

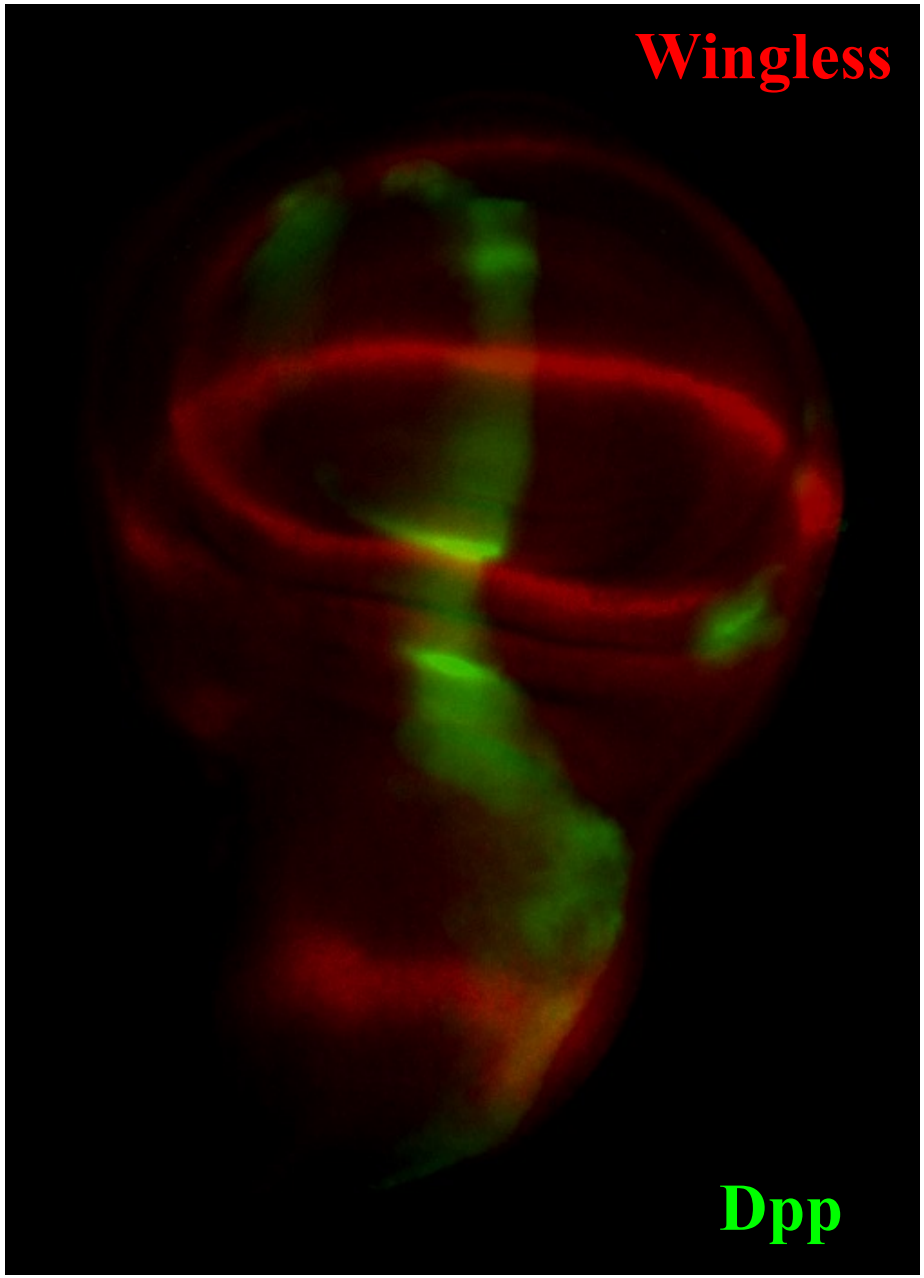
If active role: are mechanical forces too part of the programmed changes? For example, programmed changes to ECM or cortical actin?

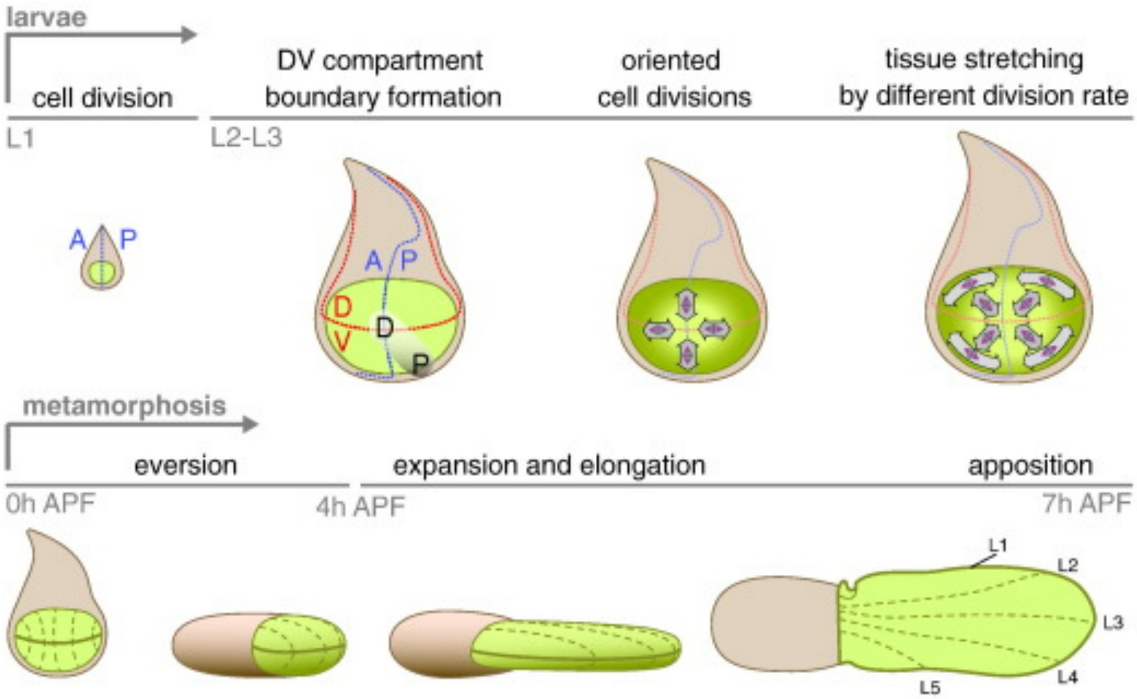


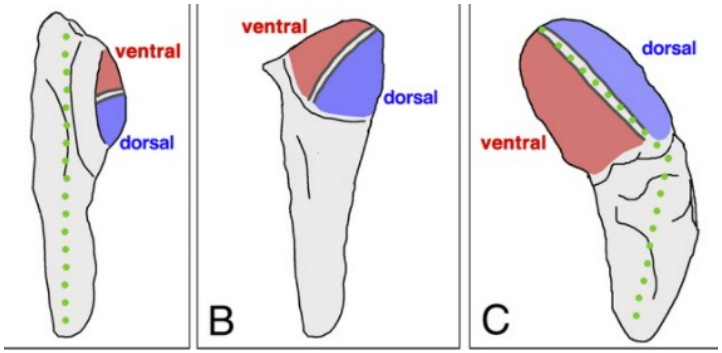


Differential development of wing and haltere is a Good system to study how organ size, shape and thereby function are specified and how these features evolve

How does Ubx modulate wing-developmental pathways?

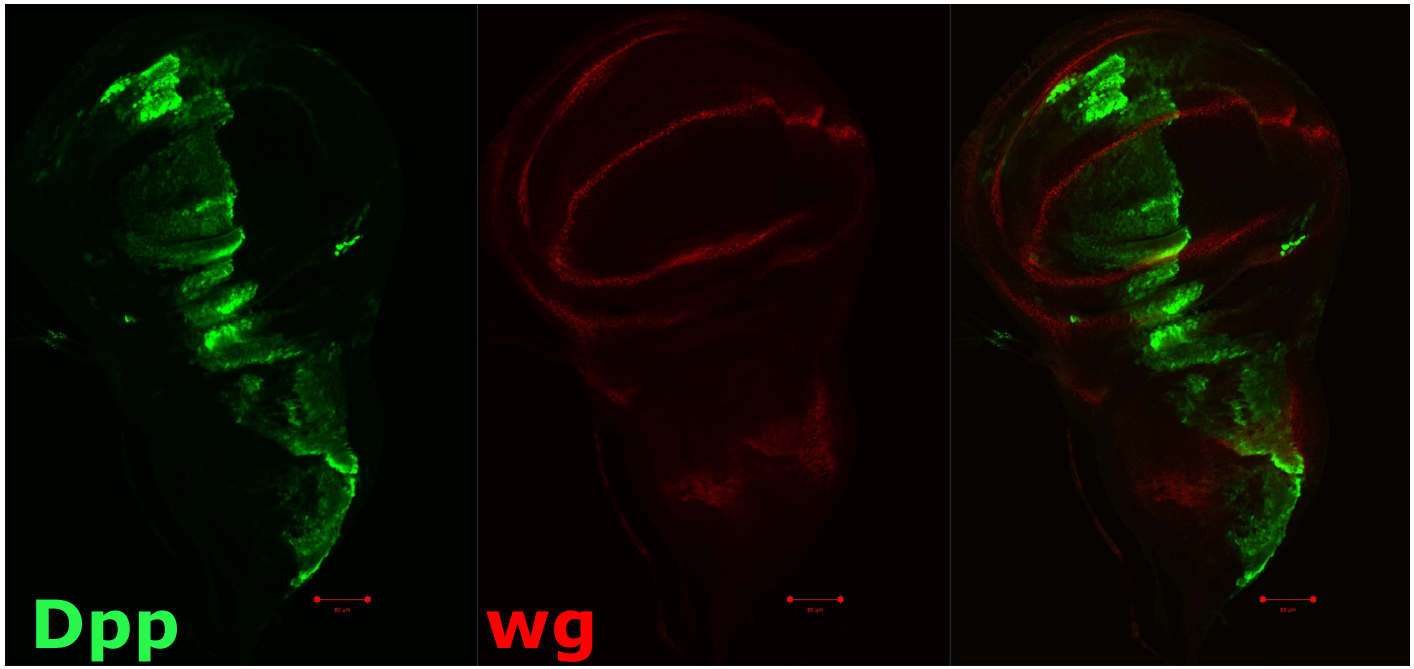




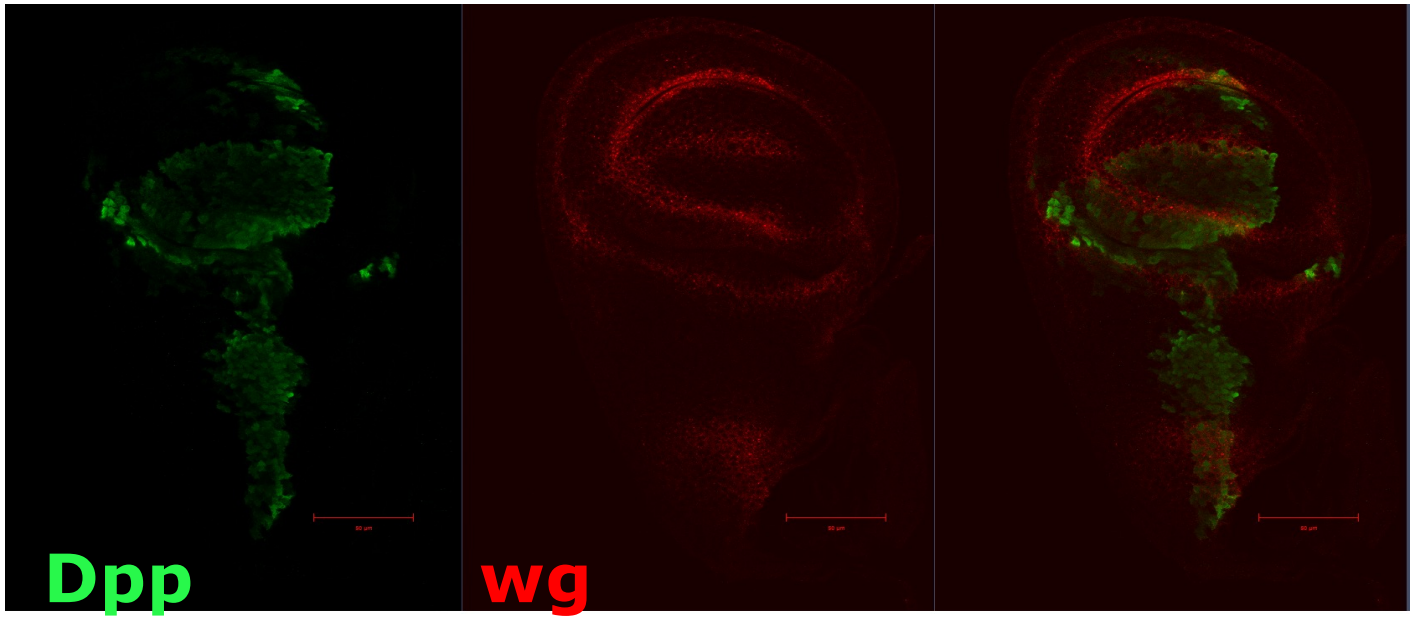


Diaz de la Loza & Thompson, 2017, S Aldaz · 2010

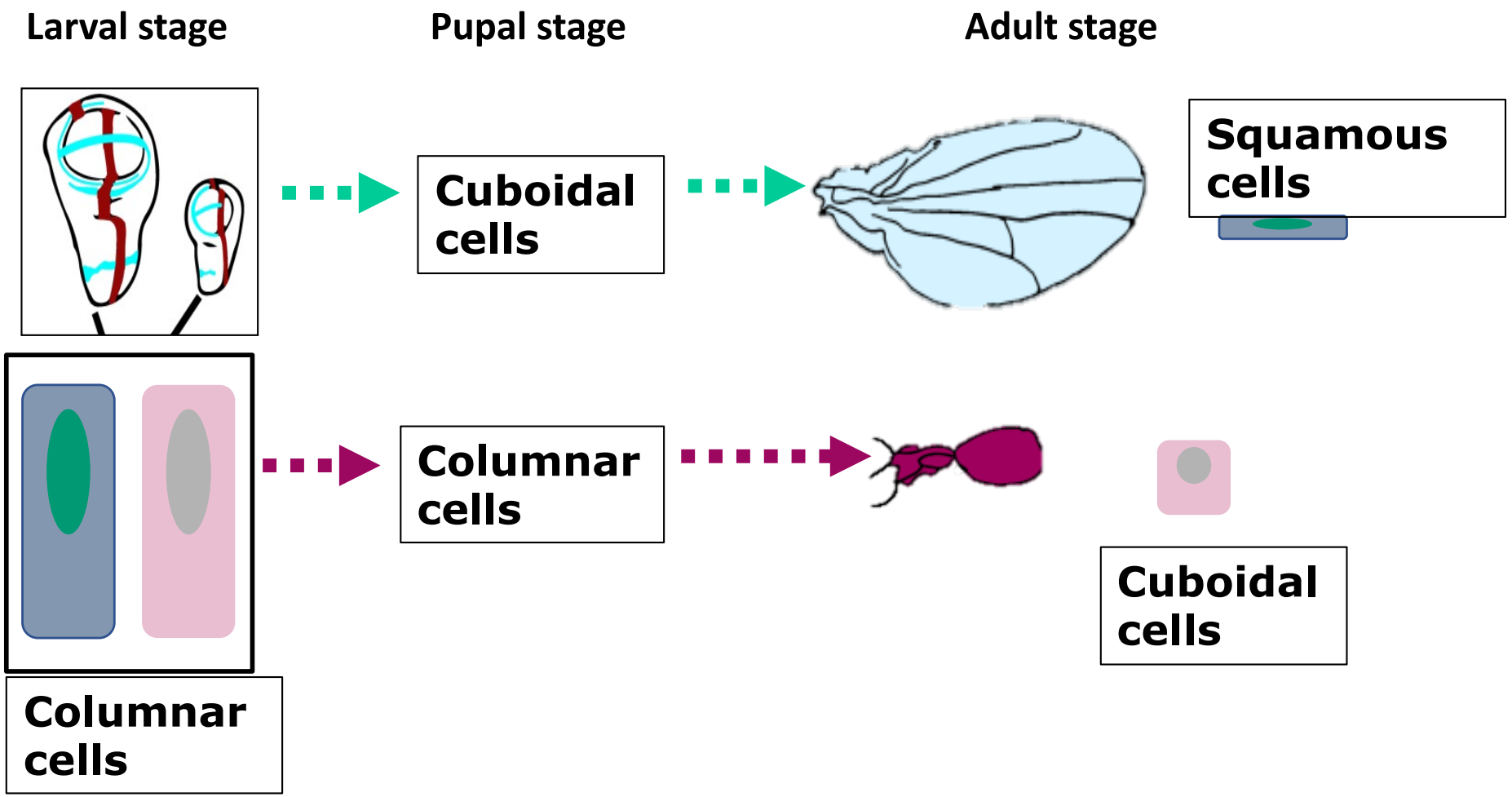
Wing



Haltere



Shape of wing and haltere cells at different developmental stages

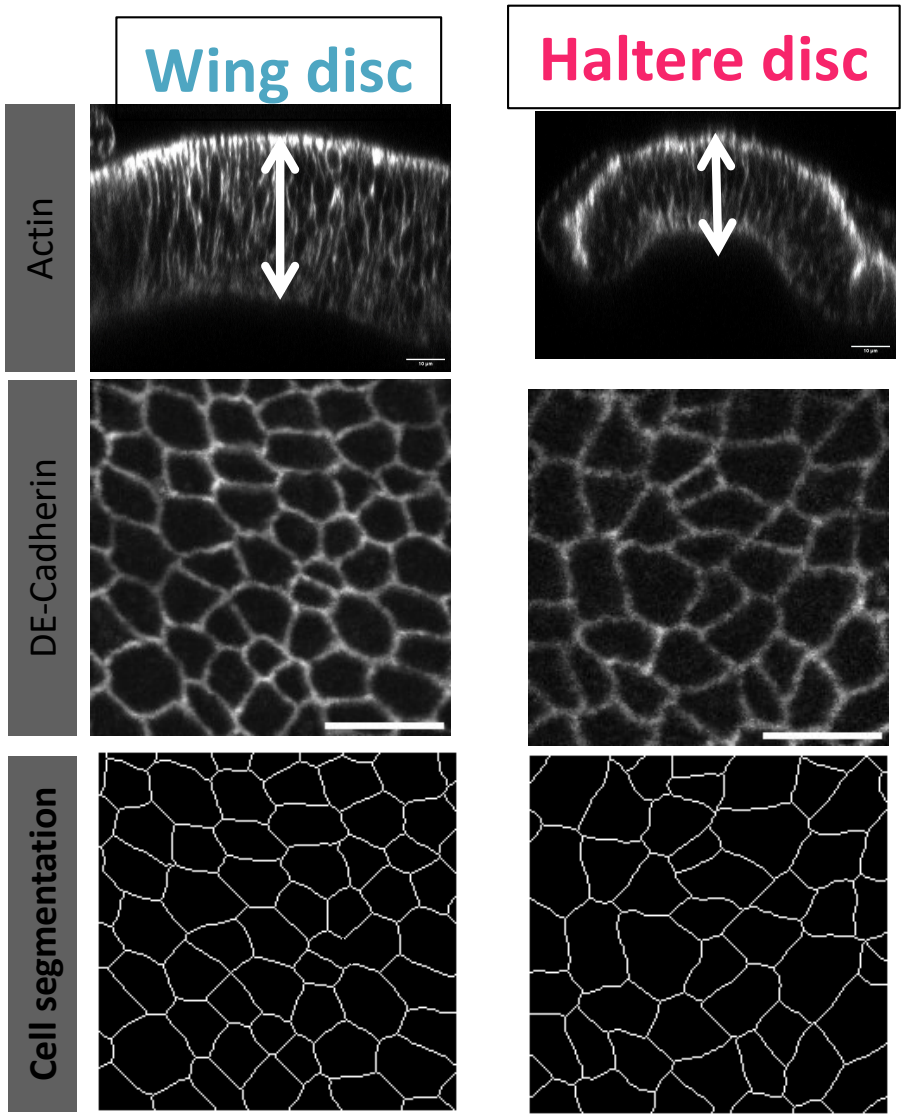


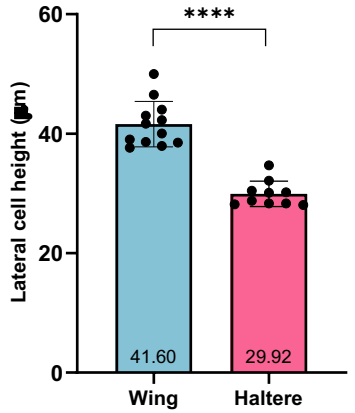
Cellular factors influencing epithelial morphogenesis

- Initial cell constraints such as cell shape, height, size and tension
- Extracellular Matrix properties
- Actomyosin levels and localization
- Changes in cell-cell junction properties

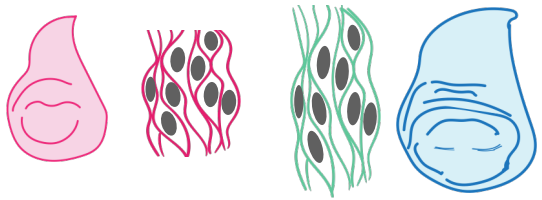
C Dilsha

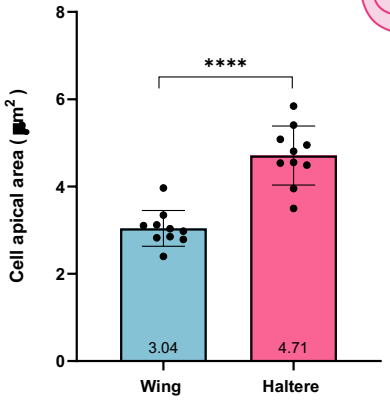
Wing disc cells are more apically constricted and laterally elongated compared to haltere cells at L3





n=12,10 for wing and haltere, respectively

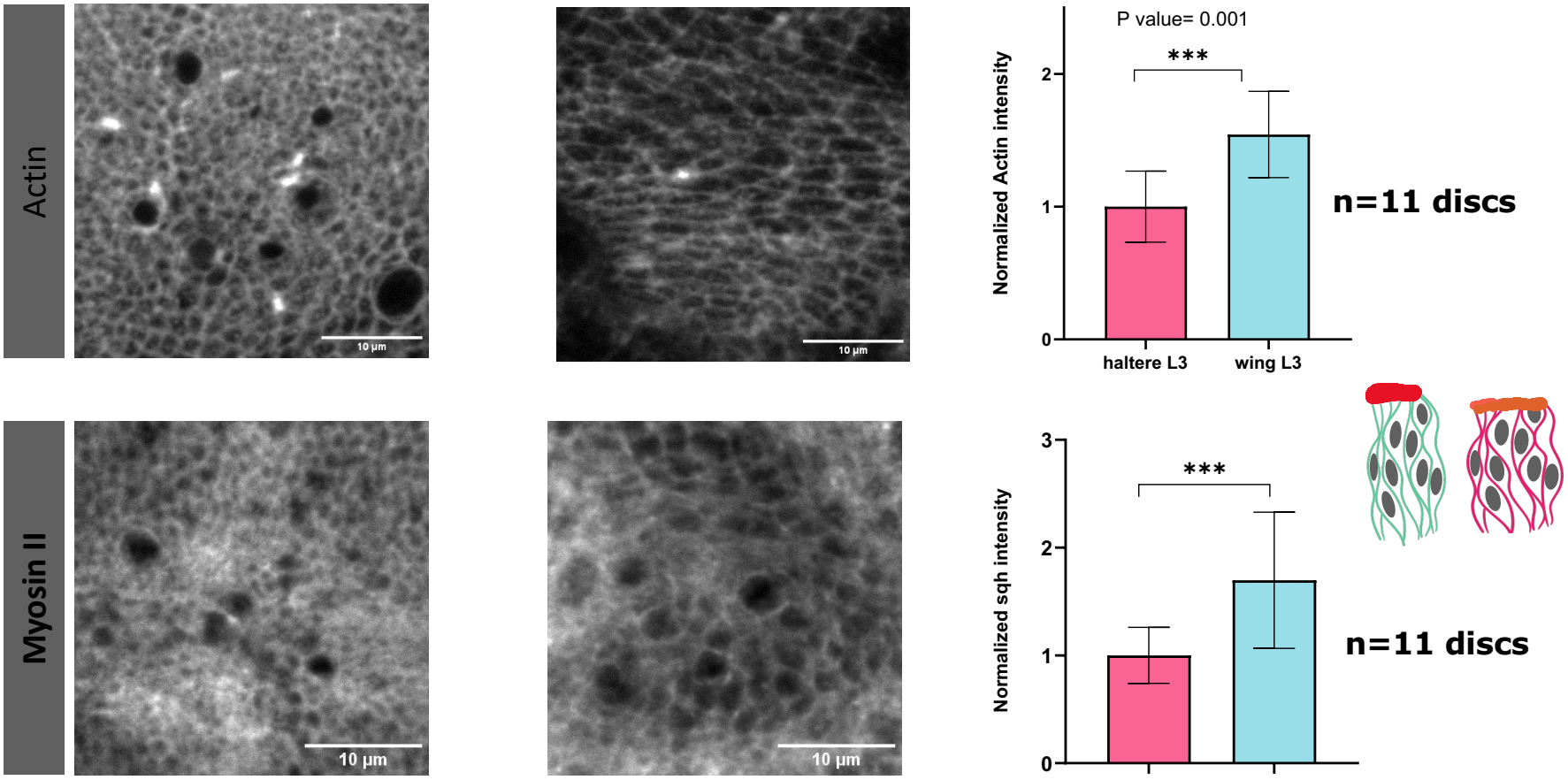




n=10

Wing disc cells have higher levels of apical actin and myosin compared to haltere cells

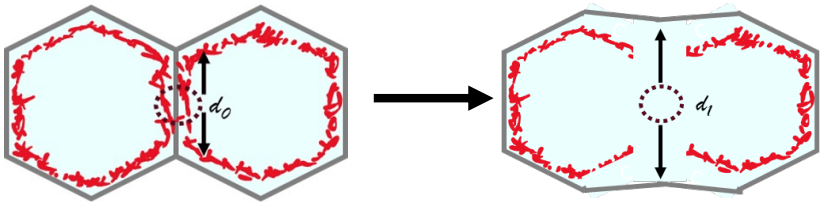
Wing disc | **Haltere disc**



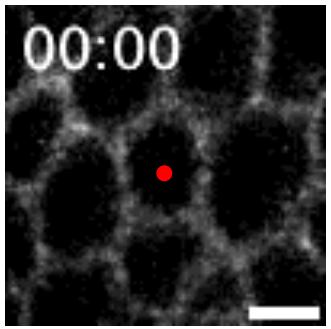
(Apical projections)

Wing disc cells displays higher apical contractility compared to haltere disc

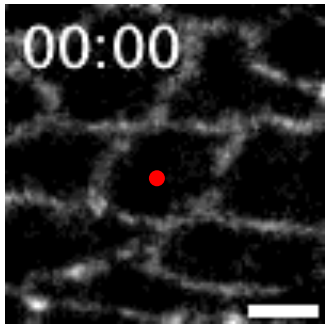
cell bond ablations



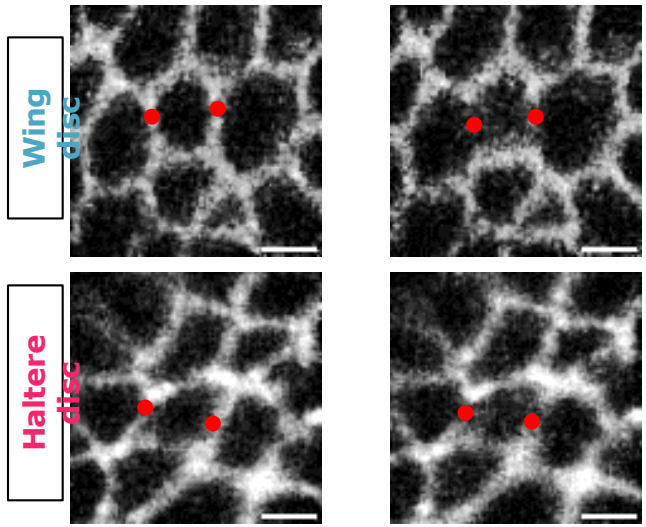
Wing disc



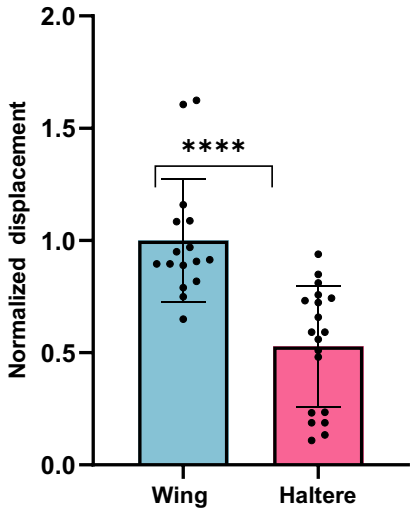
Haltere disc



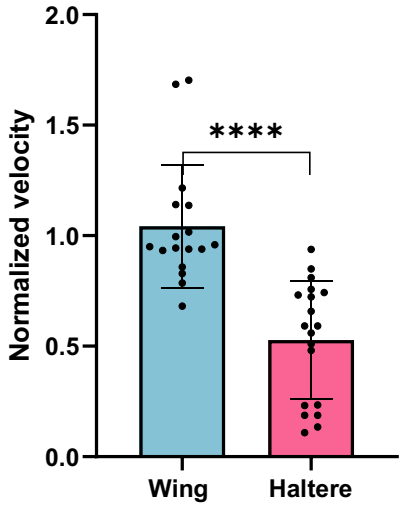
A



B



C



N=17,20 respectively for wing and haltere

Increased levels of Yki in the background of reduced Atro or Pten causes partial haltere to wing homeotic transformations

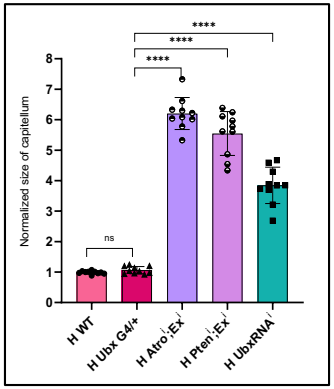
A

Ubx Gal4: +

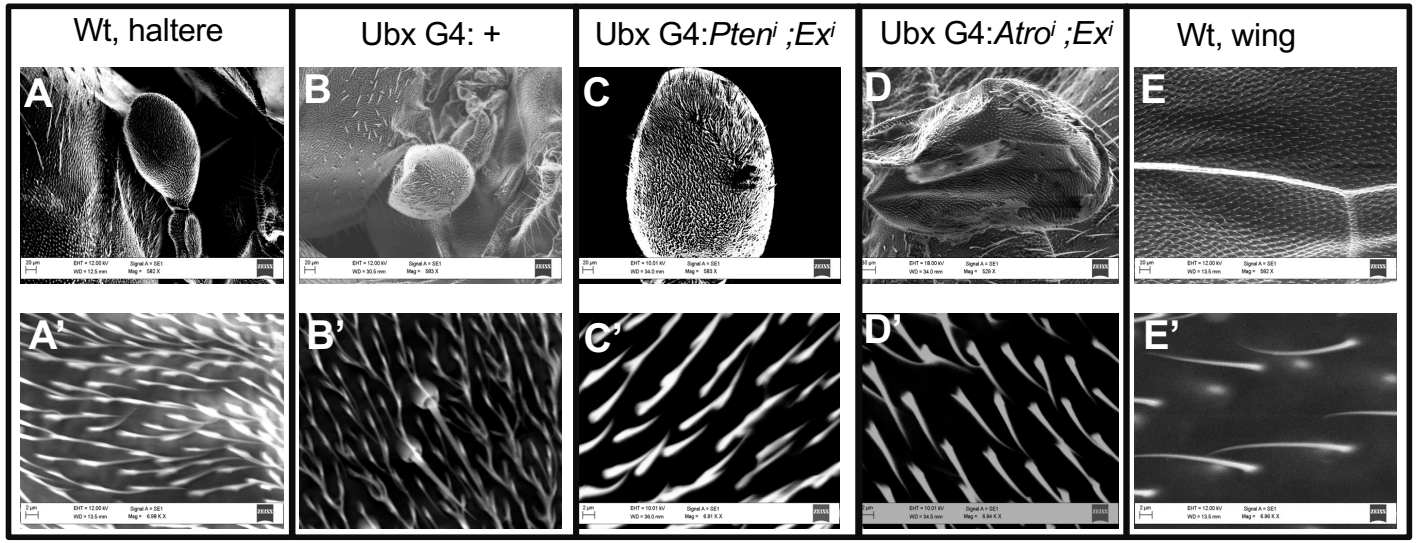
Ubx Gal4: *Pten^{i} ;Ex^{i}*

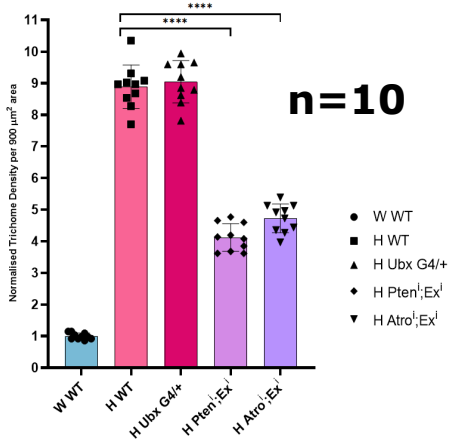
Ubx Gal4:*Atro^{i} ;Ex^{i}*

Ubx Gal4:*Ubx^{i}*

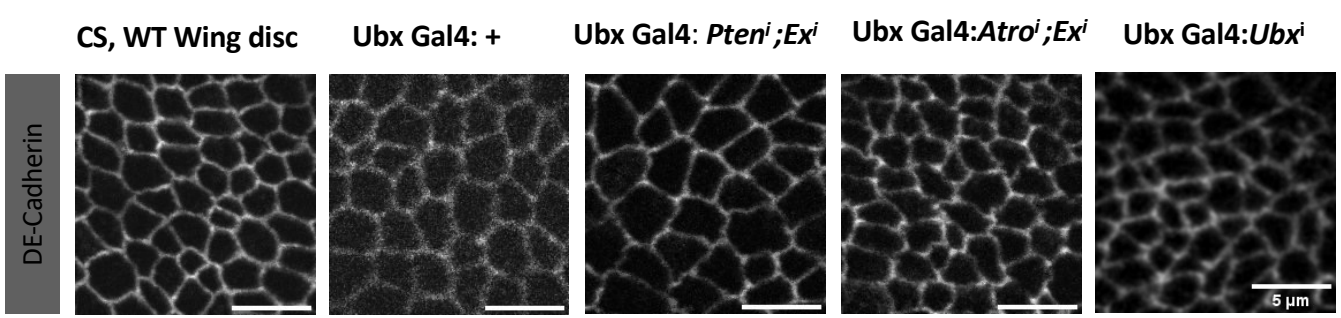


n≥ 10

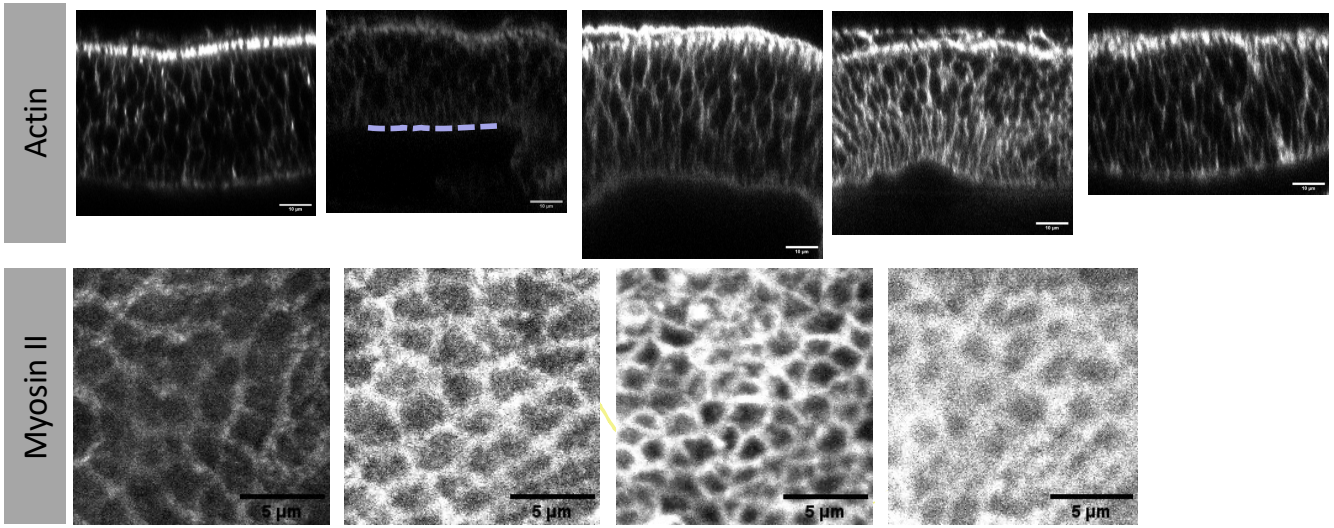


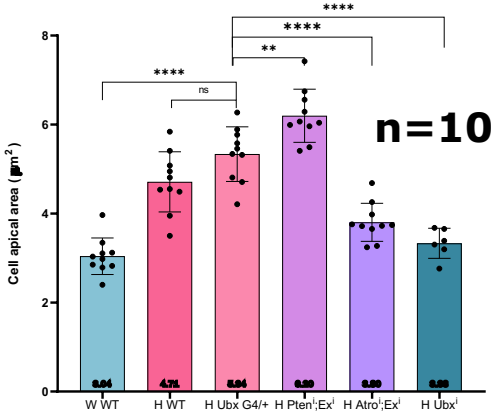


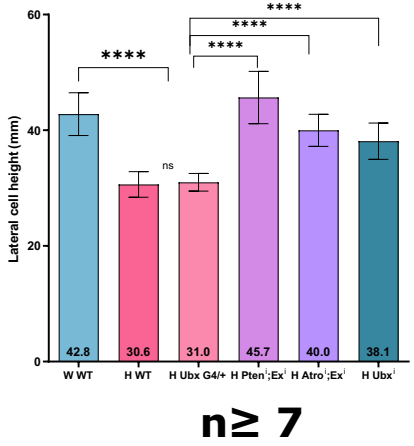
Mutant halteres show increased cell height, apical cell constriction and changes in cellular morphology



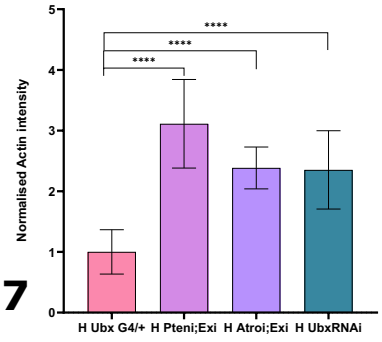
B



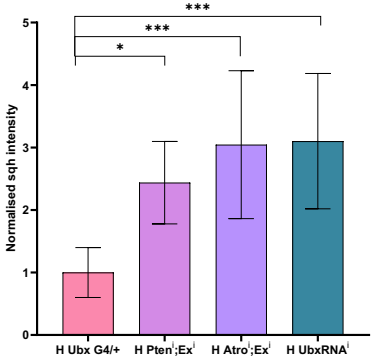




n≥ 7

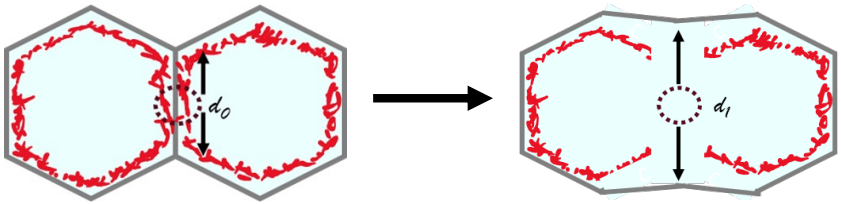


n≥ 7

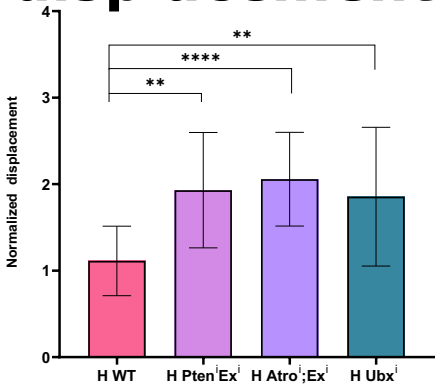


n≥ 7

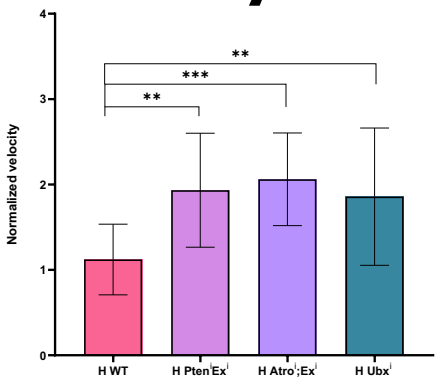
Cell apical contractility – mutant haltere discs shows higher recoil velocity compared to the control halteres



Mean displacement



Recoil velocity



n≥ 17

Differences in the mechanical properties of cells in principle can affect the morphogenesis outcome/ or in our case eversion leading to slight differences in the 3D architecture that is formed.

Apical and basal ECM remodeling is critical for changes in wing epithelia during eversion

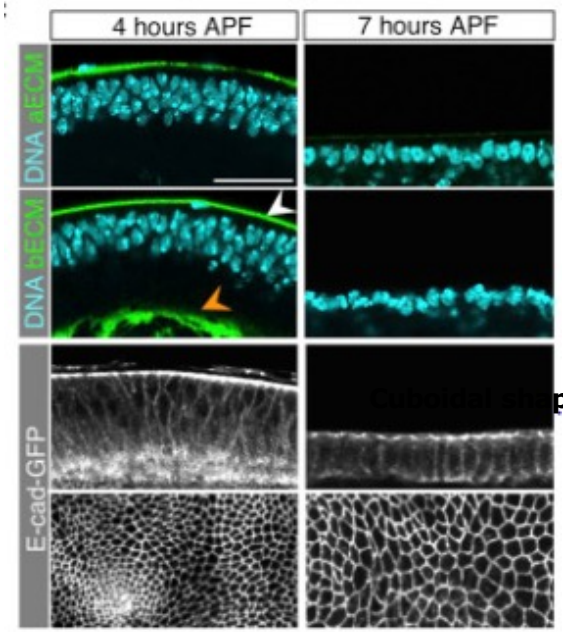
Wing disc

Disc to 4-7h APF

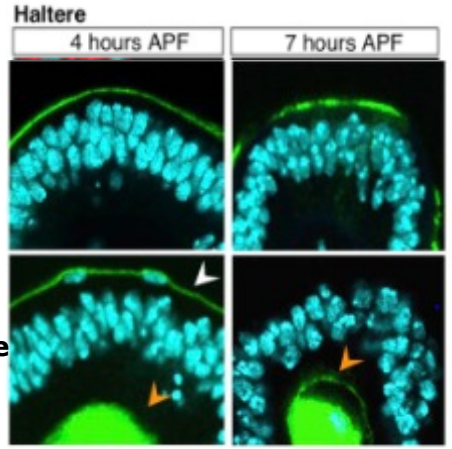
Cell shape changes

Haltere disc

Wing disc



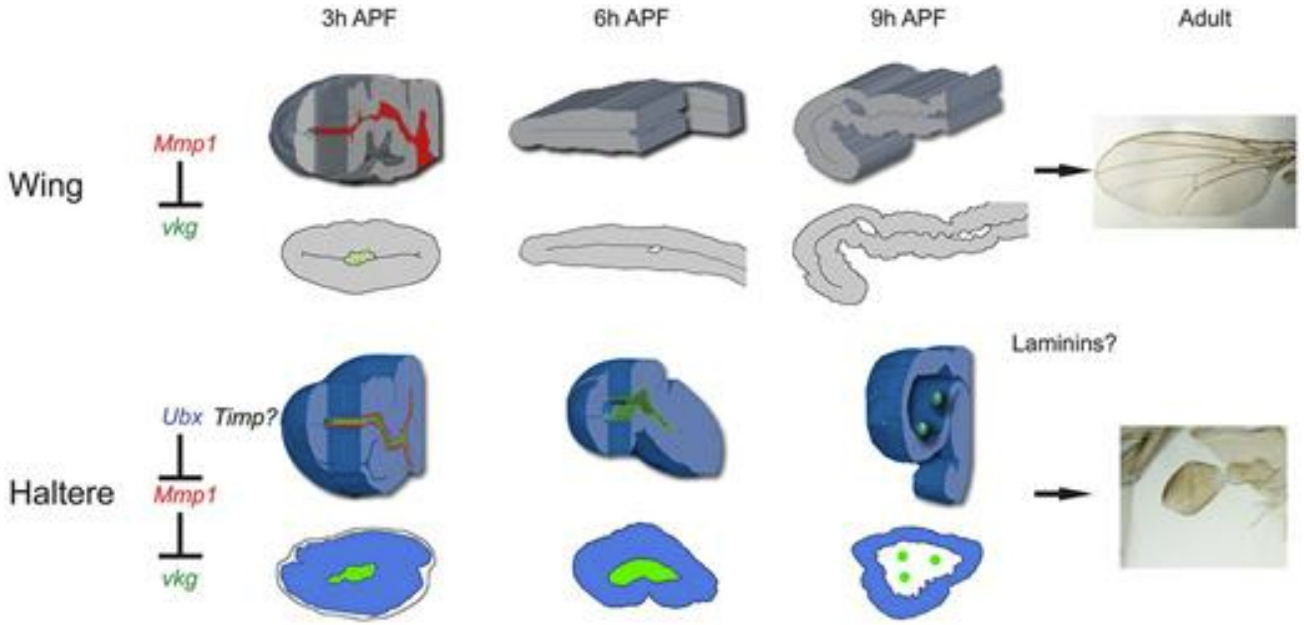
Haltere disc



Retains Columnar shape

De Las Heras, Garcia-Cortes, & Foronda, 2018; Diaz-de-la-Loza et al., 2018

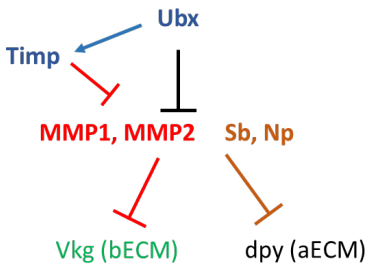
Ubx inhibits ECM remodelling in haltere discs



Wing

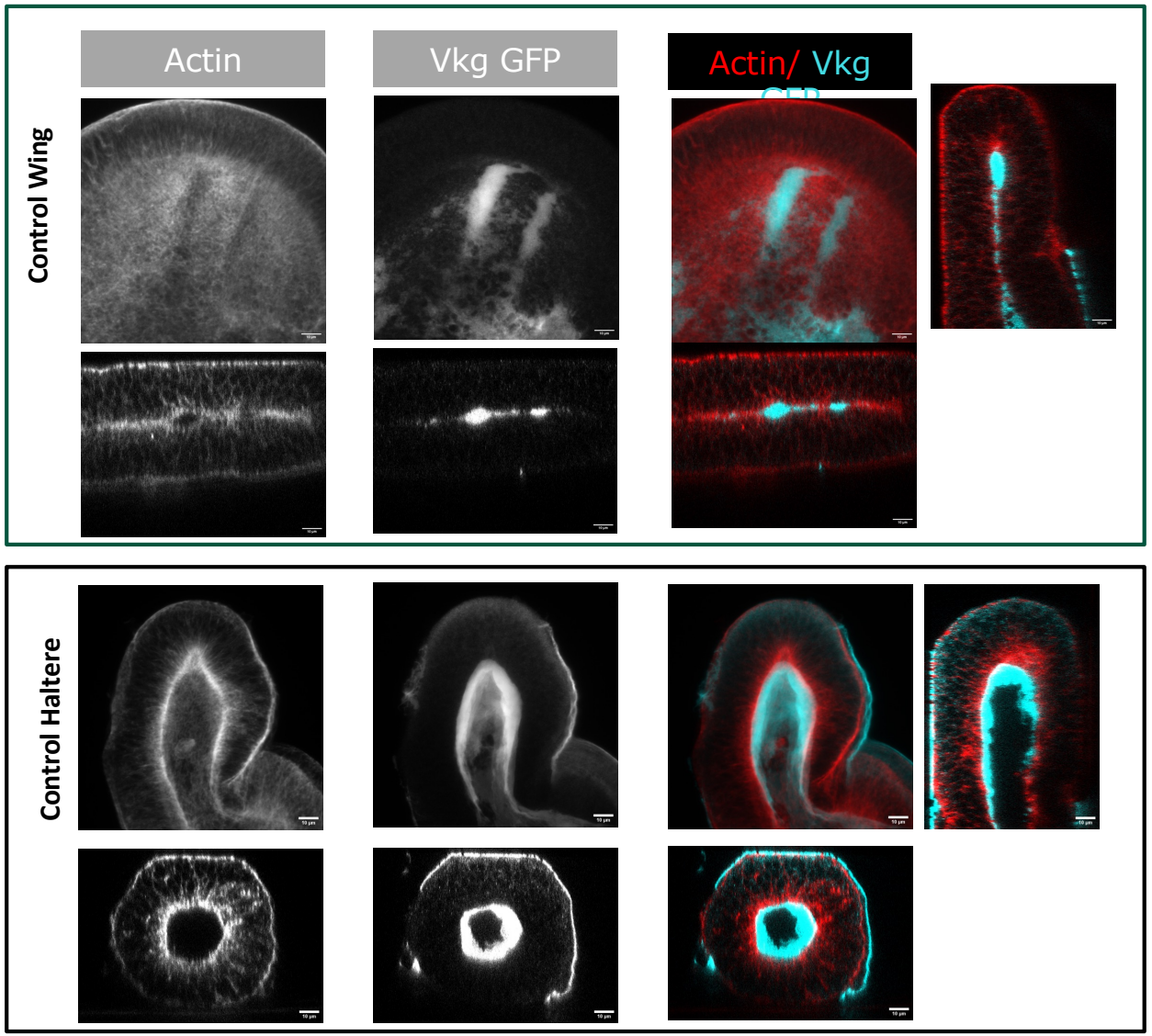
Haltere

Wing and haltere discs start looking different



De Las Heras, Garcia-Cortes, & Foronda, 2018

Wing and haltere disc undergo differential 3D tissue reorganisation at 4-6 h APF



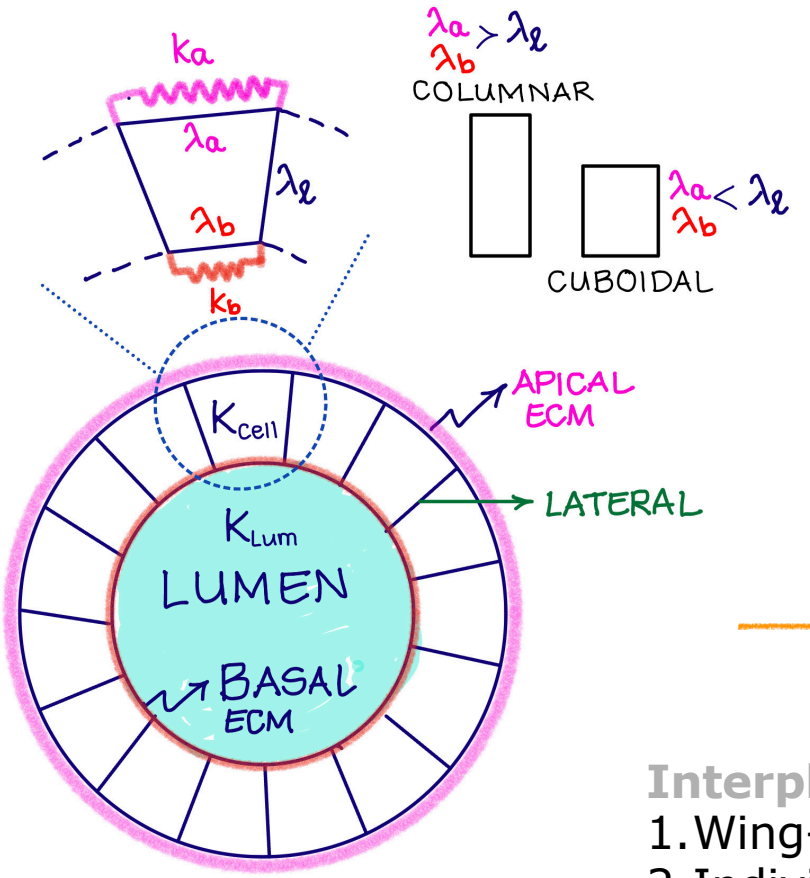
Presence of the lumen filled with basal ECM and a globular geometry

Mathematical Modeling

Mandar M. Inamdar

Professor, Civil Engineering Department, IITB

Lateral section Vertex Model



Preferred Area for cell: A_{0C}

Cell Area Stiffness: K_{cell}
surrogate for volume

Apicalcontractility: λ_a

BasalContractility: λ_b

LateralContractility: λ_l

ECM modeled as
Apical and Basal Springs

$$k_a, k_b$$

Lumen modeled as a dummy cell

Preferred Area: A_{0L} **(tuned to tune lumen size)**

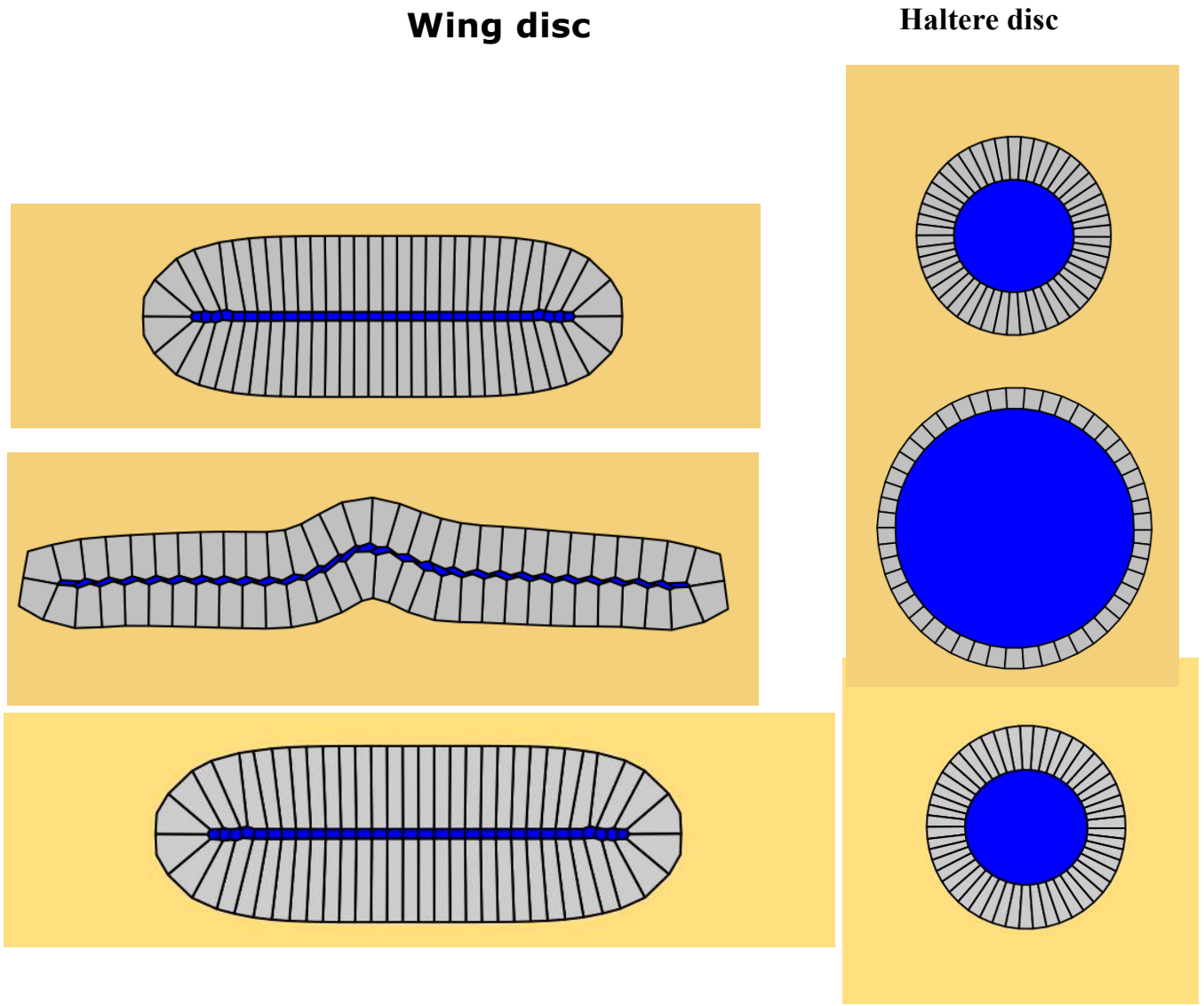
Lumen stiffness: K_{Lum}

Qualitative physical picture

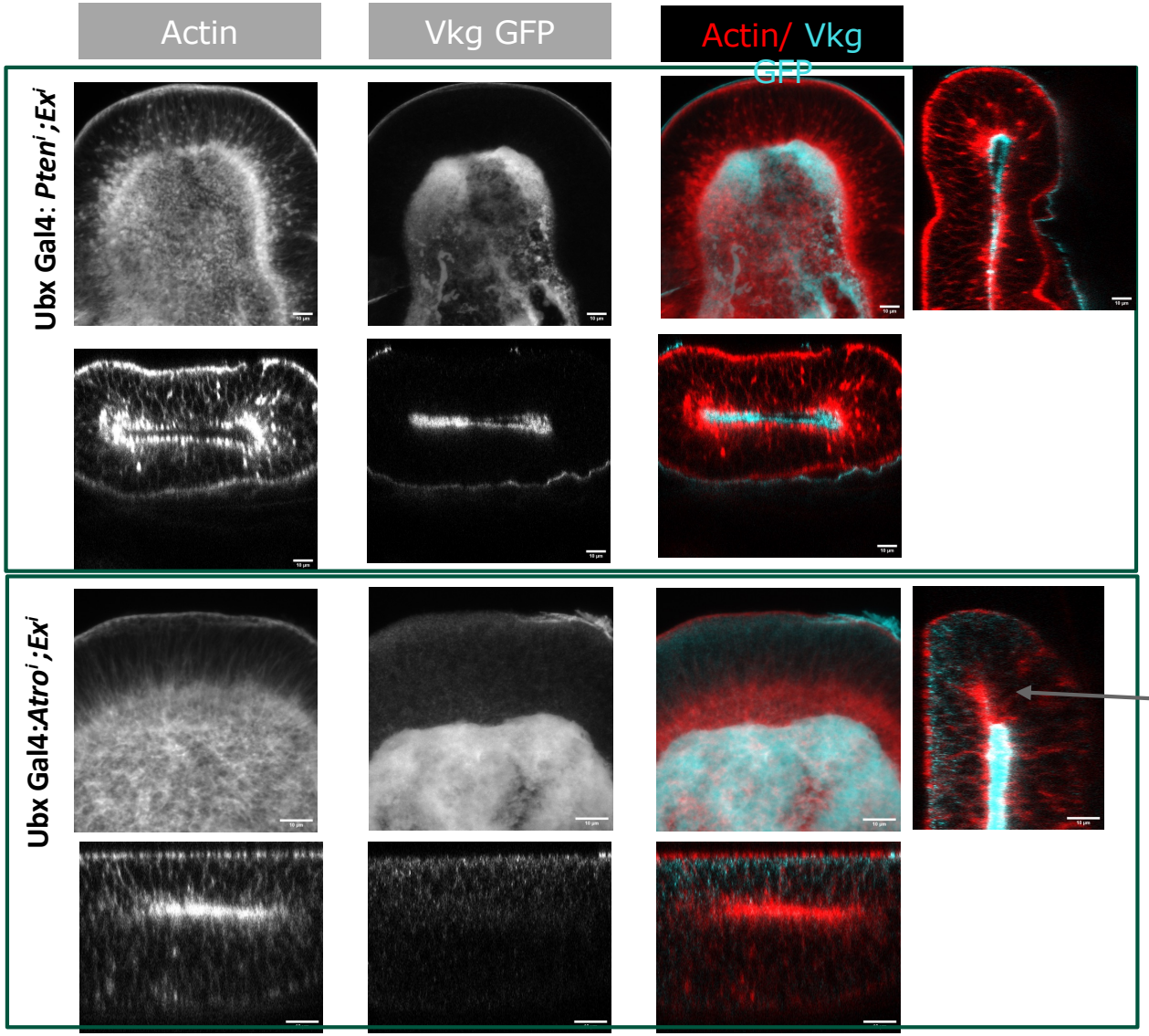
Interplay:

1. Wing-like flat or Haltere like Globular morphology?
2. Individual cell morphologies

Modelling cell shape transitions and organ morphogenesis



Atrophin and Expanded double knockdown induce basal ECM remodelling and DV apposition

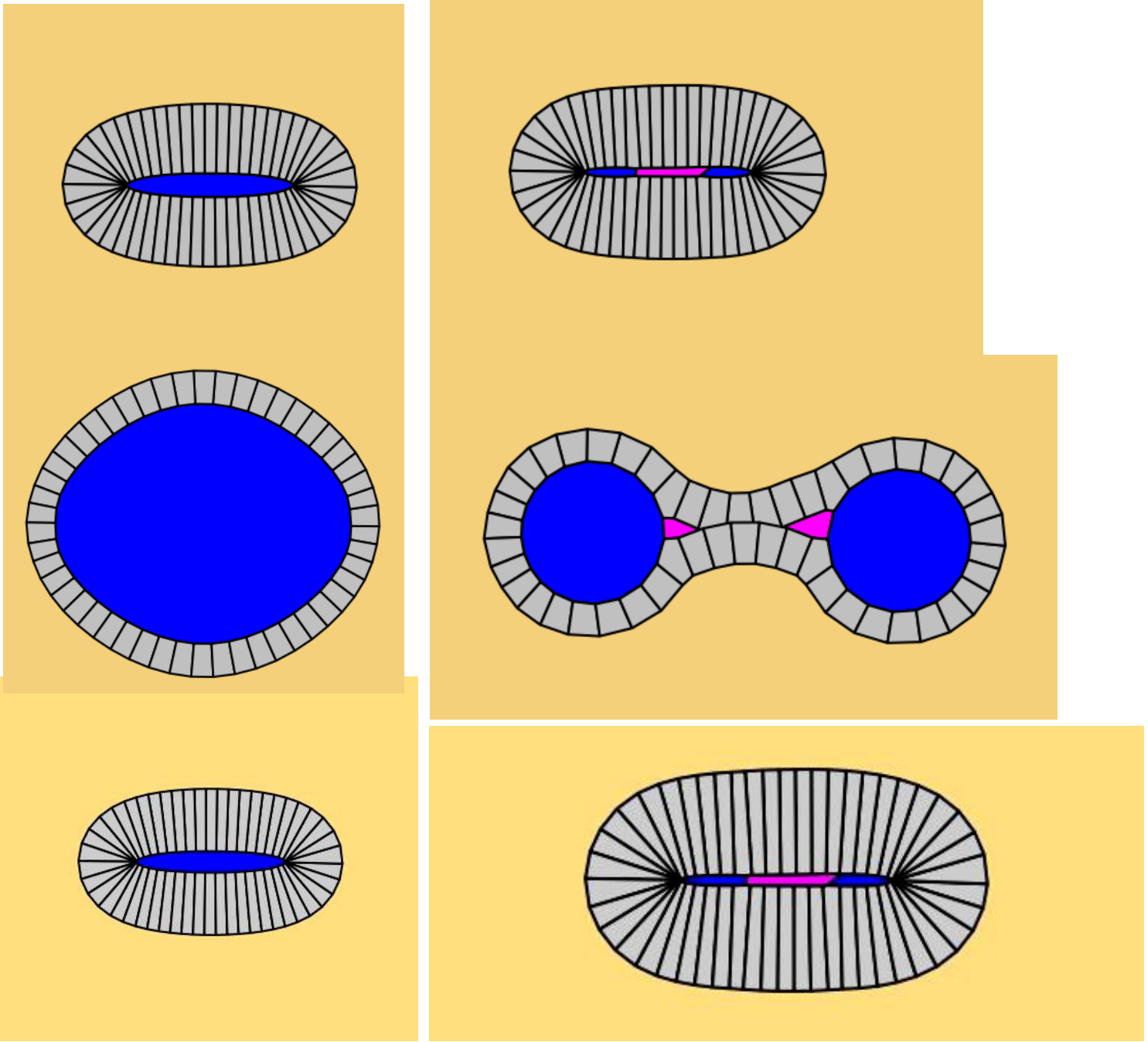


Shows bECM clearance and zippering in some areas

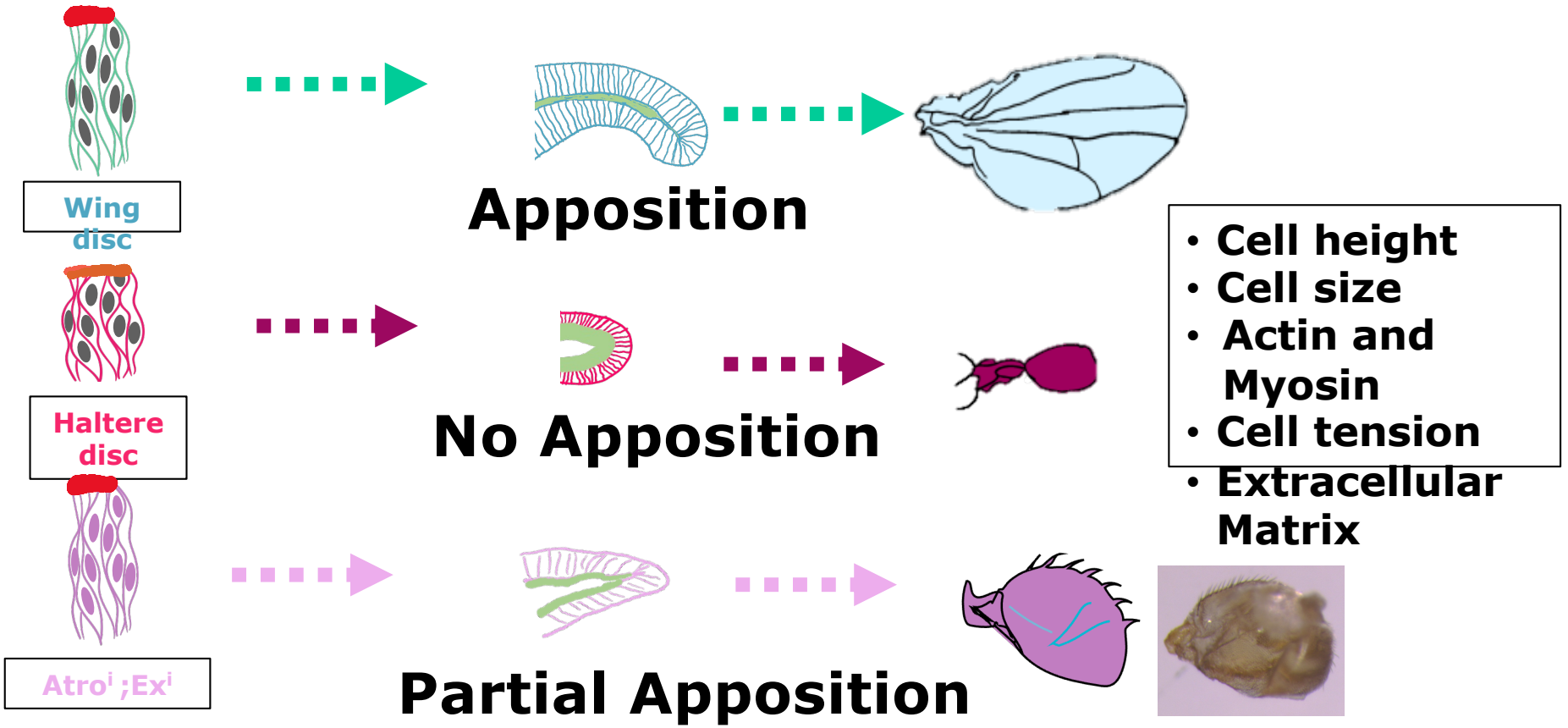
Modelling cell shape transitions and organ morphogenesis

H $Pten^{RNAi}$;ex^{RNAi}

H $Atro^{RNAi}$;ex^{RNAi}



Summary


Wing disc
Apposition
Haltere disc
No Apposition
Atro^{i} ;Ex^{i}
Partial Apposition
• Cell height
• Cell size
• Actin and Myosin
• Cell tension
• Extracellular Matrix