Tissue Size
&
Morphogen Gradients

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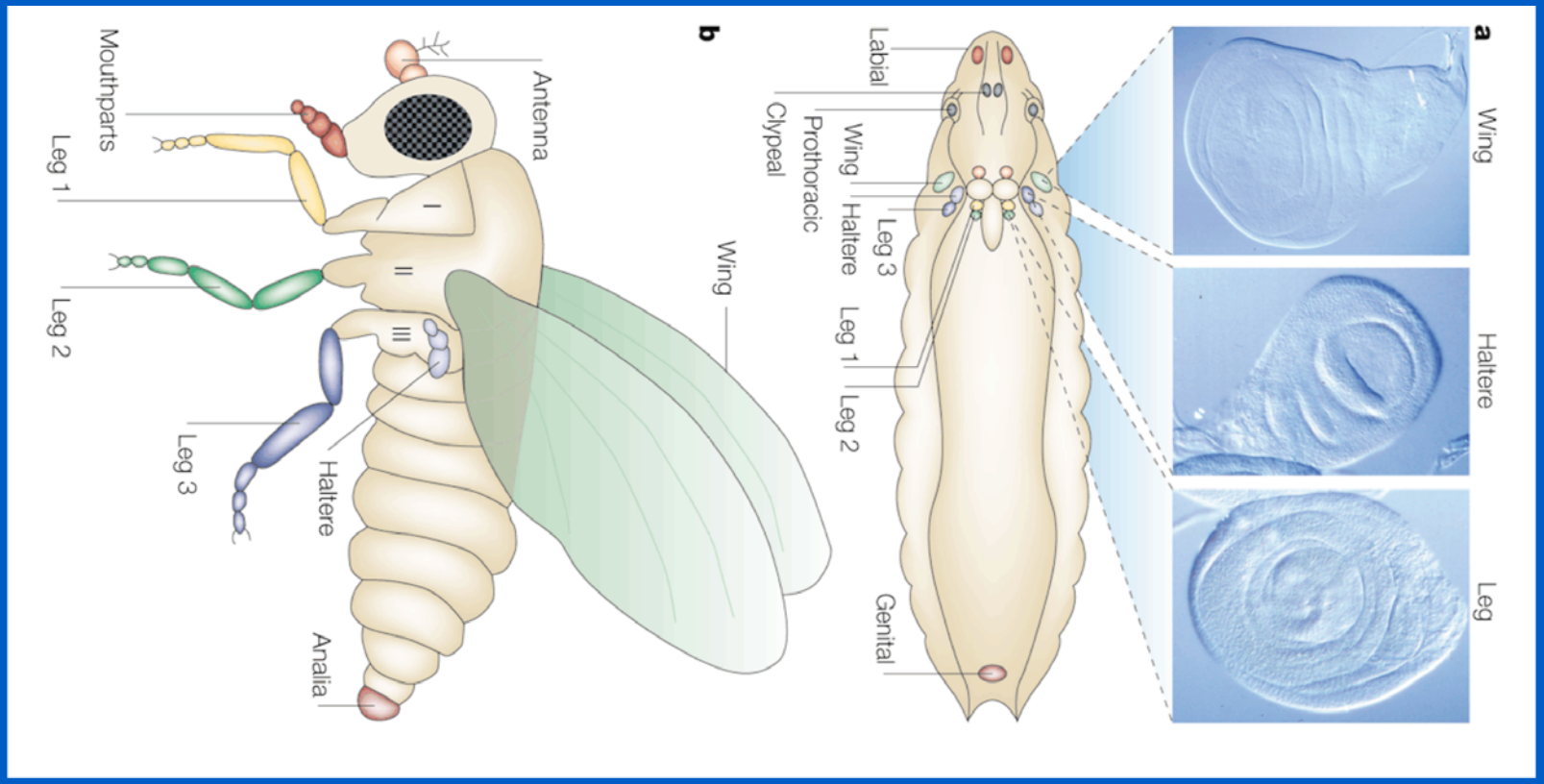
IN THE HELMHOLTZ ASSOCIATION

Problem of organ size determination

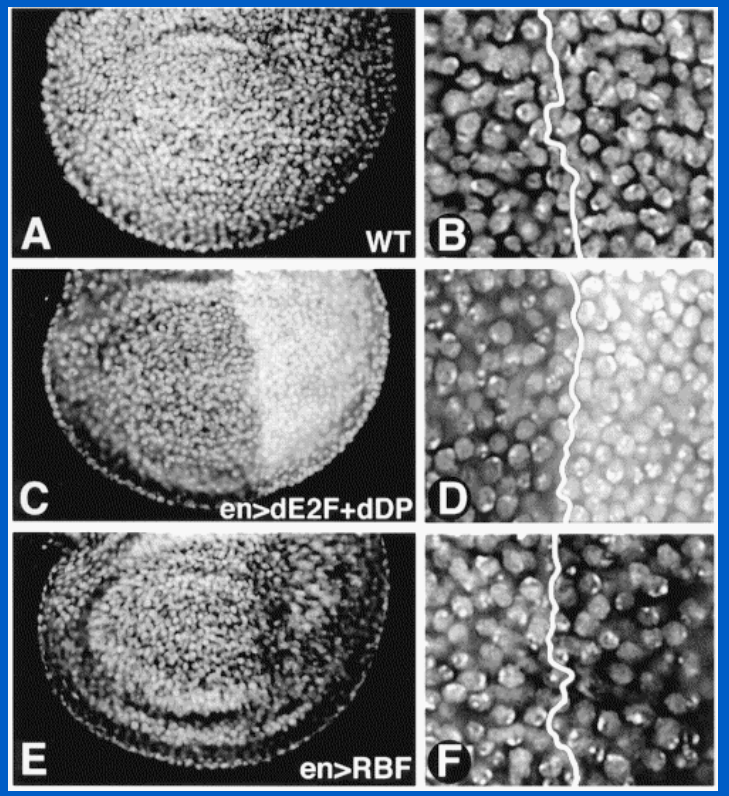
Drosophila Development Synopsis



Nature Reviews/Molecular Cell Biology 2:89-97

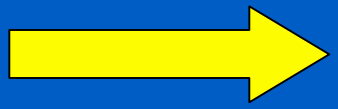
How it does NOT work

- counting cell divisions
  - cell cycle manipulation
- measuring time
  - Minutes



Neufeld TP, de la Cruz AF, Johnston LA, Edgar BA. Cell 1998

Features of how it DOES work

Experiment		Feature
Transplantation		Autonomous
Clones & competition		Compartments as size units
Ablation		Physical dimensions measured

Conceptual framework

nutrients

insulin signaling

patterning

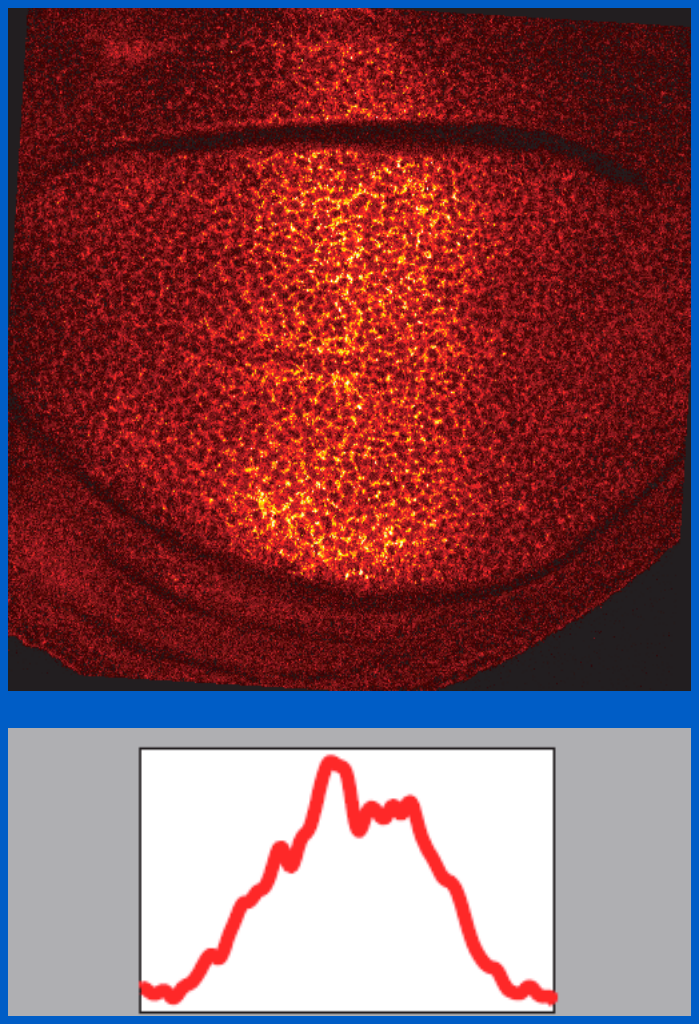
Autonomous size measurement

Hox genes

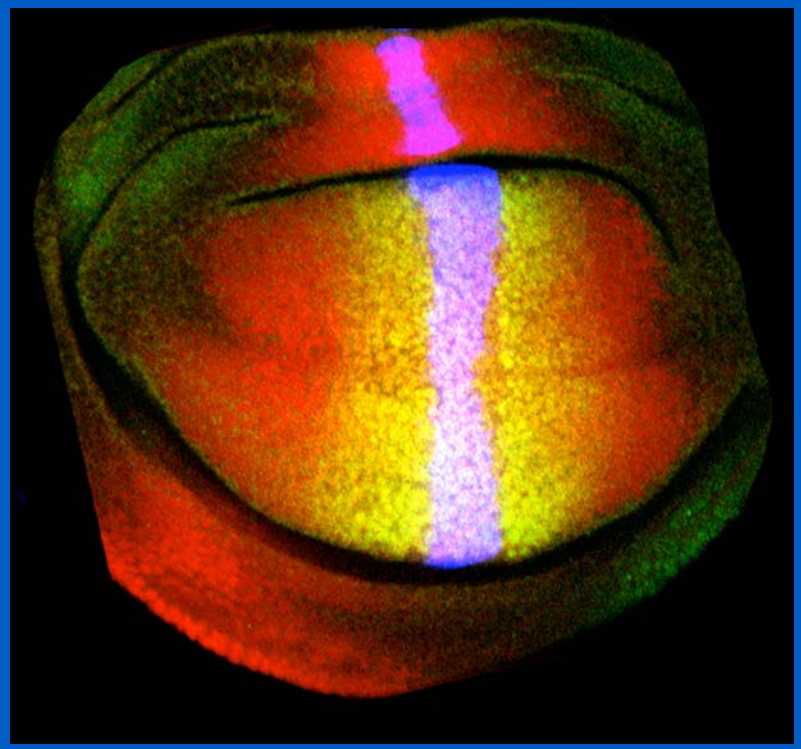
Morphogens

- Dpp

Dpp forms an extracellular gradient along A/P axis

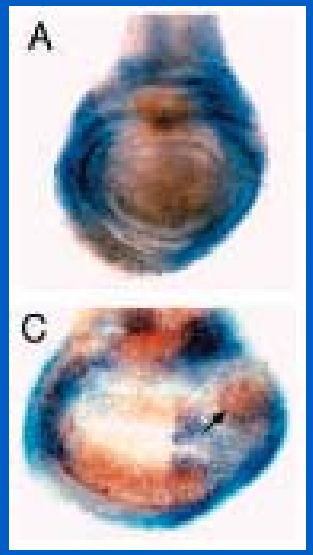


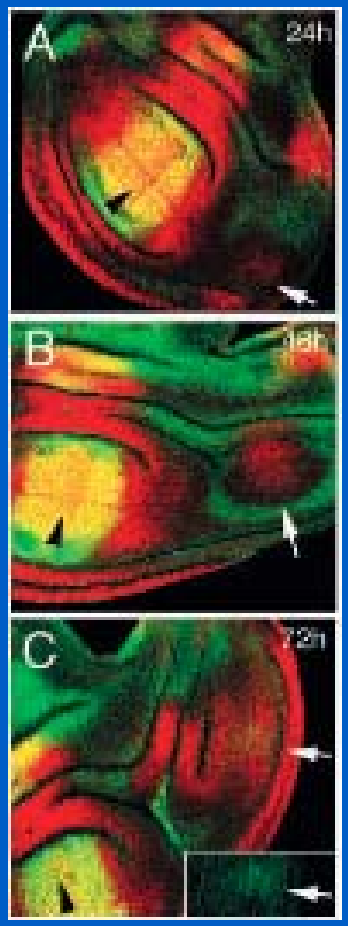
Dpp gradient in the wing disc



dpp expression domain
Spalt omb

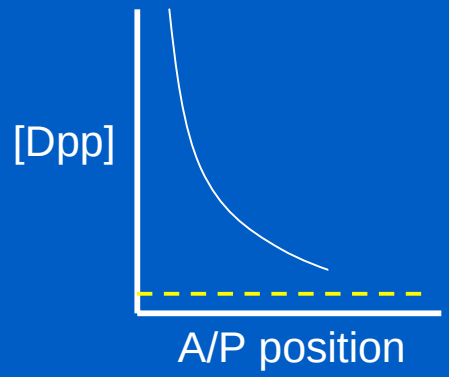
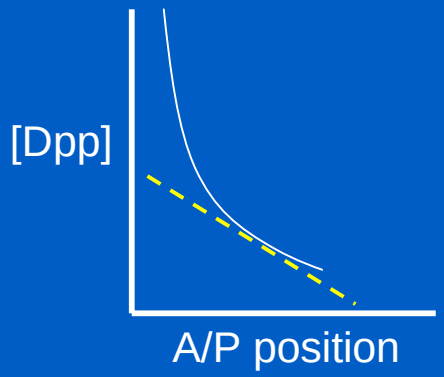
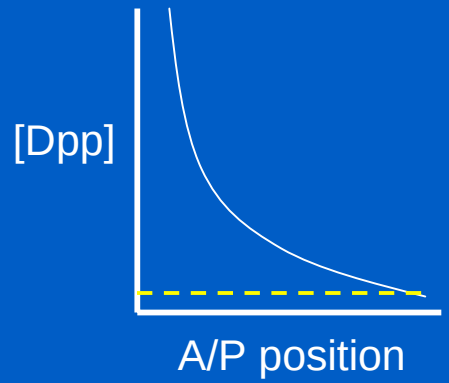
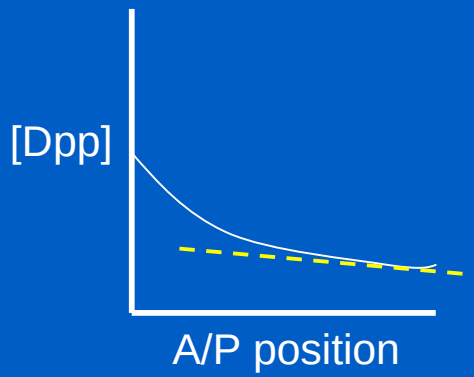
Dpp drives massive tissue overgrowth



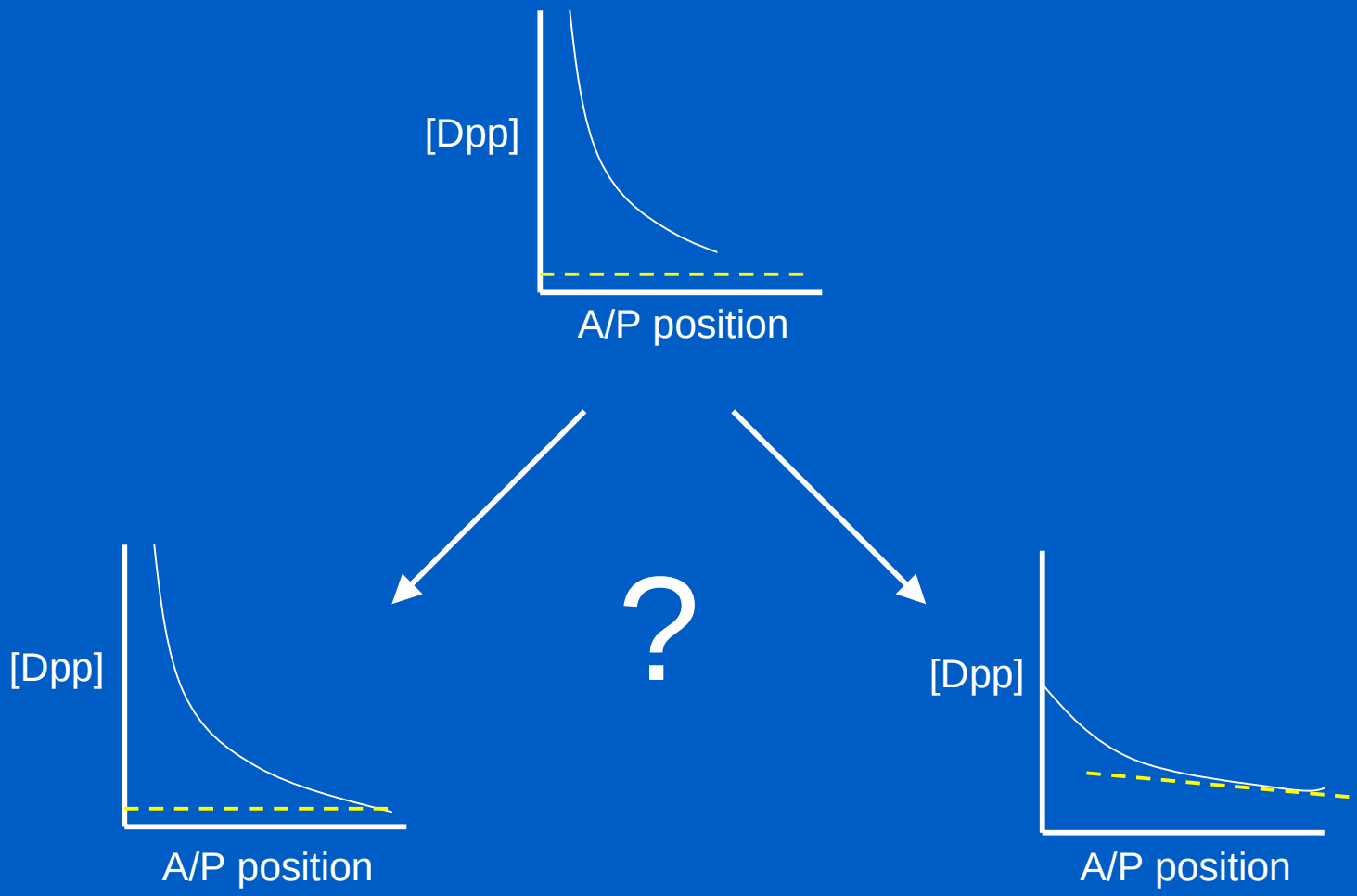


Lecuit & Cohen. Development 1998

Two models for how Dpp drives tissue growth

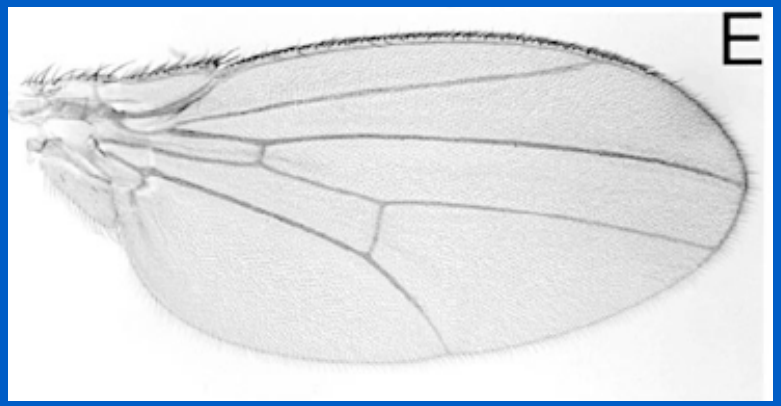
Growth depends on:	Dpp levels	Dpp gradient
Growing disc:		
Growth stops:		

Goal



Use of a functional Dpp-GFP fusion

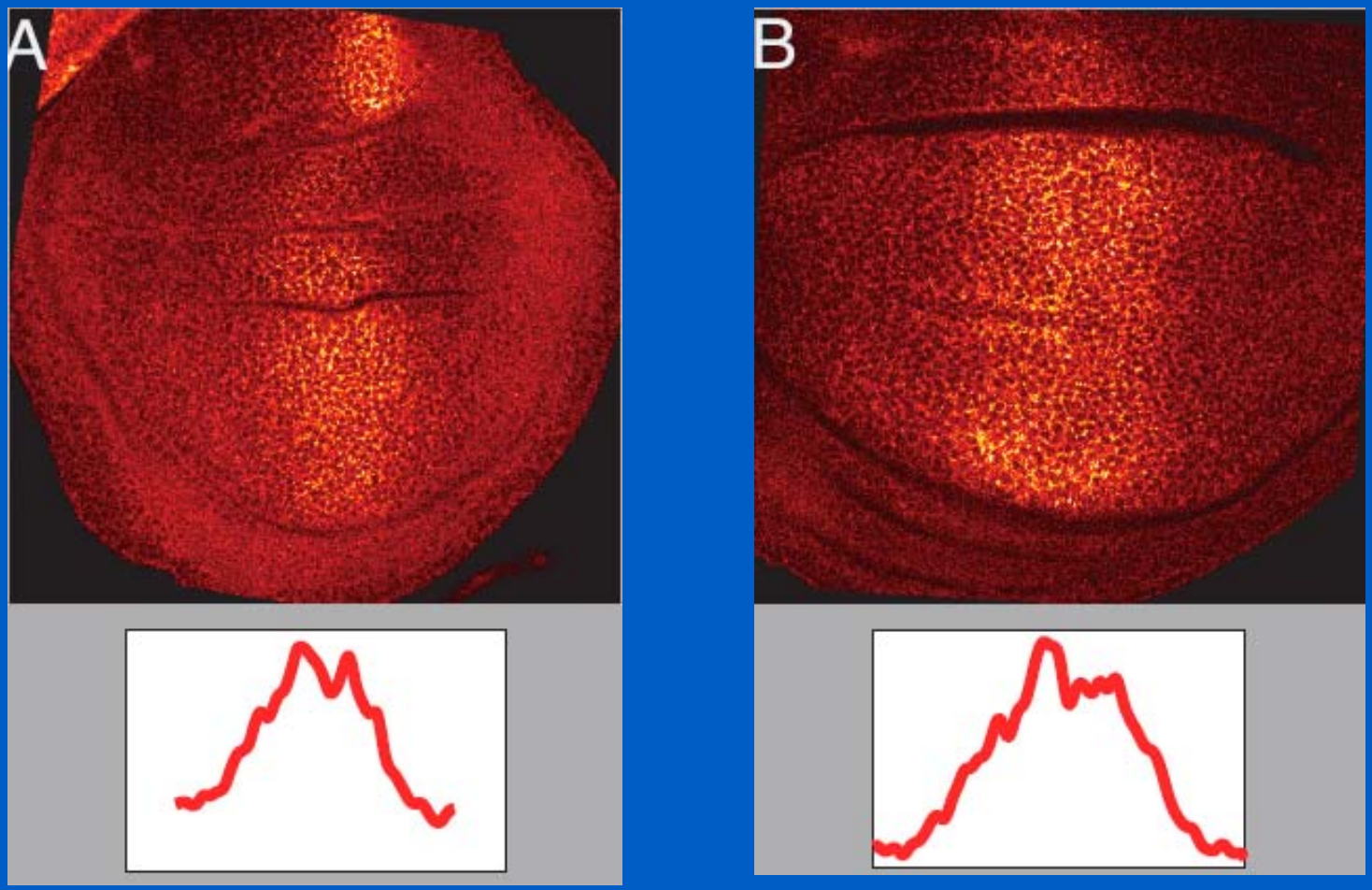
wildtype



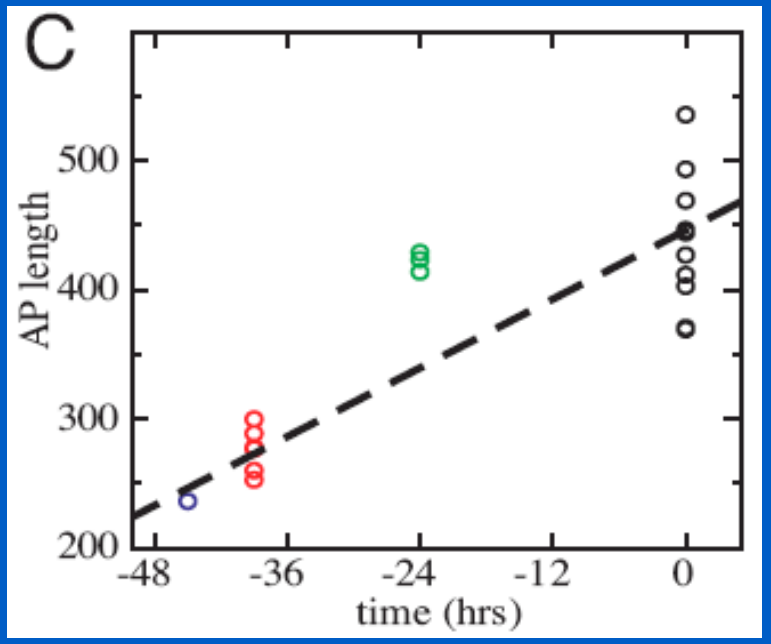
dpp^{-}

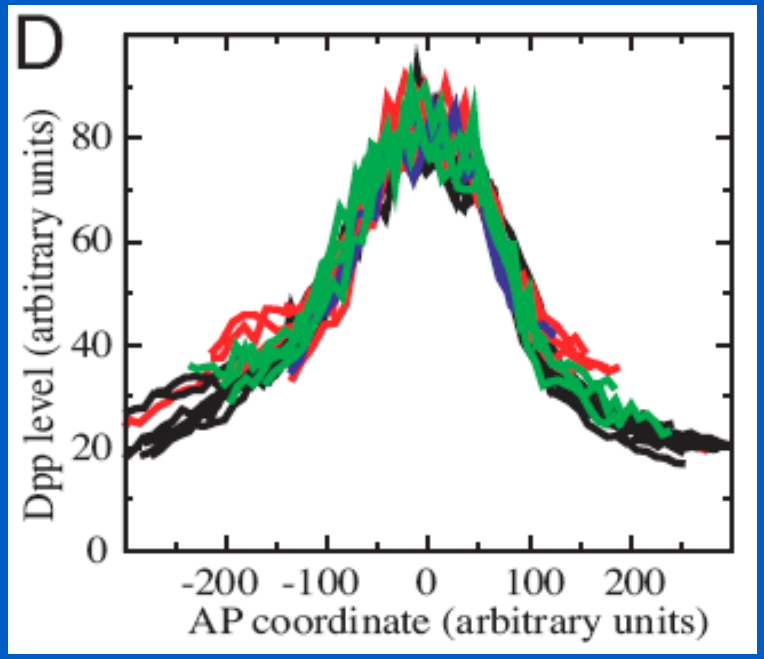
dpp^{-} + Dpp-GFP

Dpp-GFP in small & large discs

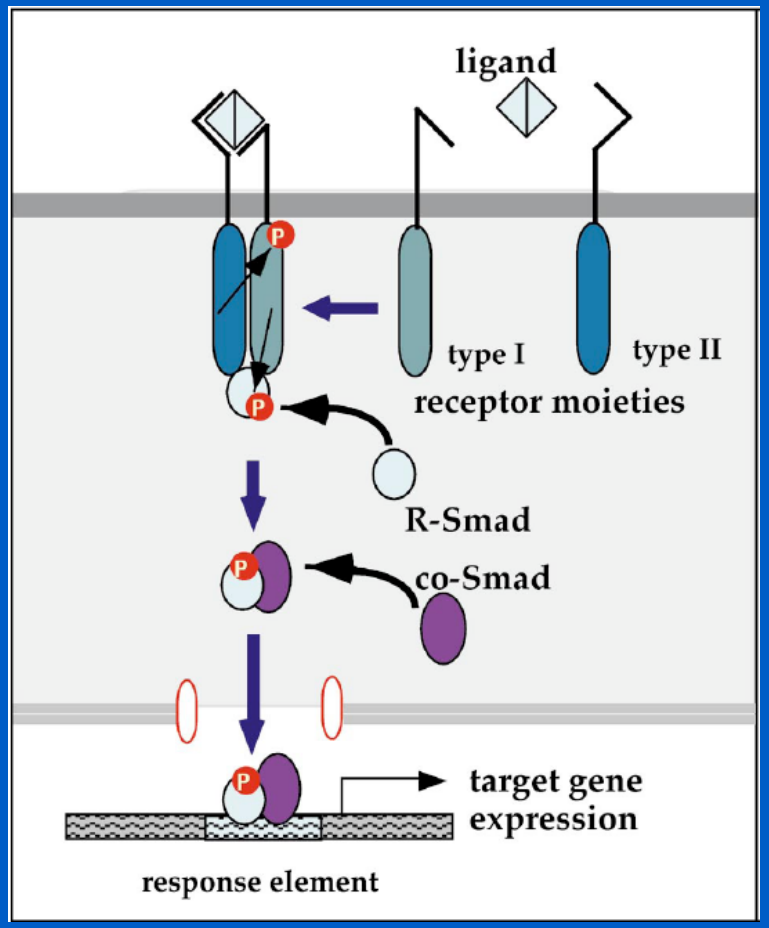


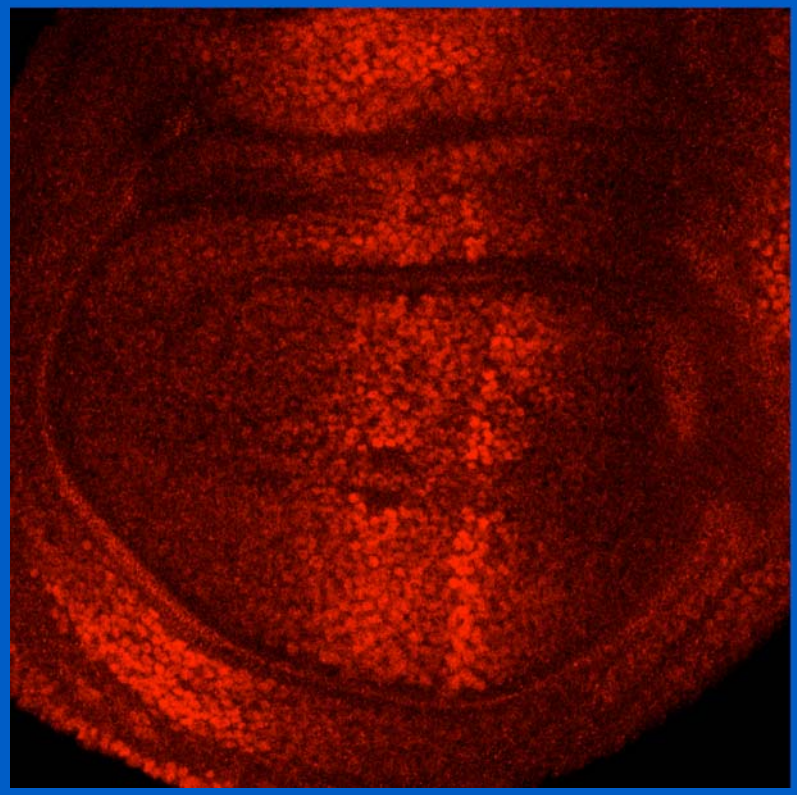
Dpp-GFP gradients of small & large discs overlap



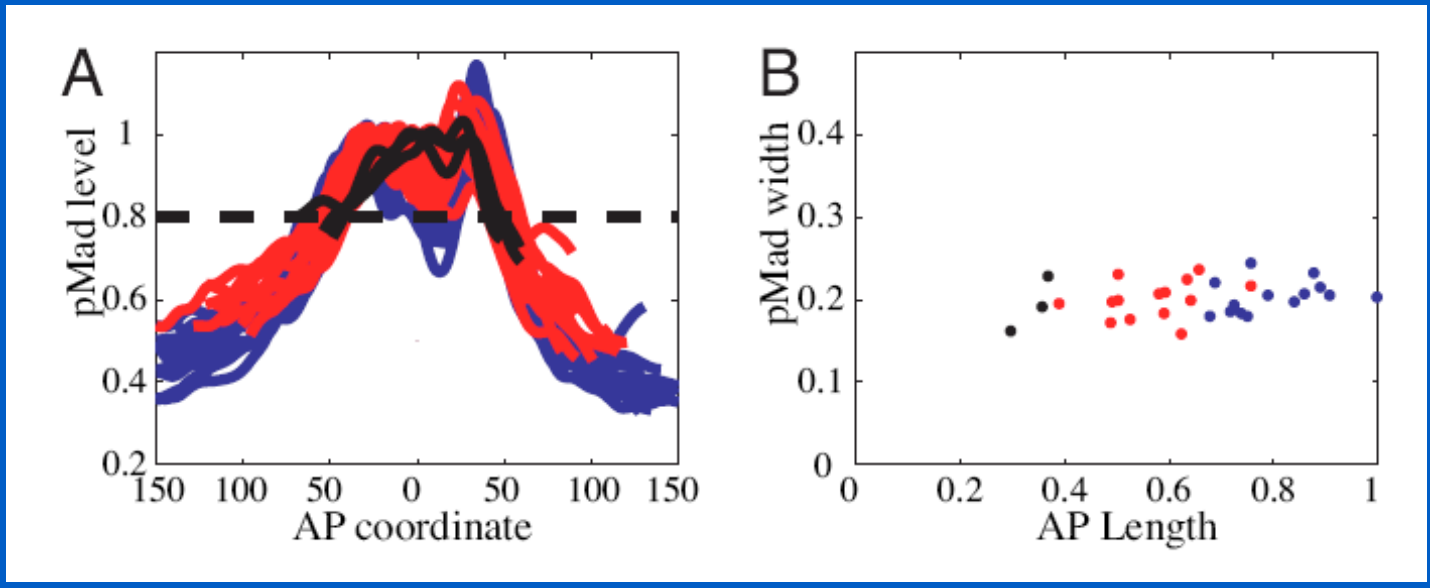


Endogenous Dpp signaling measured by phospho-Mad

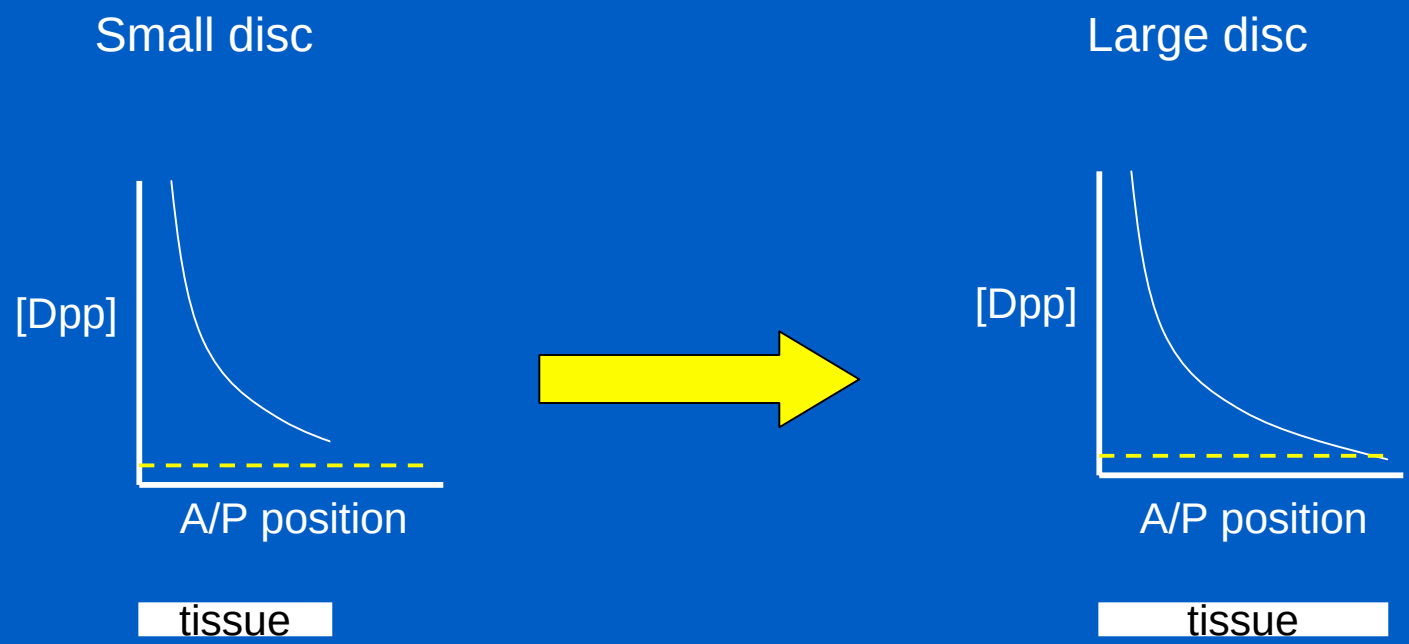




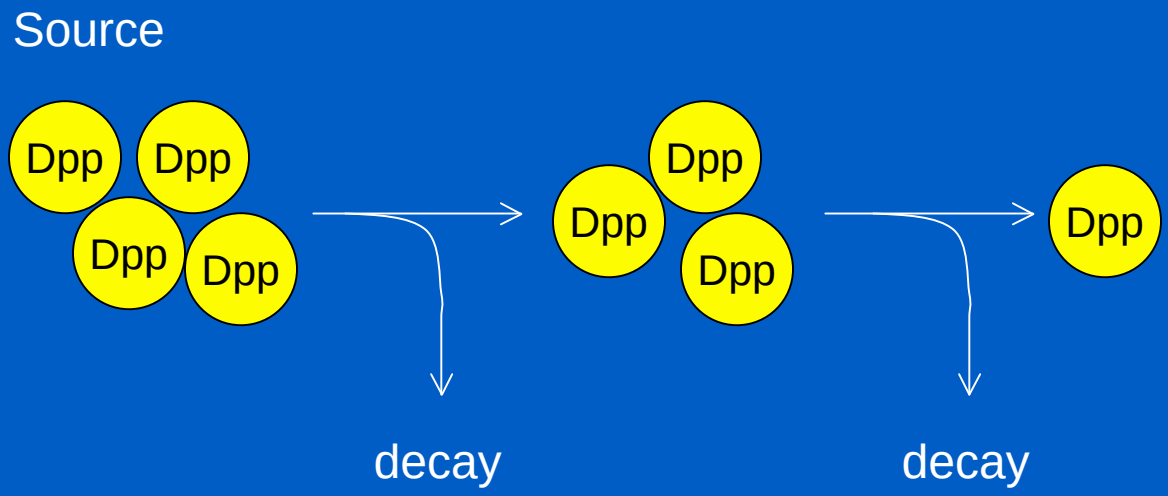
pMad gradient does not flatten during disc growth



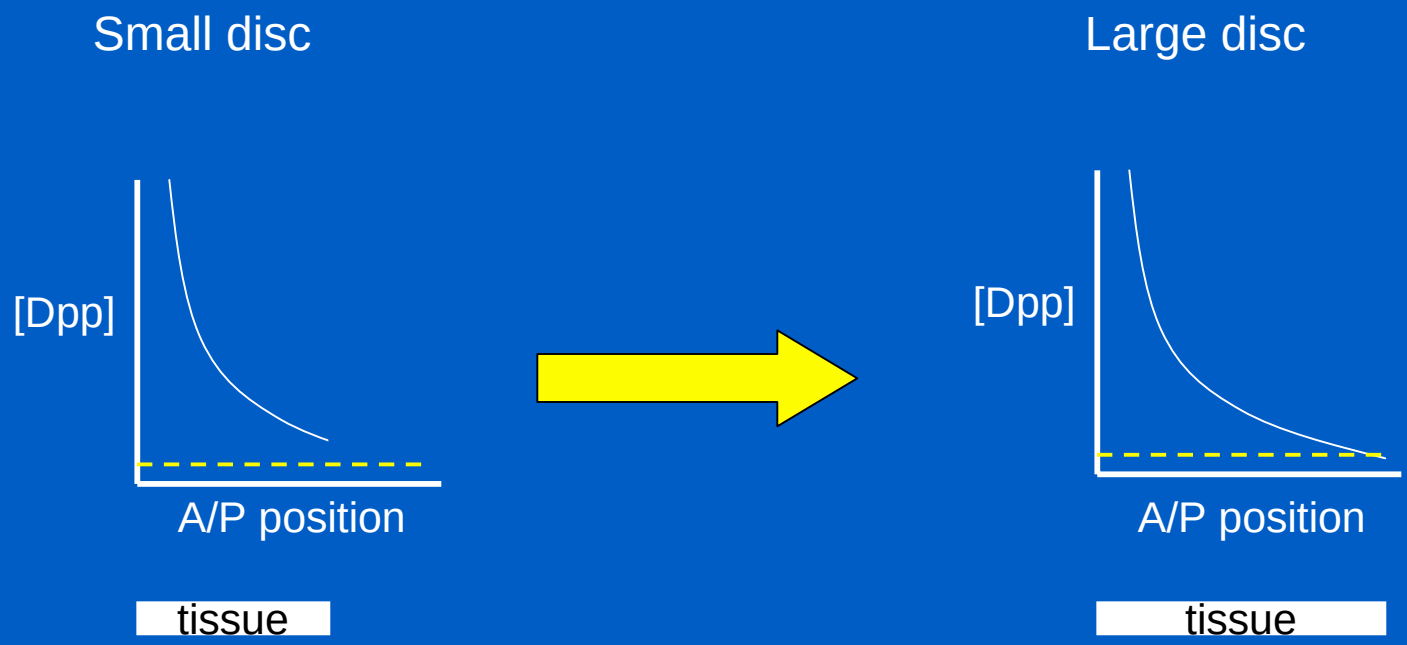
Dpp gradient does not flatten during tissue growth



Dpp gradient shape determined by rate of spreading vs rate of decay



Conundrum: how do cells near the Dpp source know when to stop growing?



- signaling molecule
- physical coupling

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