

Gene Activity during Embryonic Development

NICHD

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Eric Wieschaus

**Focus on the Future
(unanswered questions)**

Gene activity, transcription networks and pattern

Gene activity and cellular mechanics

Understanding Early Development

Patterning - Maternal gradients provide positional cues



Transcriptional response at MBT controls cell fate



Understanding Early Development

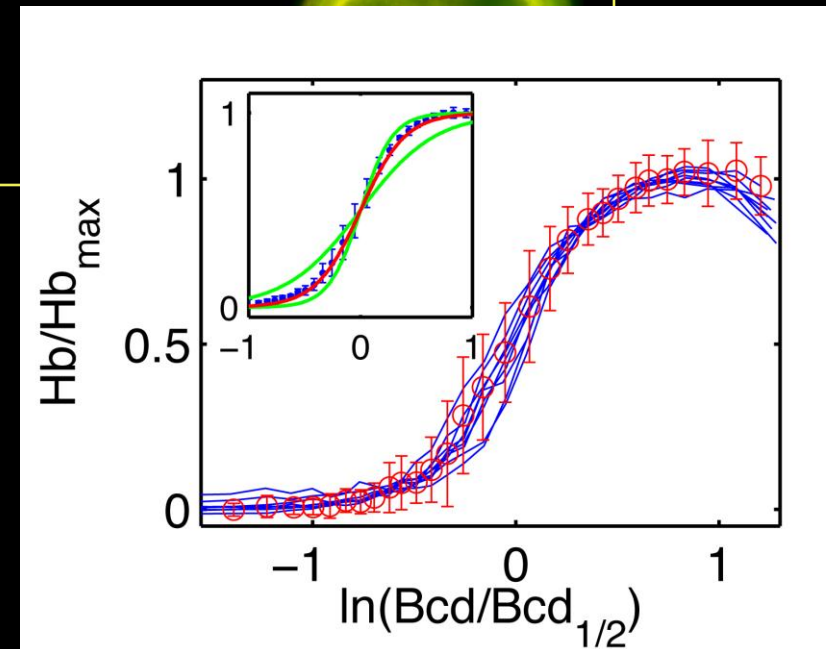
Patterning - Maternal gradients provide positional cues



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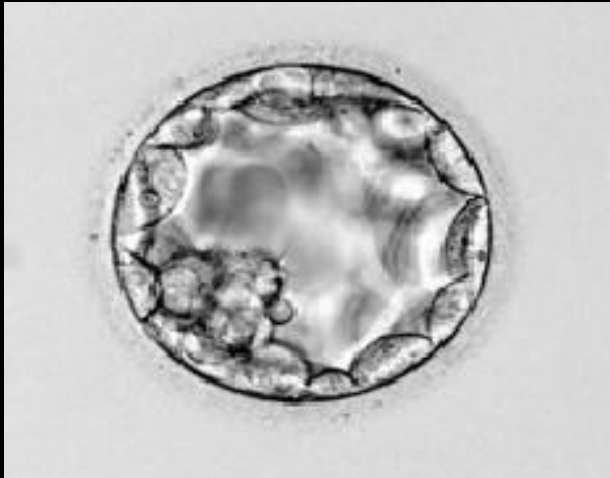


Biophysical measurements of
input Bcd concentration and
HB transcriptional output
(Gregor et al 2007)



How do transcriptional patterns arise in mammalian embryos?

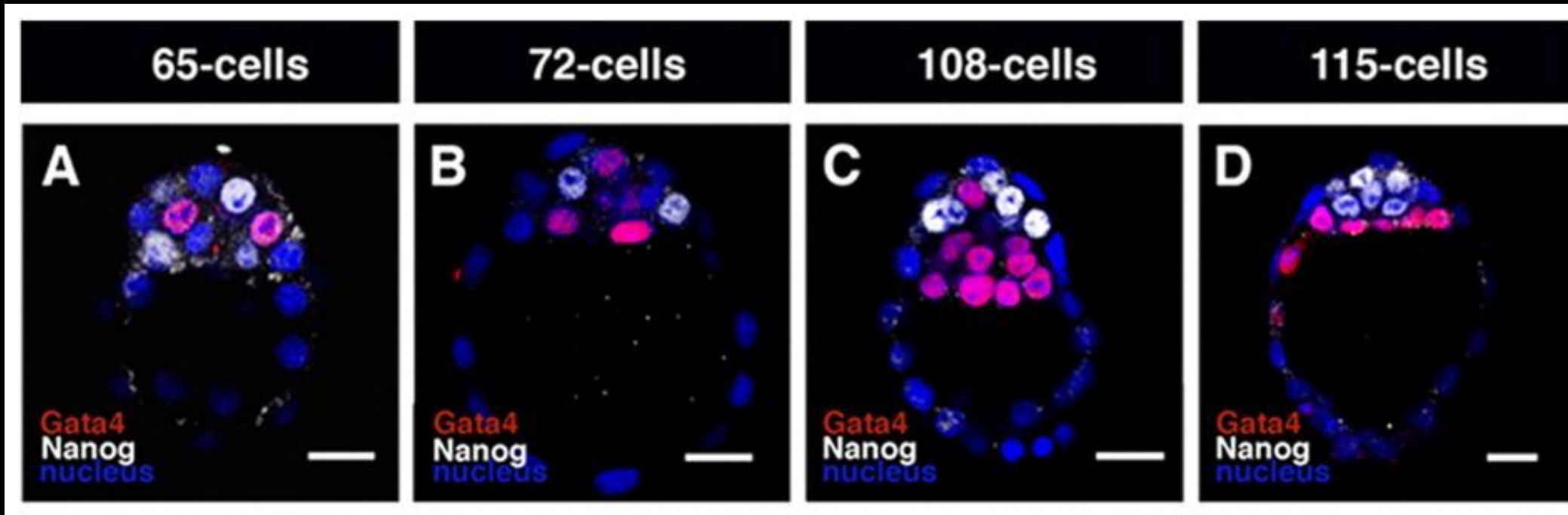
In flies, pattern of the embryo comes from pre-determined distributions in the unfertilized egg.



Is this possible in mammalian eggs where only a tiny fraction of the maternally supplied RNA and protein is incorporated into the inner cell mass and embryonic epiblast?

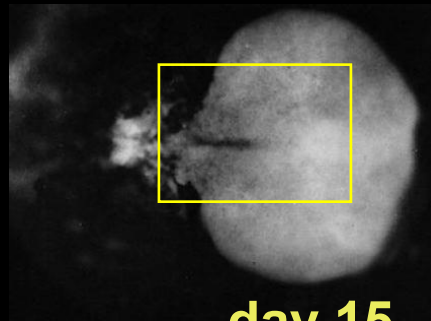
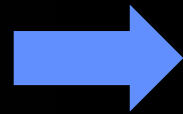
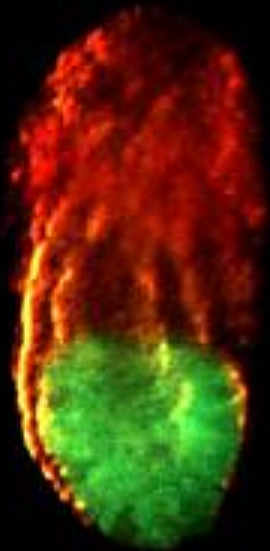
Where does the embryonic pattern come from in human embryos?

Localized patterns of expression arise in the inner cell mass through a gradual process cell communication circuits and sorting out



Anna-Katerina Hadjantonakis, Sloan-Kettering Institute

Can cell signaling within the epiblast also account for the establishment of the head-tail axis in mammalian embryos?

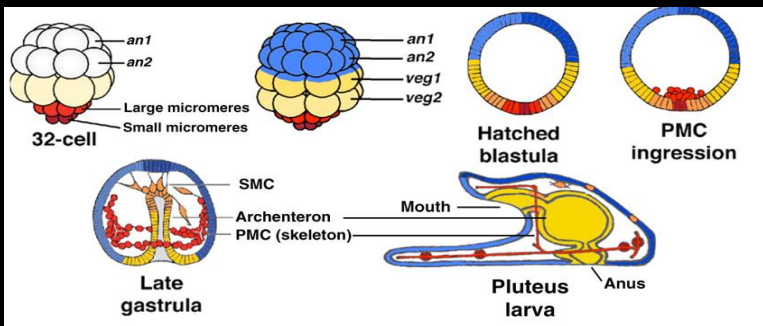


day 15



day 24

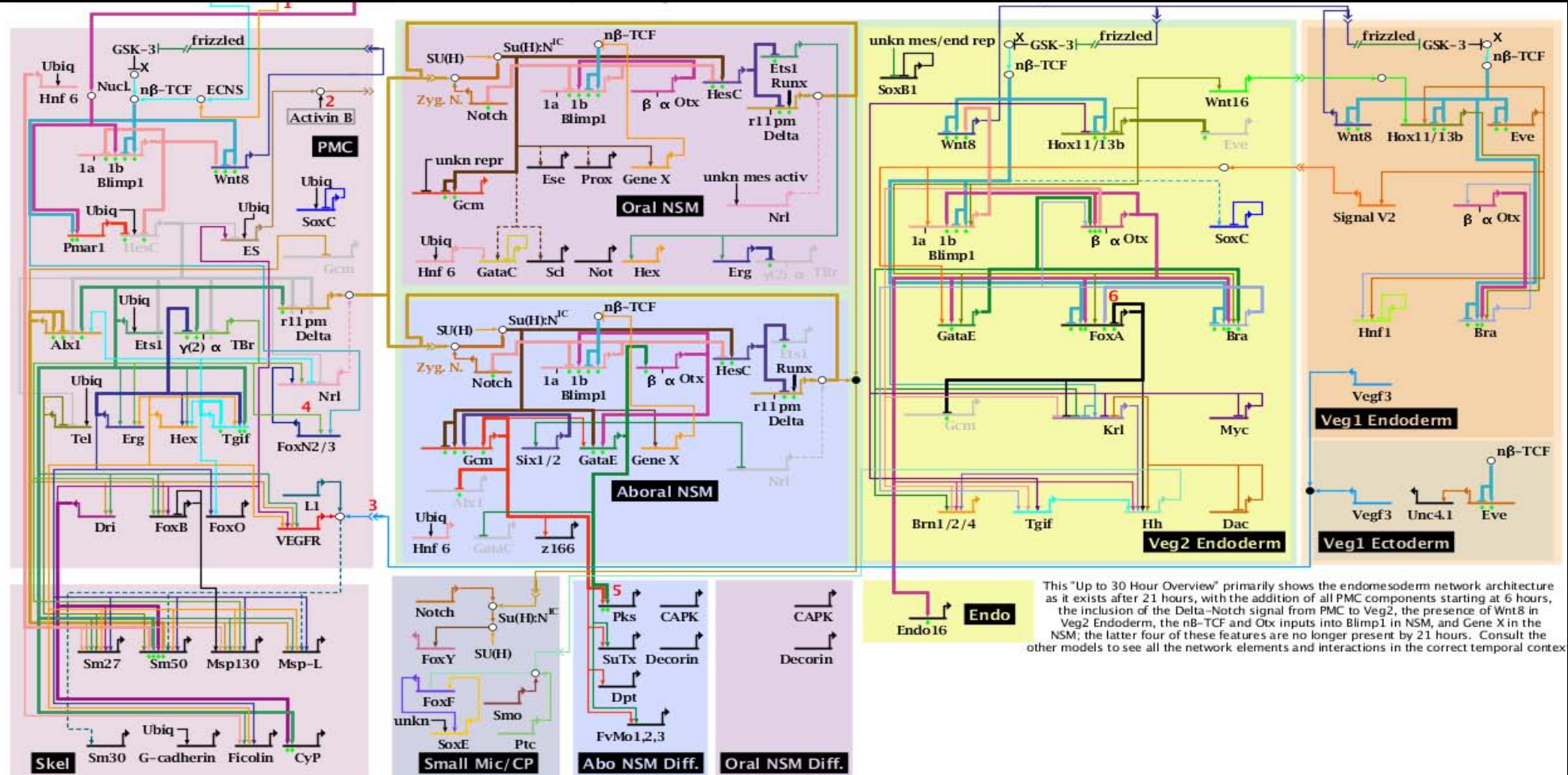
Can cell signaling circuits generate patterns where no patterns previously existed?



cell signaling networks in sea urchins

A systems biological approach

David McClay-Eric Davidson

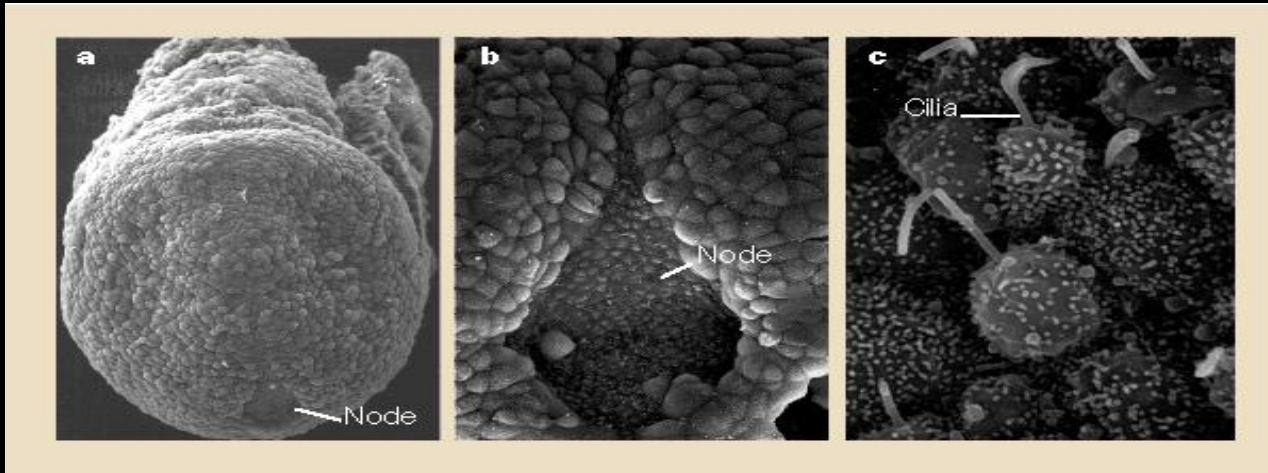


This "Up to 30 Hour Overview" primarily shows the endomesoderm network architecture as it exists after 21 hours, with the addition of all PMC components starting at 6 hours, the inclusion of the Delta-Notch signal from PMC to Veg2, the presence of Wnt8 in Veg2 Endoderm, the nβ-TCF and Otx inputs into Blimp1 in NSM, and Gene X in the NSM; the latter four of these features are no longer present by 21 hours. Consult the other models to see all the network elements and interactions in the correct temporal context.

Ubiqu=ubiquitous; Mat = maternal; activ = activator; rep = repressor.

**Can physical properties and mechanical aspects
provide the spatial cues that pattern gene
expression?**

RL patterning in mouse or fish require motile cilia in the node or in Kupfer's vesicle

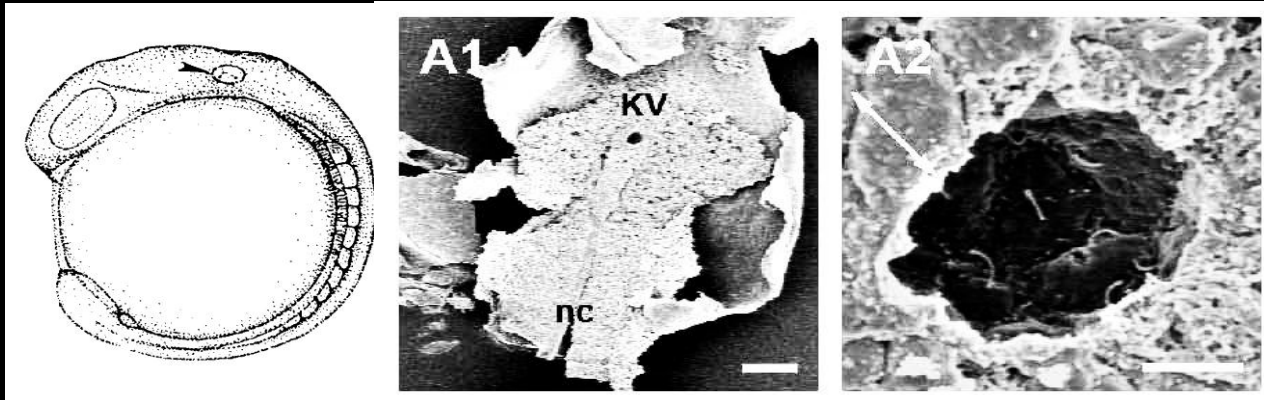


Primary cilia in the mouse node

Cliff Tabin Harvard Med School

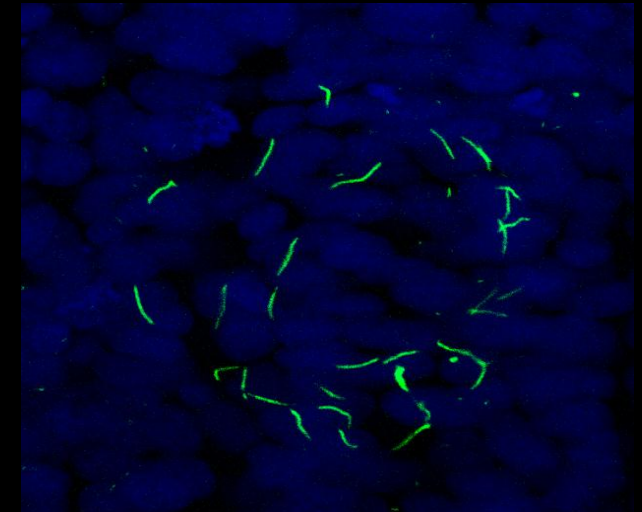
(Micrographs -K. Sulik & T. Poe, U North Carolina.)

Cilia at KV

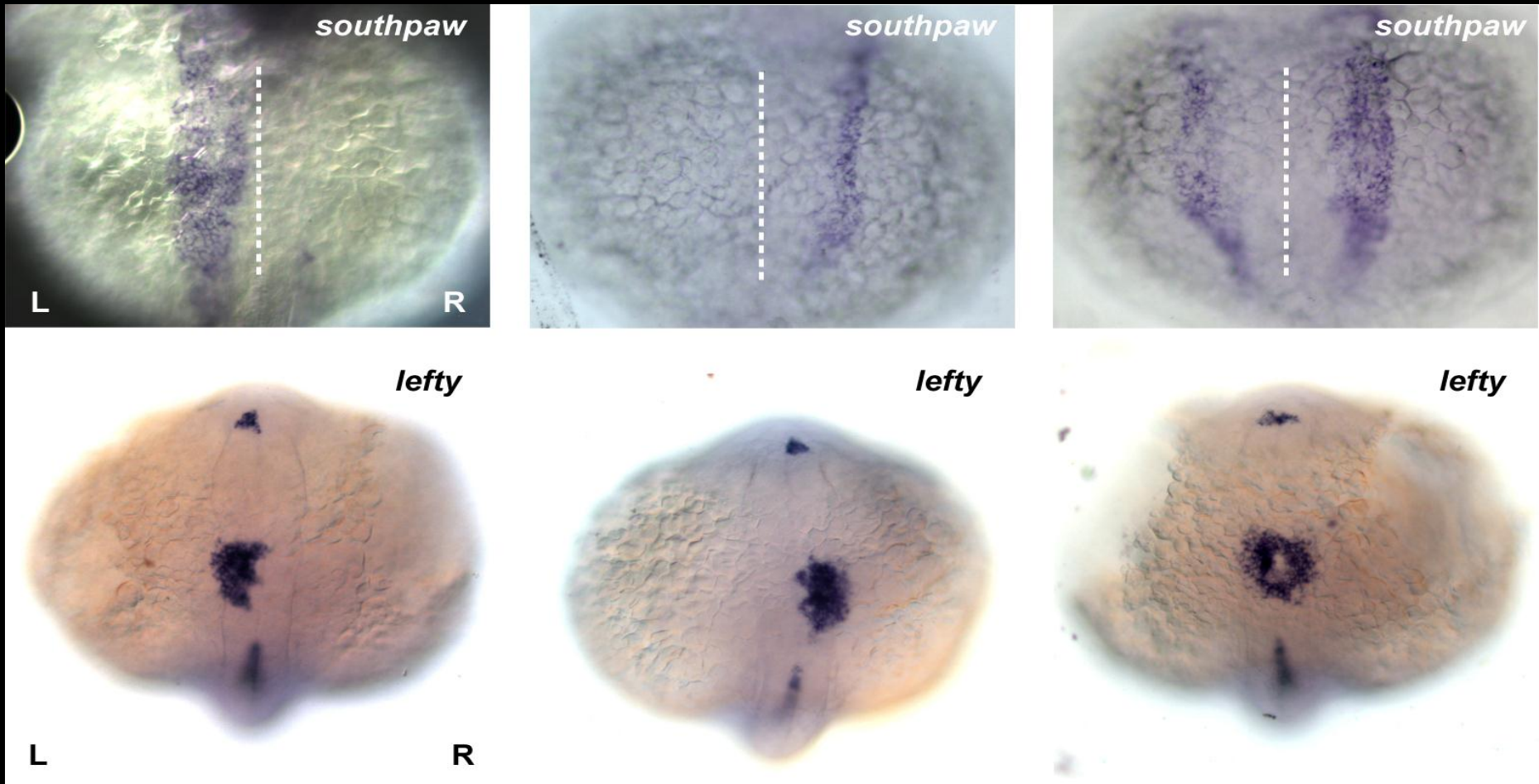


cilia in the zebrafish Kupfer's vesicle

(Rebecca Burdine, Princeton)



Defects in cilia motility affect asymmetric gene expression



Schottenfeld, Sullivan-Brown and Burdine, *Development* 2007

Sullivan-Brown et al, *Dev Biol* 2008 , Serluca* and Xu* et al, *Development* 2009

Gene Activity => Cellular Mechanics

Understanding Early Development

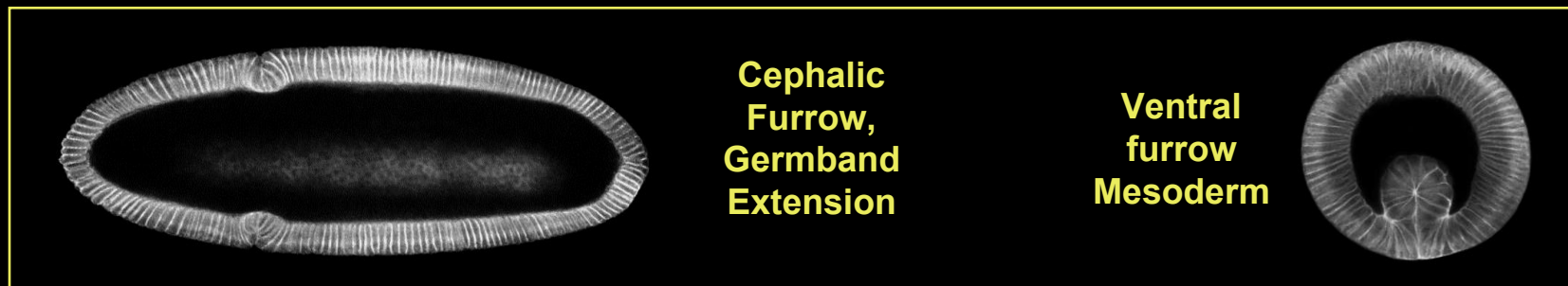
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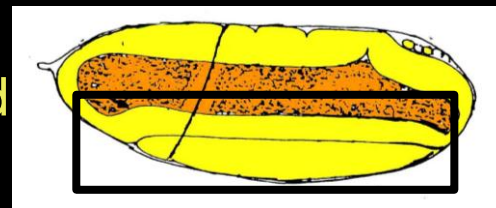
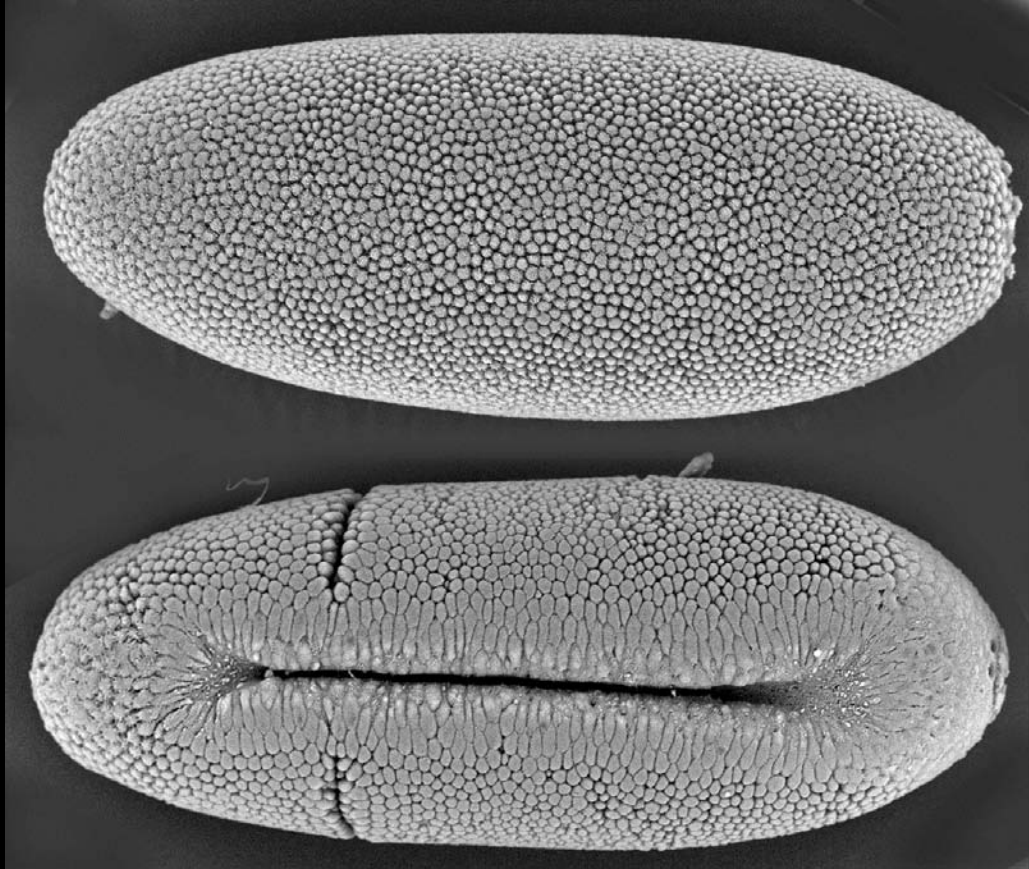
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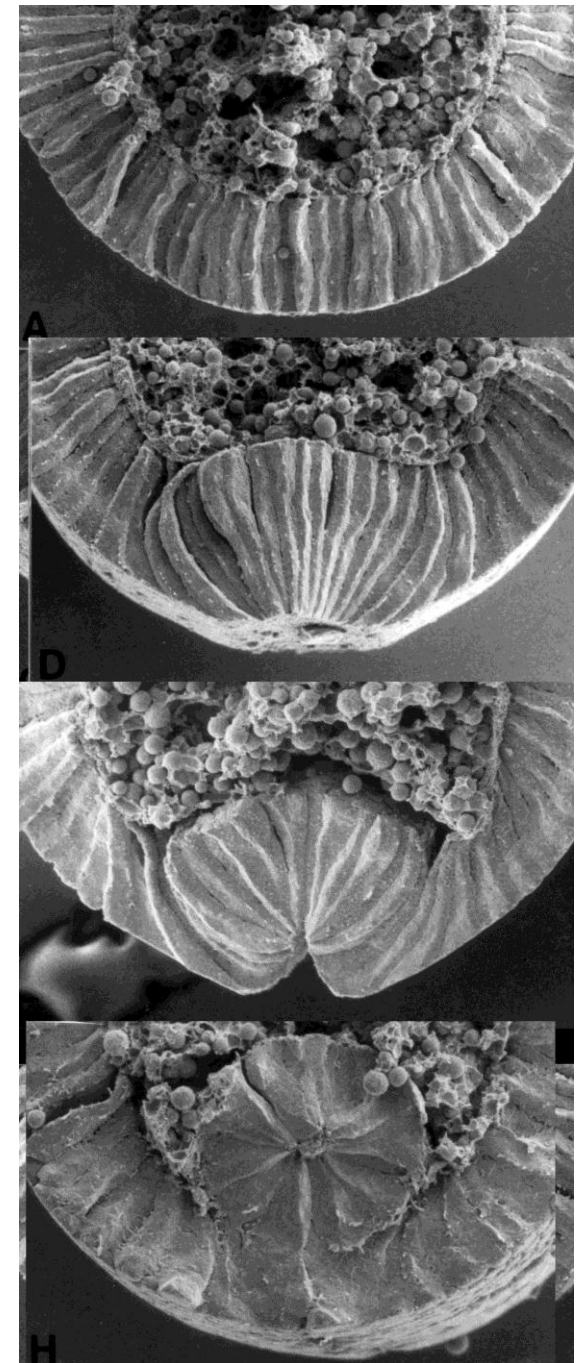
Cell fate choices are translated into cell behaviors



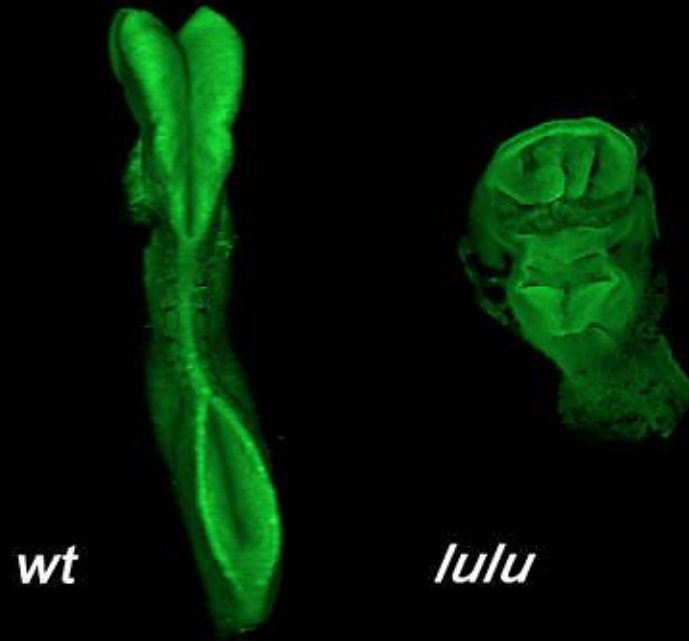
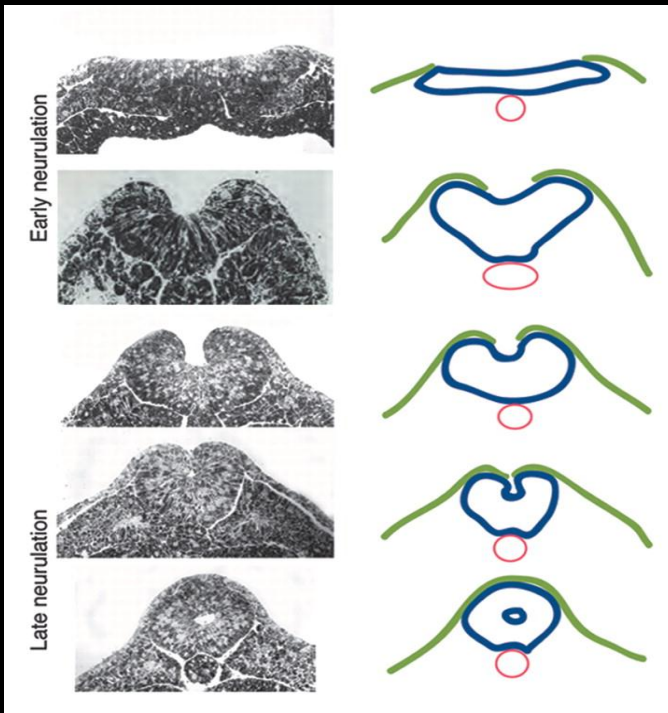
Infolding of mesoderm precursors during *Drosophila* gastrulation



Mesoderm precursors are internalized by formation of a ventral furrow

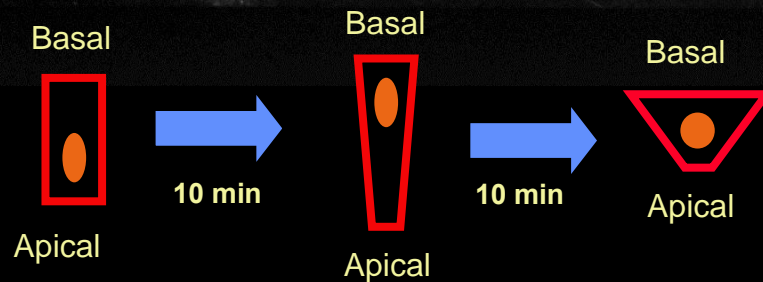
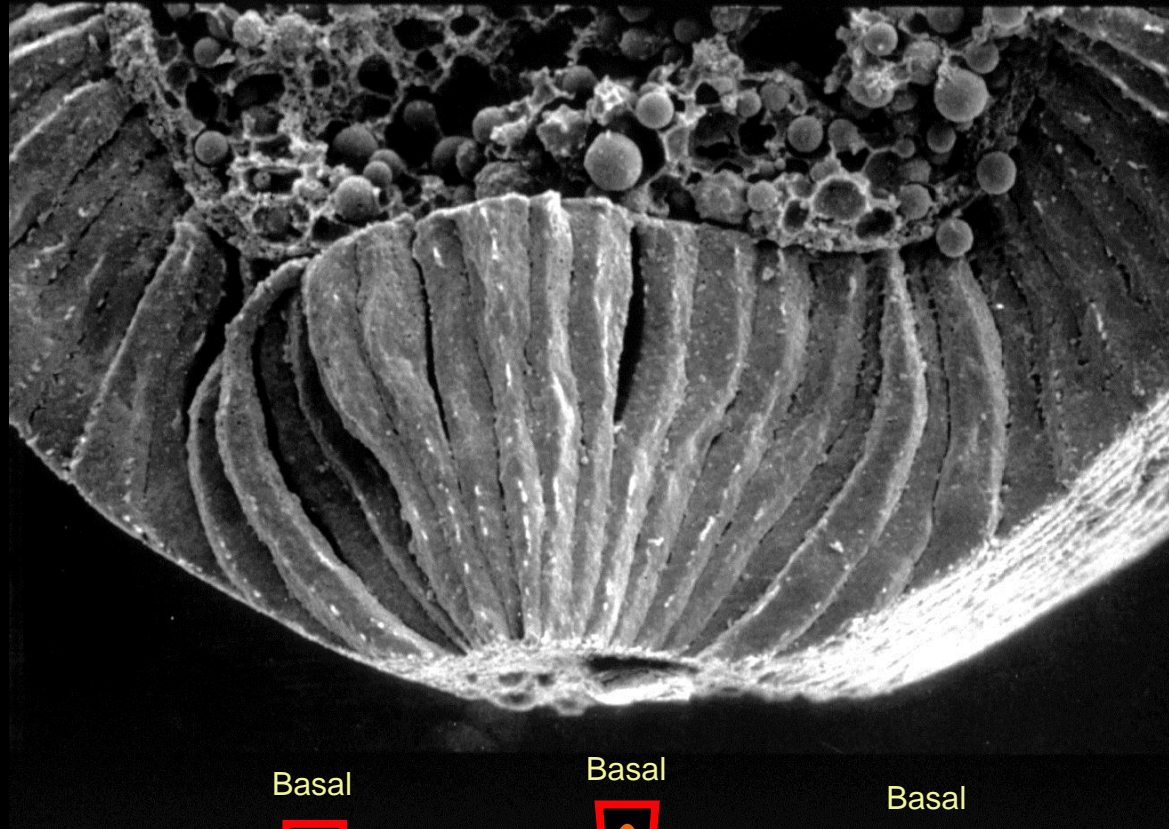


Epithelial folds during formation of neural tube

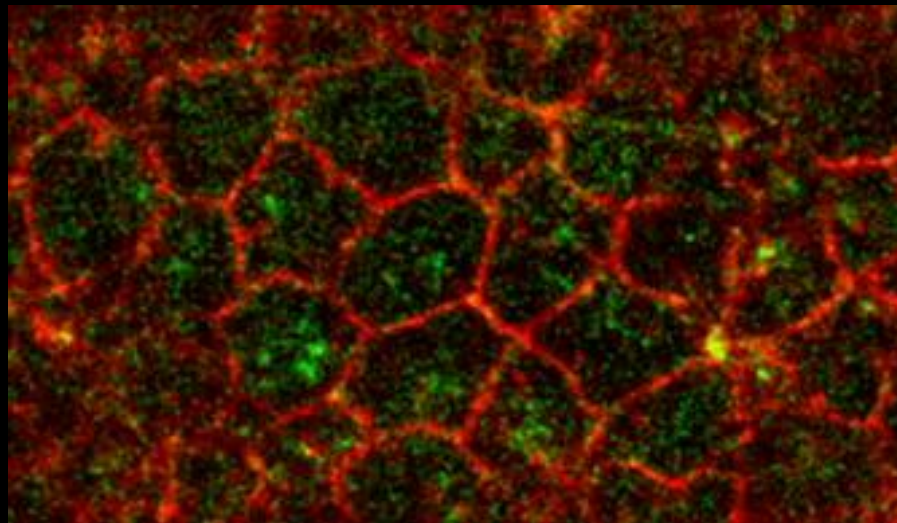
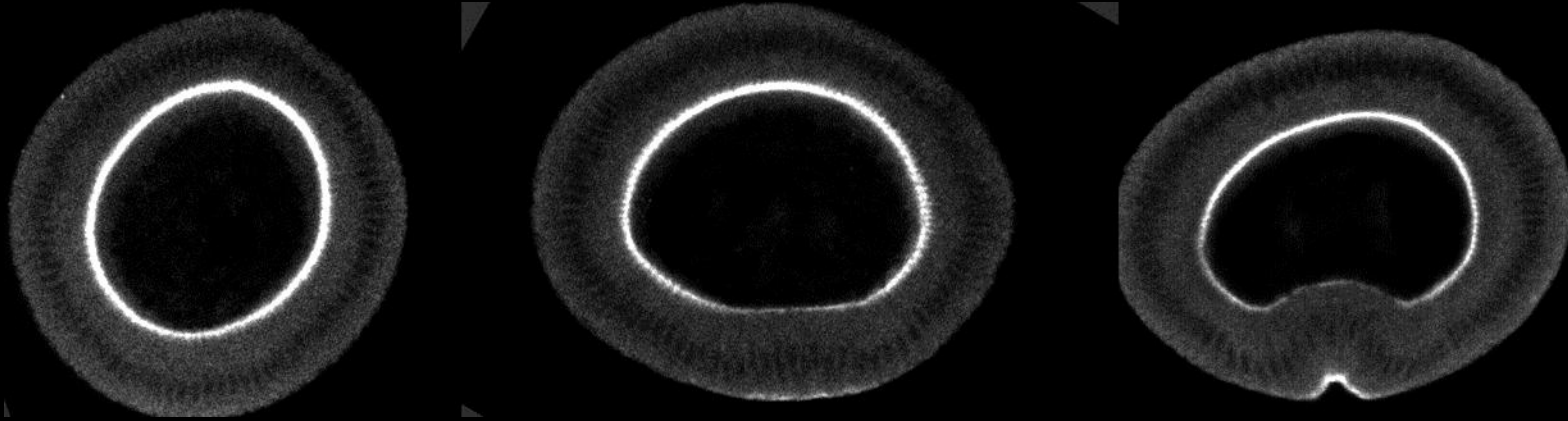


Kathryn V. Anderson
Sloan-Kettering Institute

Are there universal biophysical properties that govern cell shape changes and epithelial folding?

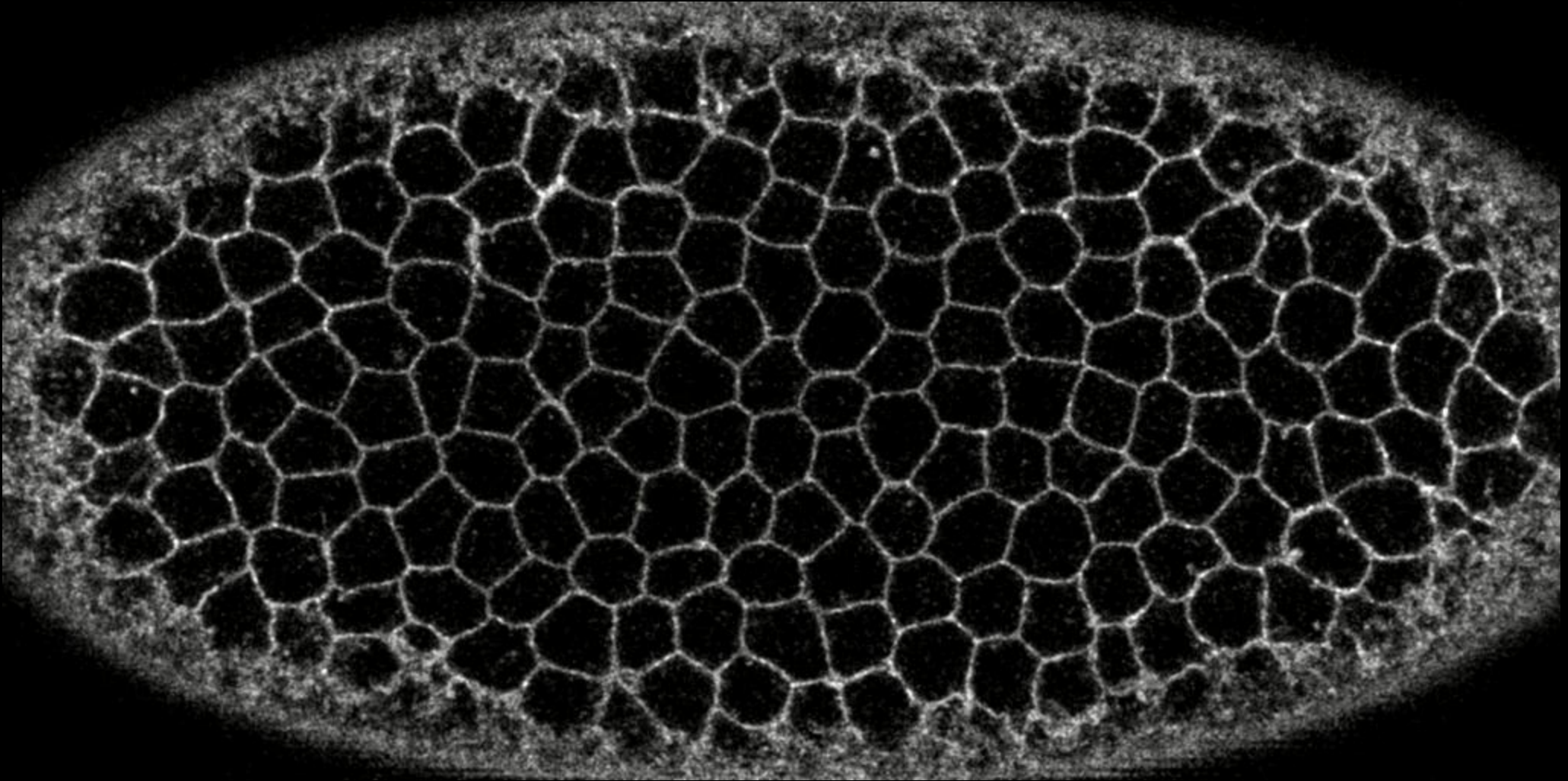


Constriction of the apical surface in ventral cells is associated with local accumulation of Myosin



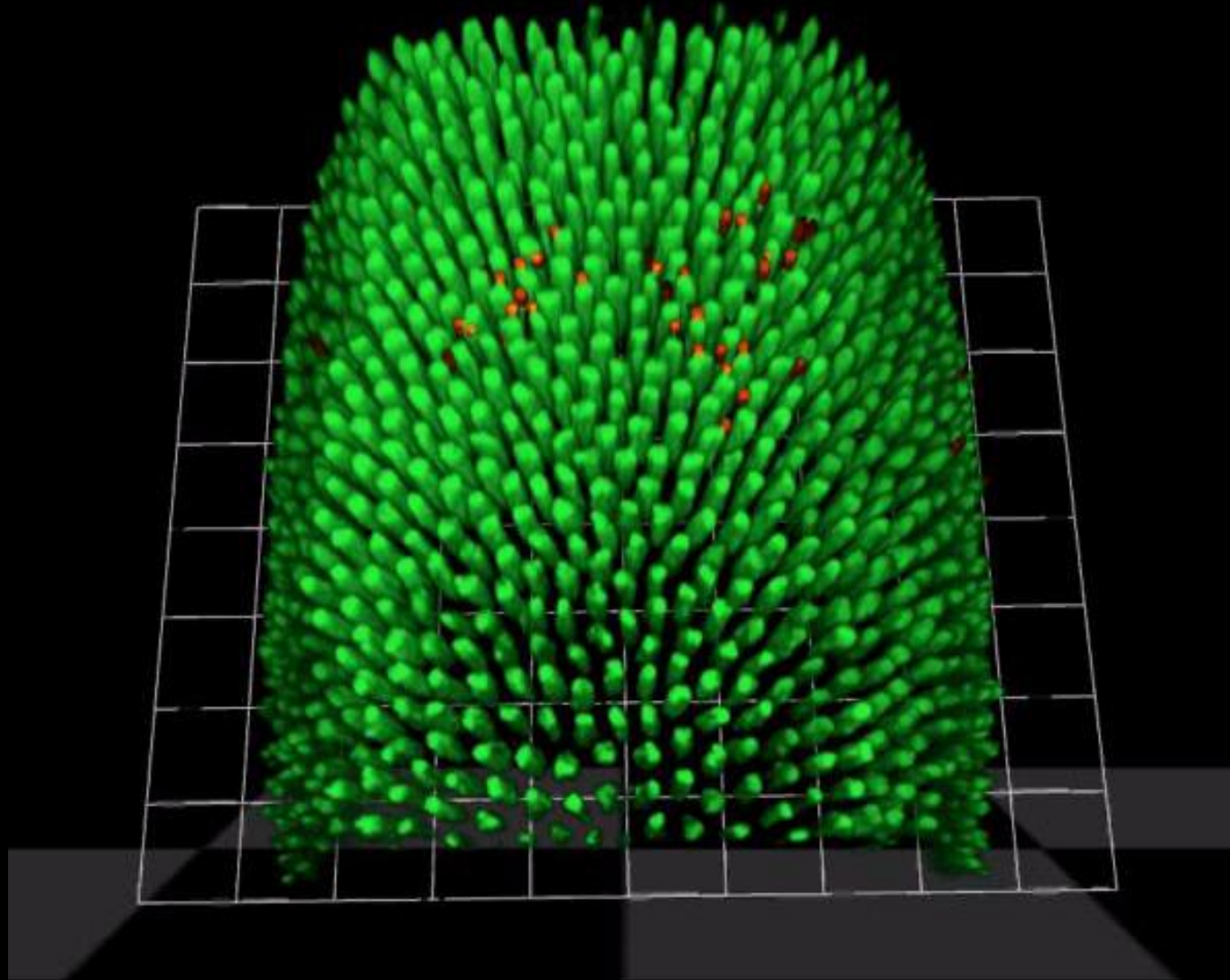
Myosin II accumulates in a network of interconnected spots on the apical surface of constricting cells

Changes in apical cell diameters drive furrow formation



Membrane-GFP (Spider)

Testing cytoplasmic properties by injection of biologically inert fluorescent beads



Embryo Development Geometry Explorer (EDGE 1)

The screenshot displays the EDGE software interface with the following components:

- Raw and processed image slices:** A central window showing a 2D image of a cell sheet with green nuclei and magenta outlines. To its right are controls for 'Show...' (Raw, Processed, Polygons, Other channels), a 'Depth' slider set to 60, and a 'Data set info' table.
- Data set info table:**

dx:	0.141	beg t:	0	btm z:	0	Ys:	700
dz:	0.5	end t:	0	top z:	86	Xs:	1024
dt:	-	ref t:	0	ref z:	37		
- Select Cells:** A panel on the right with 'neighbors order' set to 0, 'select all' and 'select manually' buttons, radio buttons for 'Individuals' (selected) and 'Averages', and 'current cell #' set to 188.
- Quantitative measurements:** A panel on the bottom left with a dropdown menu for 'Nuclei:nuclei_intensity::nuclei int...', an 'export selected cells' button, 'v-axis scale' controls (min, max), and 'Smoothing' options (smoothed, high frequency, rate of change) with a 'smoothing sigma' slider.
- nuclei intensity vs. depth graph:** A line graph showing 'Cell/nuclei intensity(intensity units) x 10⁴' on the y-axis (0 to 18) and 'height (microns)' on the x-axis (0 to 40). A red curve peaks at approximately 16.5 units at a height of 30 microns, marked by a vertical dashed line.
- 3D view:** A panel on the bottom right showing a 3D reconstruction of the cell sheet. It includes 'Show...' controls (Membranes, Surface, Vertices, Centroids, Centroid fit) and 'spatial'/'temporal' view options. A 'take picture' button is present. The z-axis is labeled 'z (microns)' with values 10 and 40.

EDGE – Michael Gelbart & Matthias Kaschube

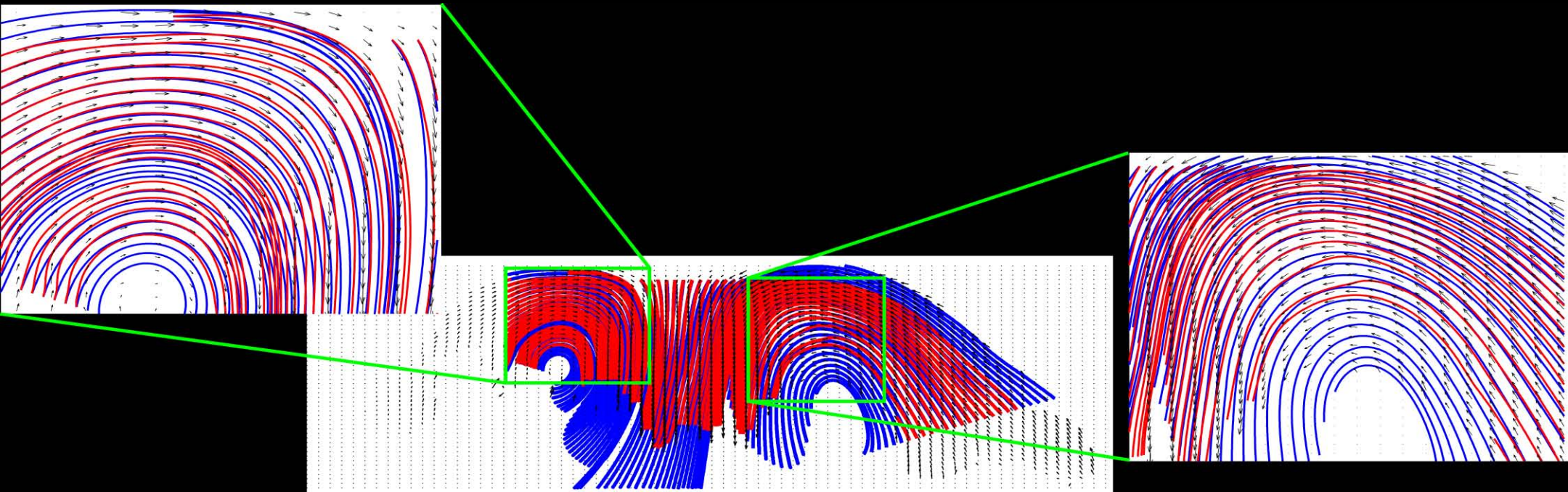
Very suitable for planar cell sheets

Performs tracking in space and time

Computational representations vertex based--Nth-order neighbors

Allows to integrate additional channels (nuclei, myosin, ...)

Global flow of cytoplasm follow patterns predicted by Navier–Stokes equations



This is surprising because the equations assume that the fluid being studied is infinitely divisible and not composed of particles (or cells!)

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