Gene Activity during Embryonic Development

NICHD

December 5, 2012

Eric Wieschaus

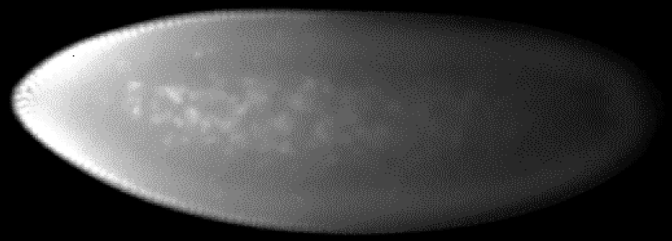
Focus on the Future
(unanswered questions)

Gene activity, transcription networks and pattern

Gene activity and cellular mechanics

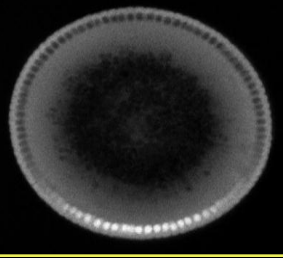
Understanding Early Development

Patterning - Maternal gradients provide positional cues

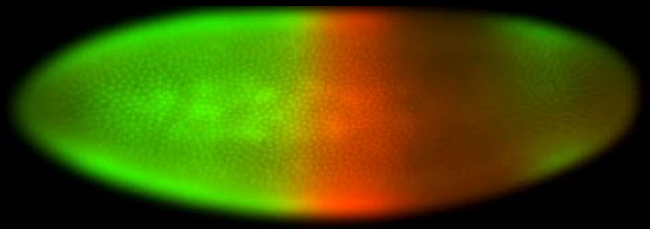


Maternal
Bicoid

Maternal
Dorsal

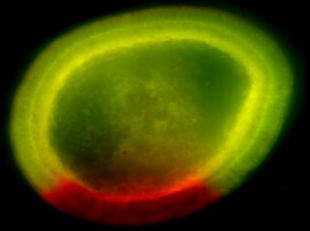


Transcriptional response at MBT controls cell fate



Hb and Kr
Gap genes

twist
(snail)



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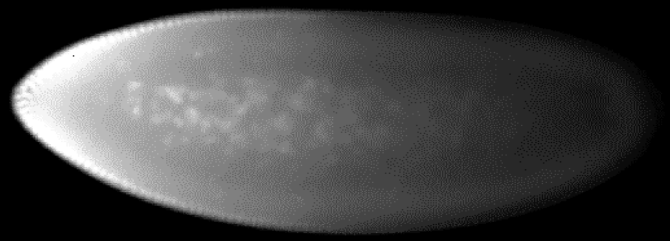

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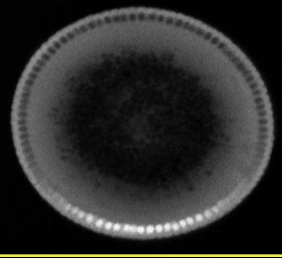

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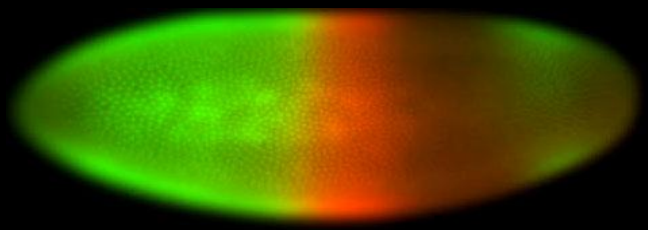
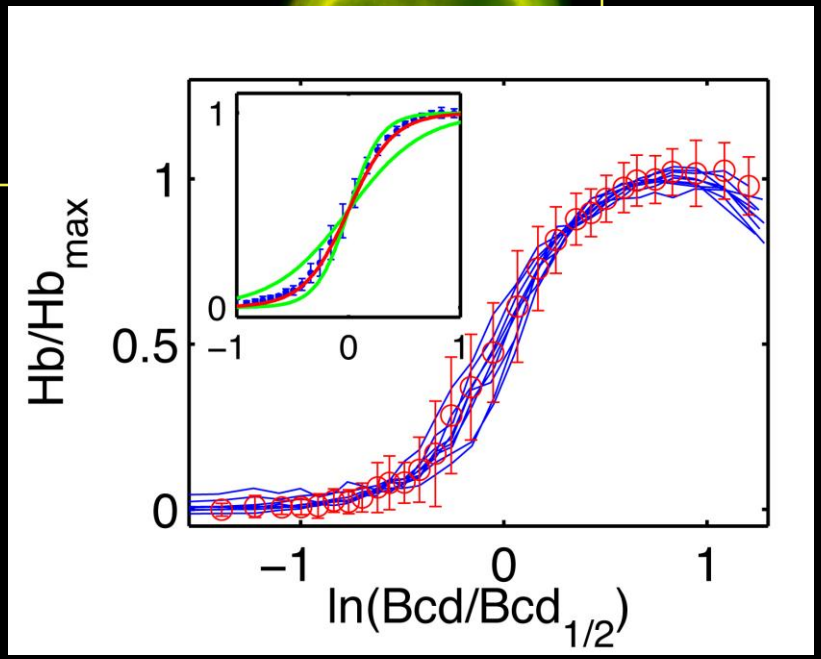


Hb and Kr
Gap genes

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



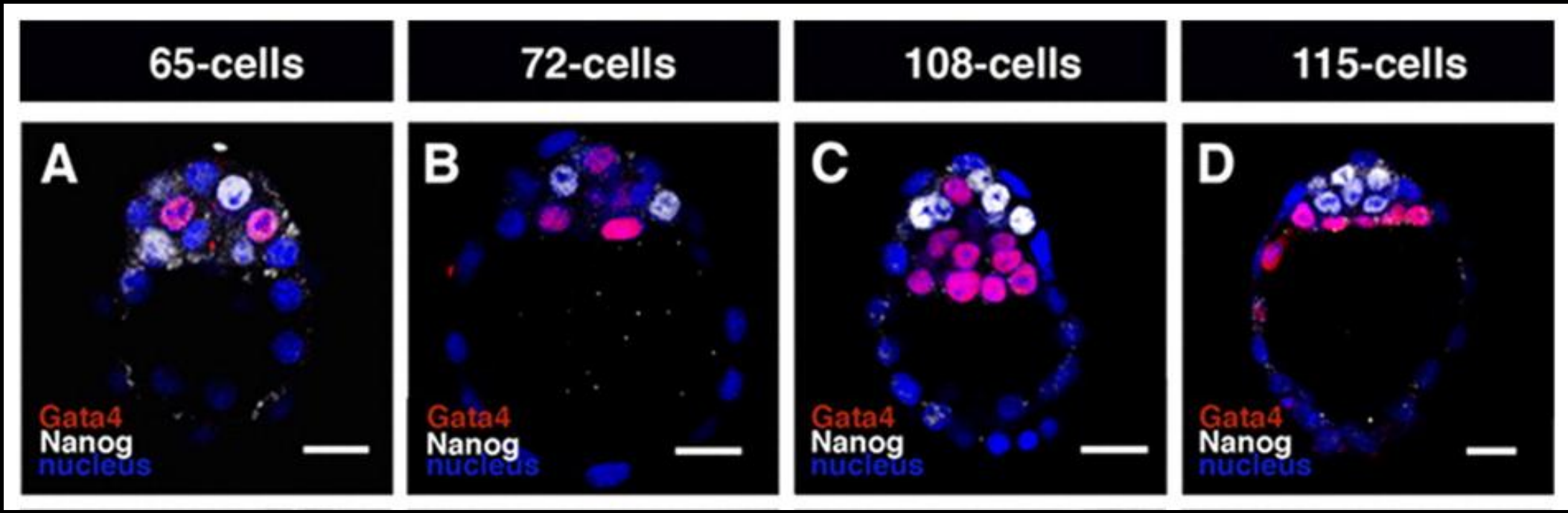
How do transcriptional patterns arise in mammalian embryos?

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?

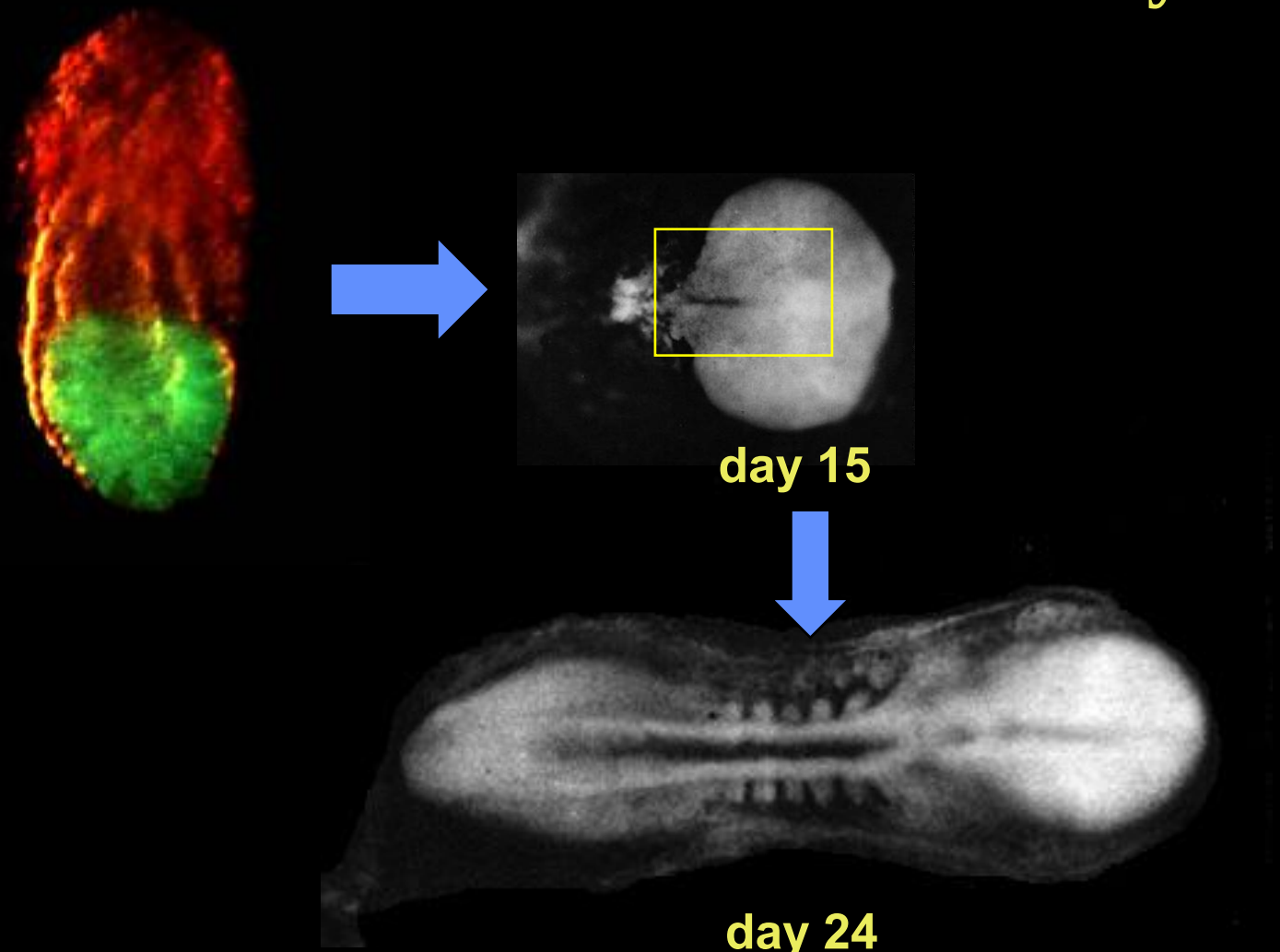
Where does the embryonic pattern come from in human embryos?

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

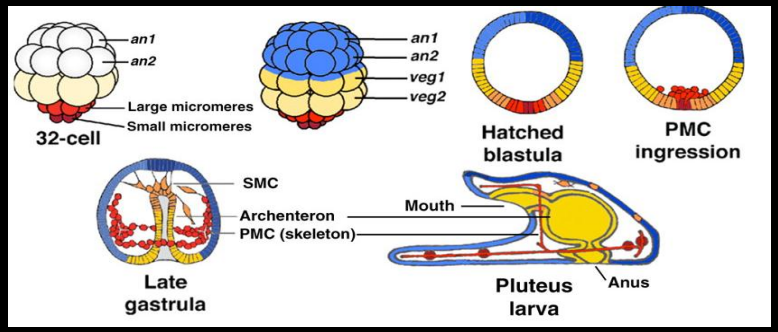


Anna-Katerina Hadjantonakis, Sloan-Kettering Institute

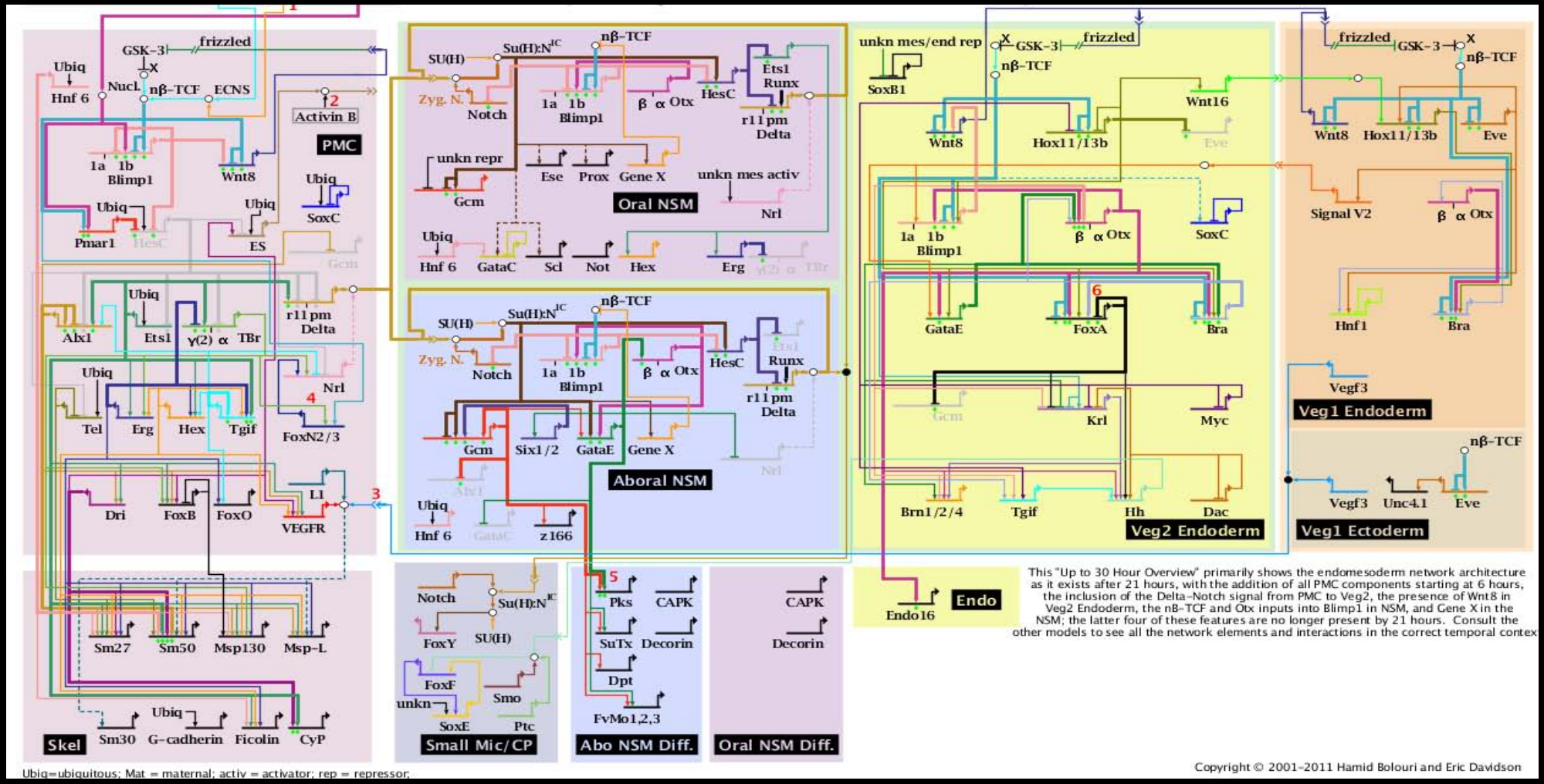
Can cell signaling within the epiblast also account for the establishment of the head-tail axis in mammalian embryos?



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

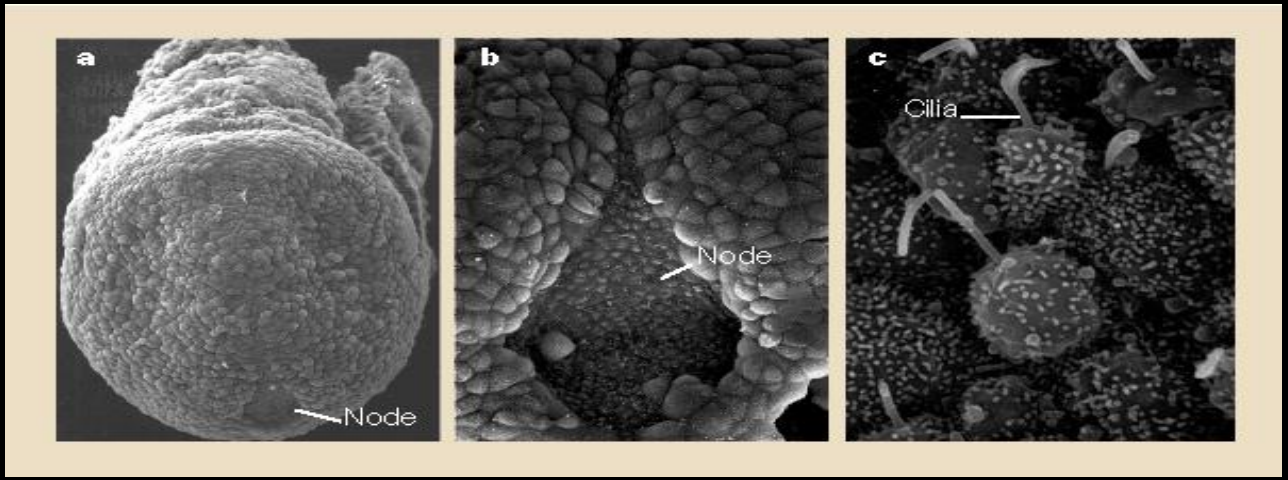


cell signaling networks in sea urchins
A systems biological approach
David McClay-Eric Davidson



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

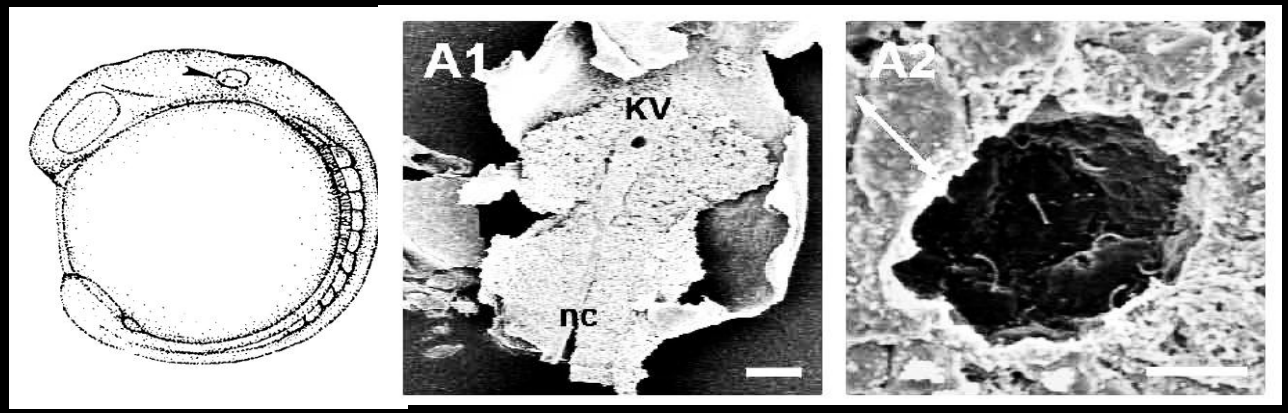
RL patterning in mouse or fish require motile cilia in the node or in Kupfer's vesicle



Primary cilia in the mouse node

Cliff Tabin Harvard Med School

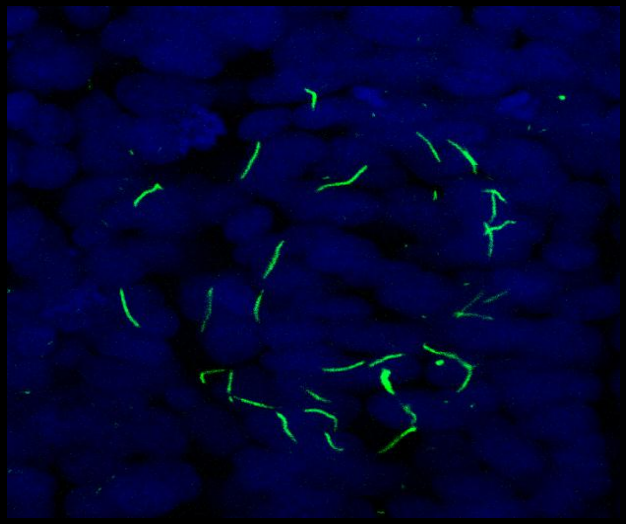
(Micrographs -K. Sulik & T. Poe, U North Carolina.)



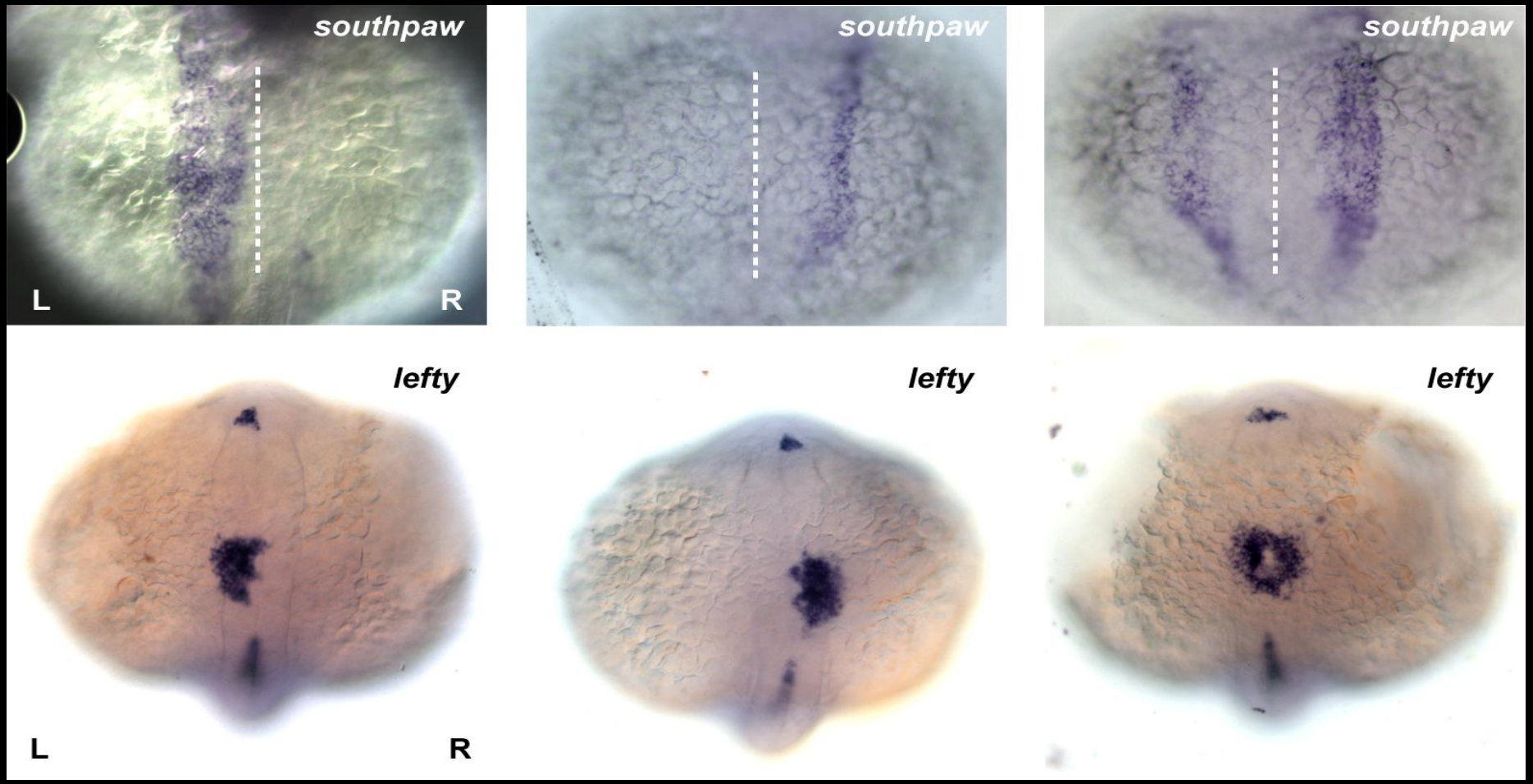
cilia in the zebrafish Kupfer's vesicle

(Rebecca Burdine, Princeton

Cilia at KV



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

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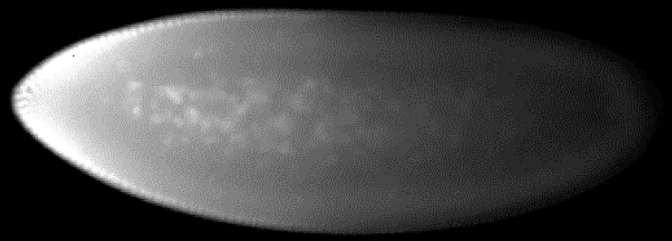

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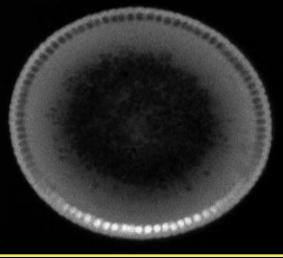

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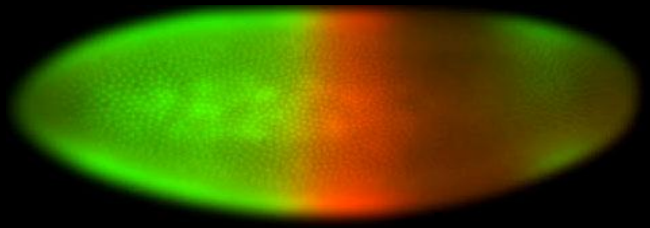

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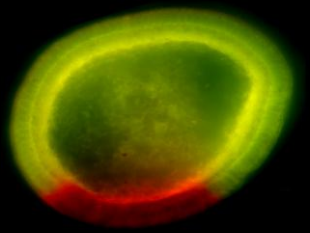
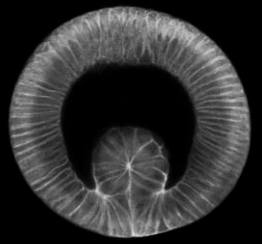


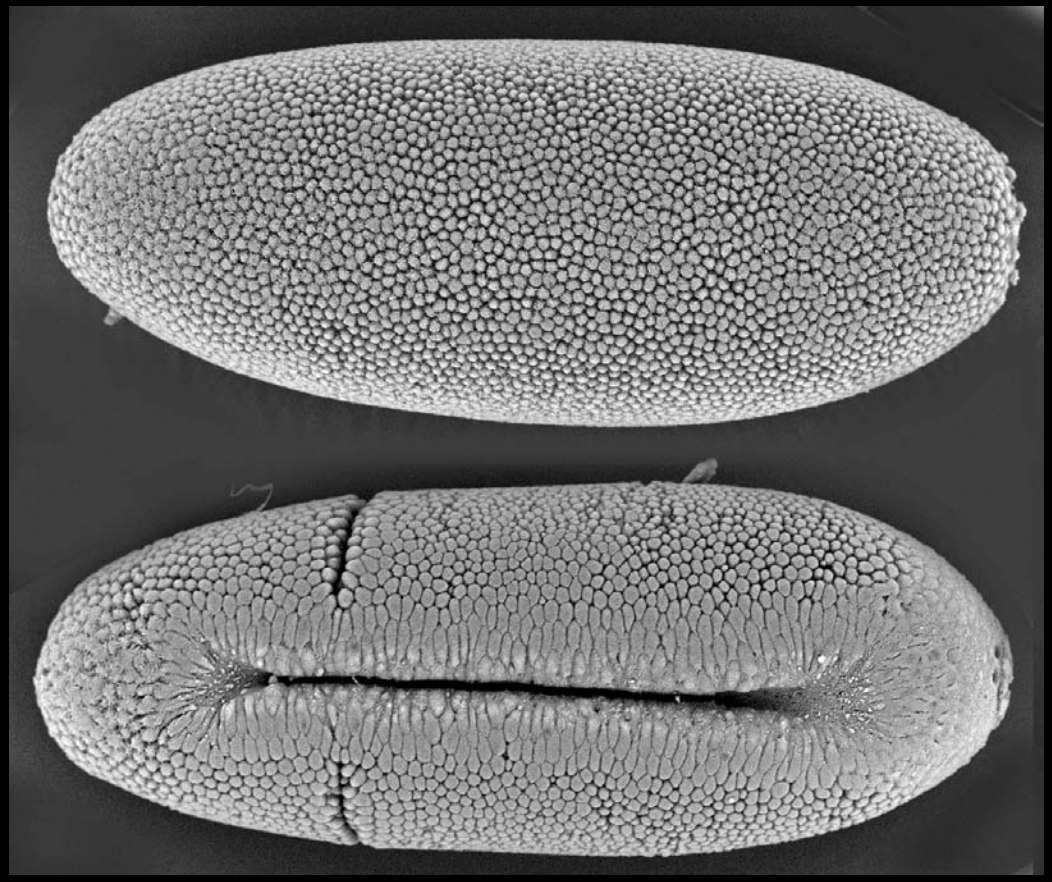
Cell fate choices are translated into cell behaviors

Cephalic
Furrow,
Germband
Extension

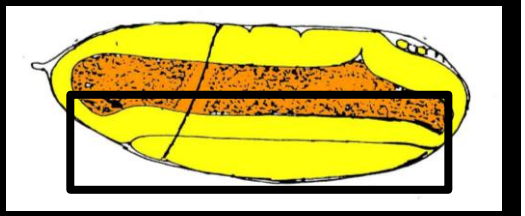
Ventral
furrow
Mesoderm

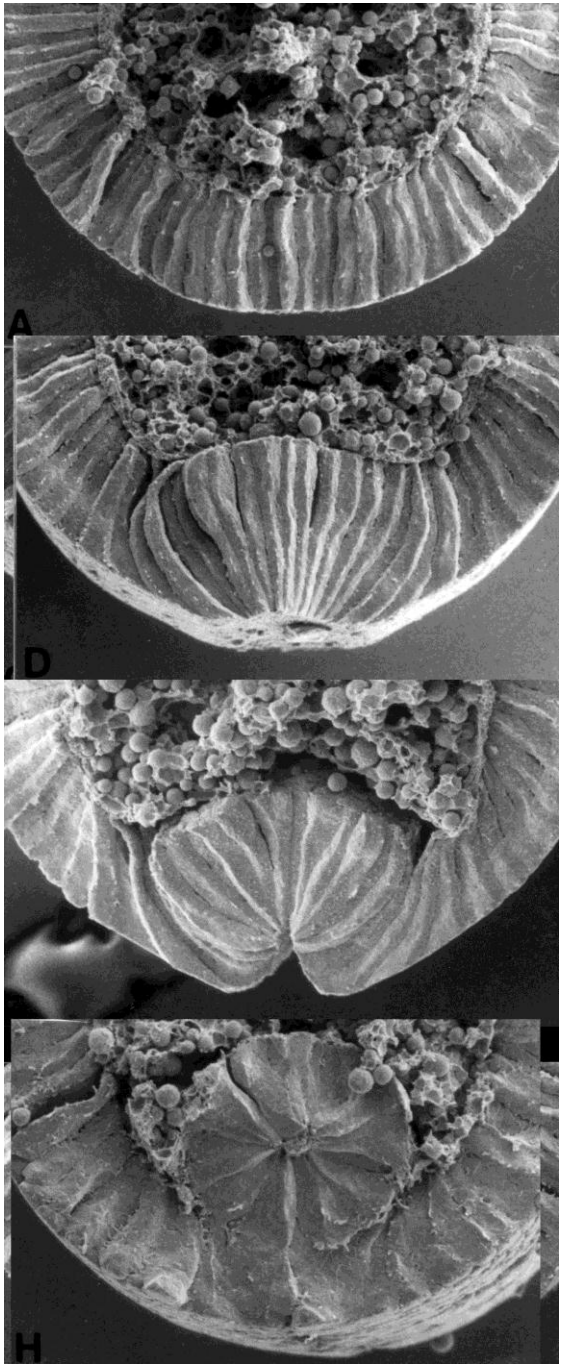


Infolding of mesoderm precursors during Drosophila gastrulation

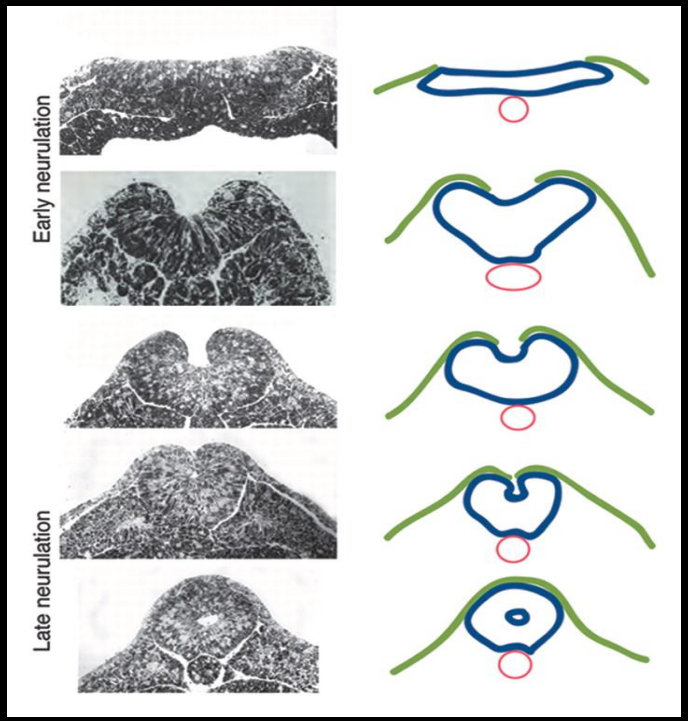


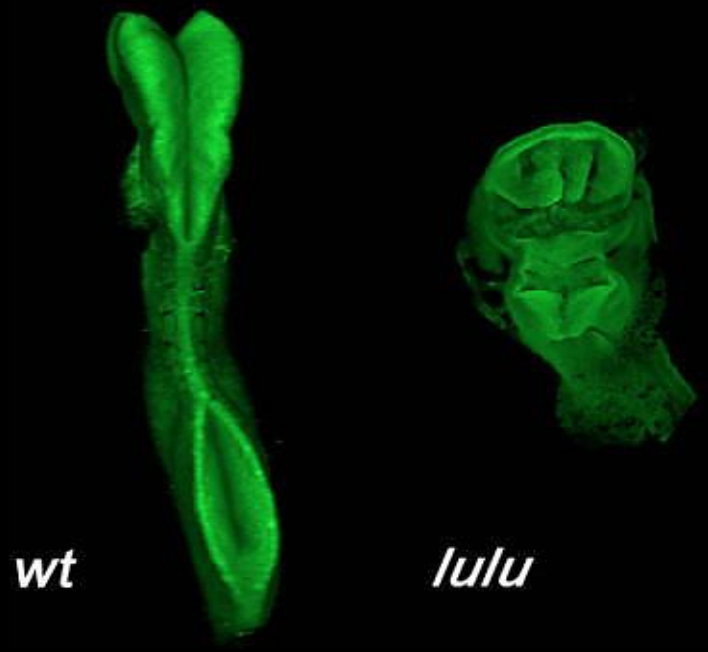
Mesoderm precursors are internalized by formation of a ventral furrow





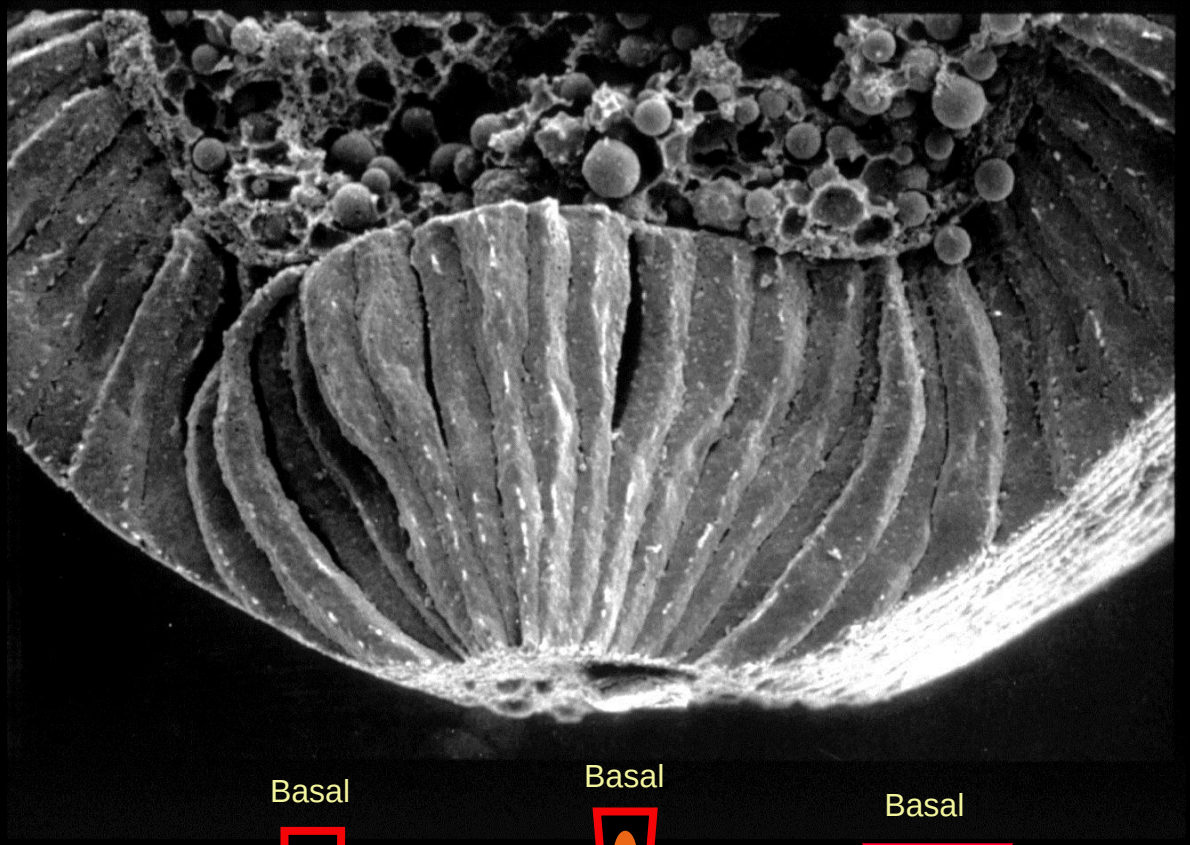
Epithelial folds during formation of neural tube



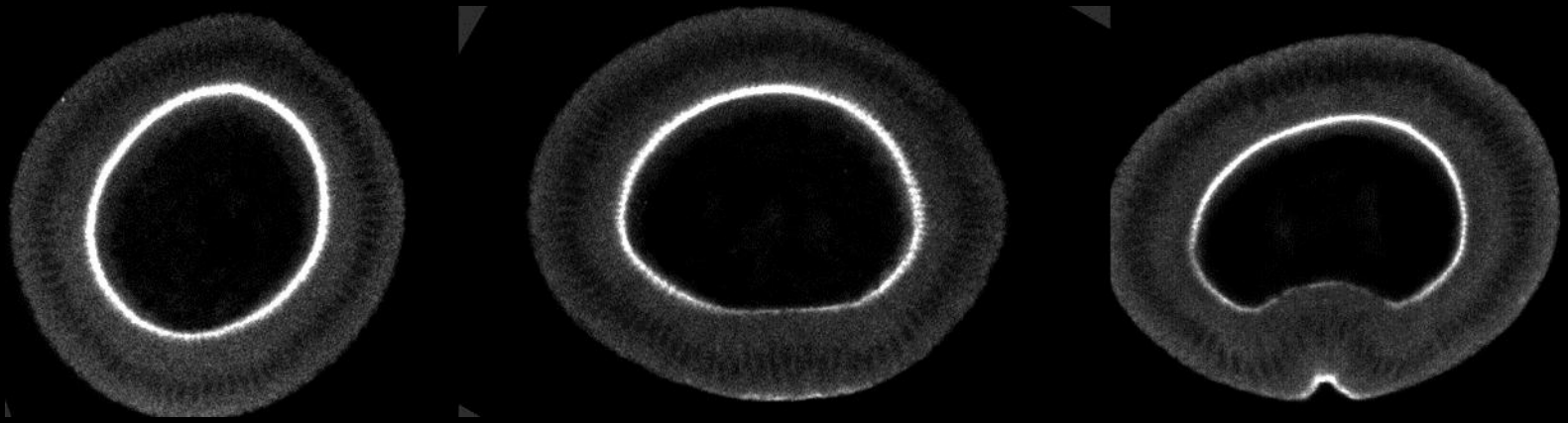


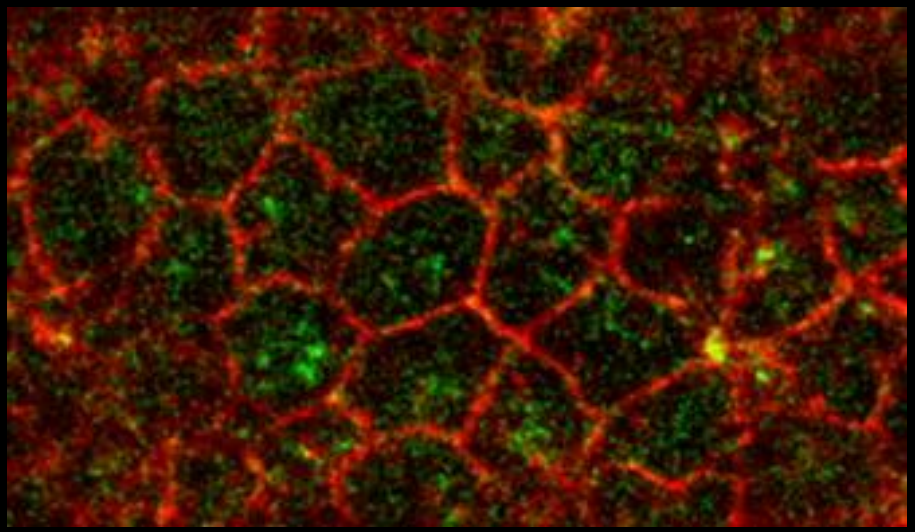
Kathryn V. Anderson
Sloan-Kettering Institute

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



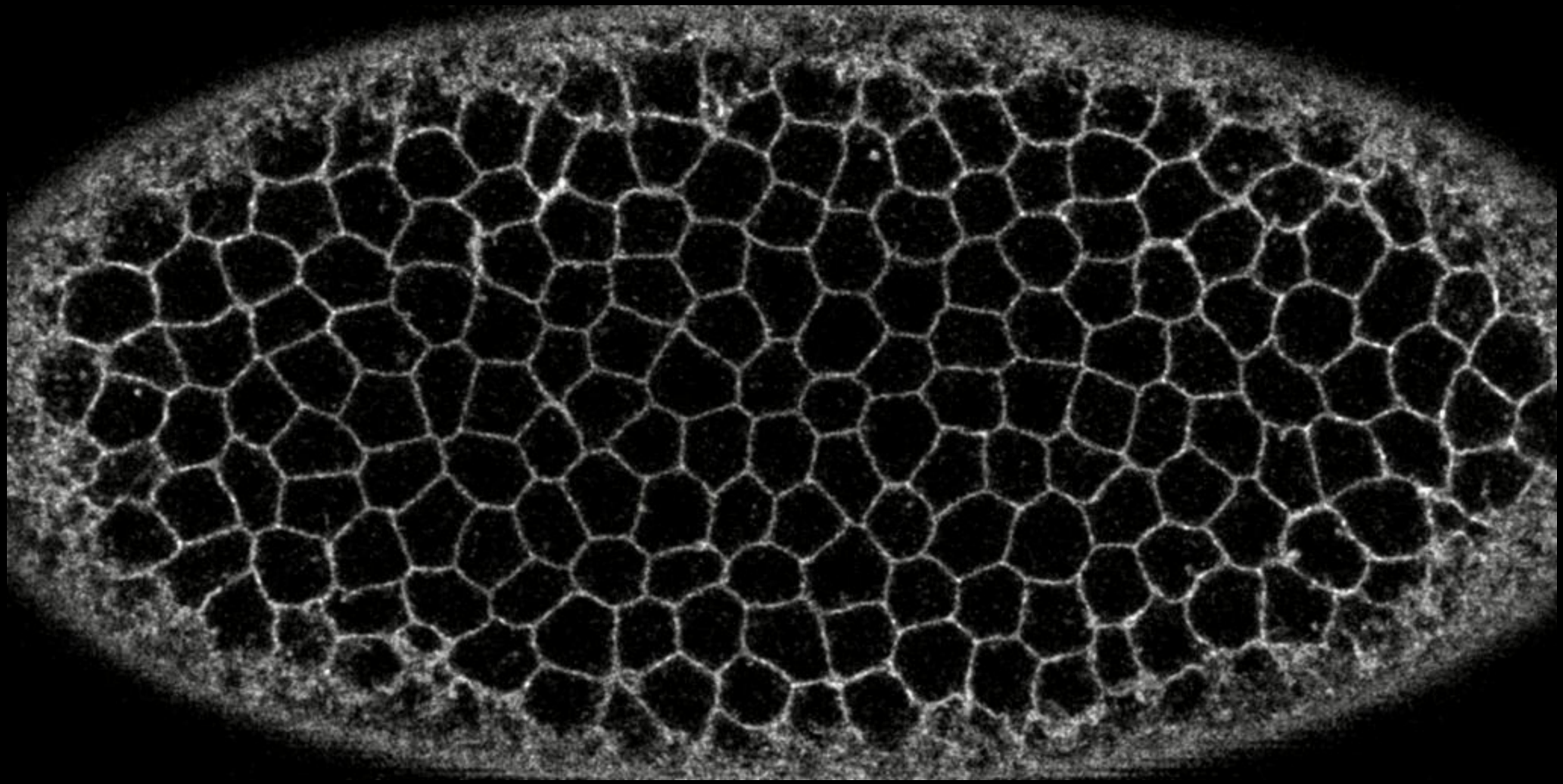
Constriction of the apical surface in ventral cells is associated with local accumulation of Myosin





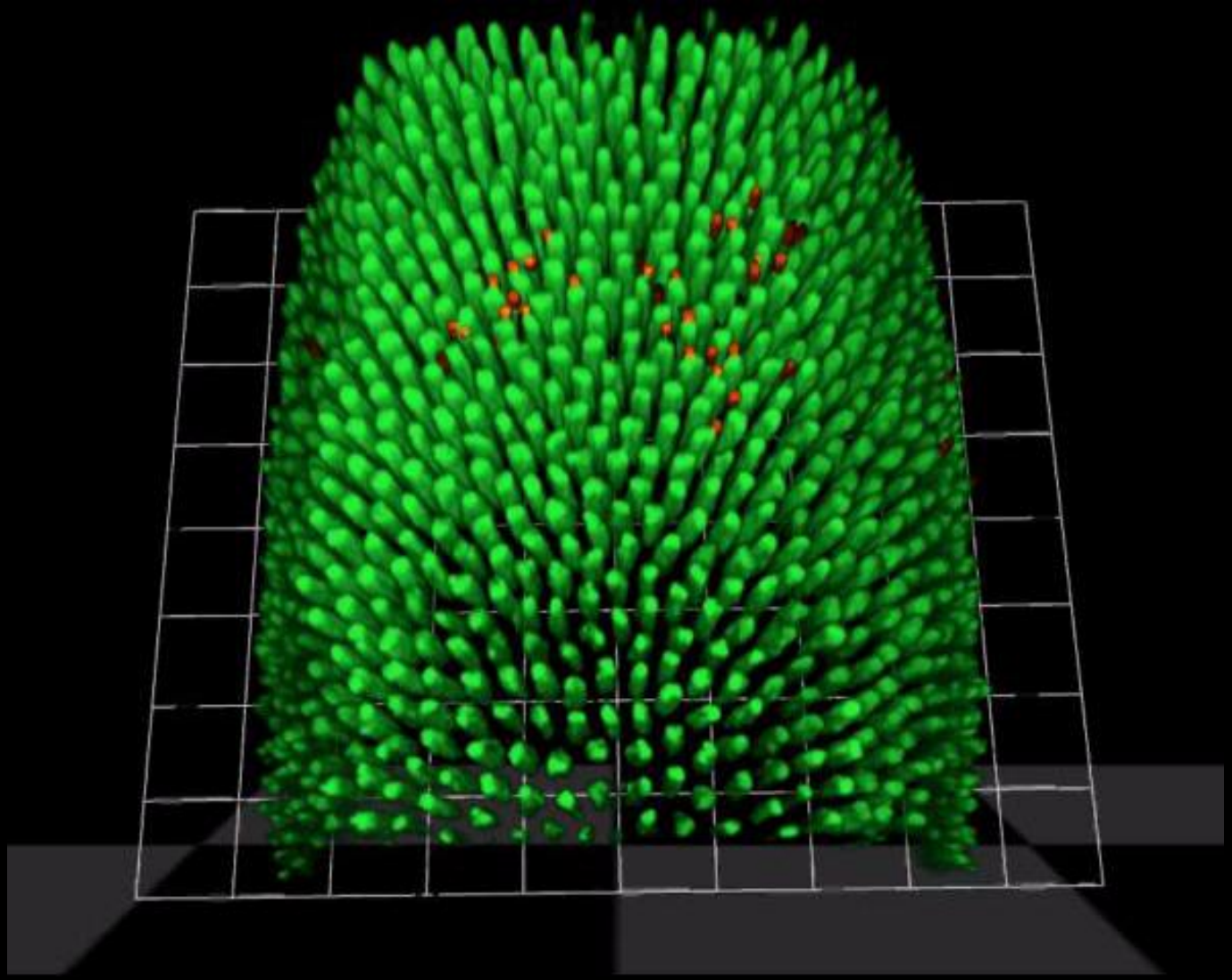
Myosin II accumulates in a network of interconnected spots on the apical surface of constricting cells

Changes in apical cell diameters drive furrow formation



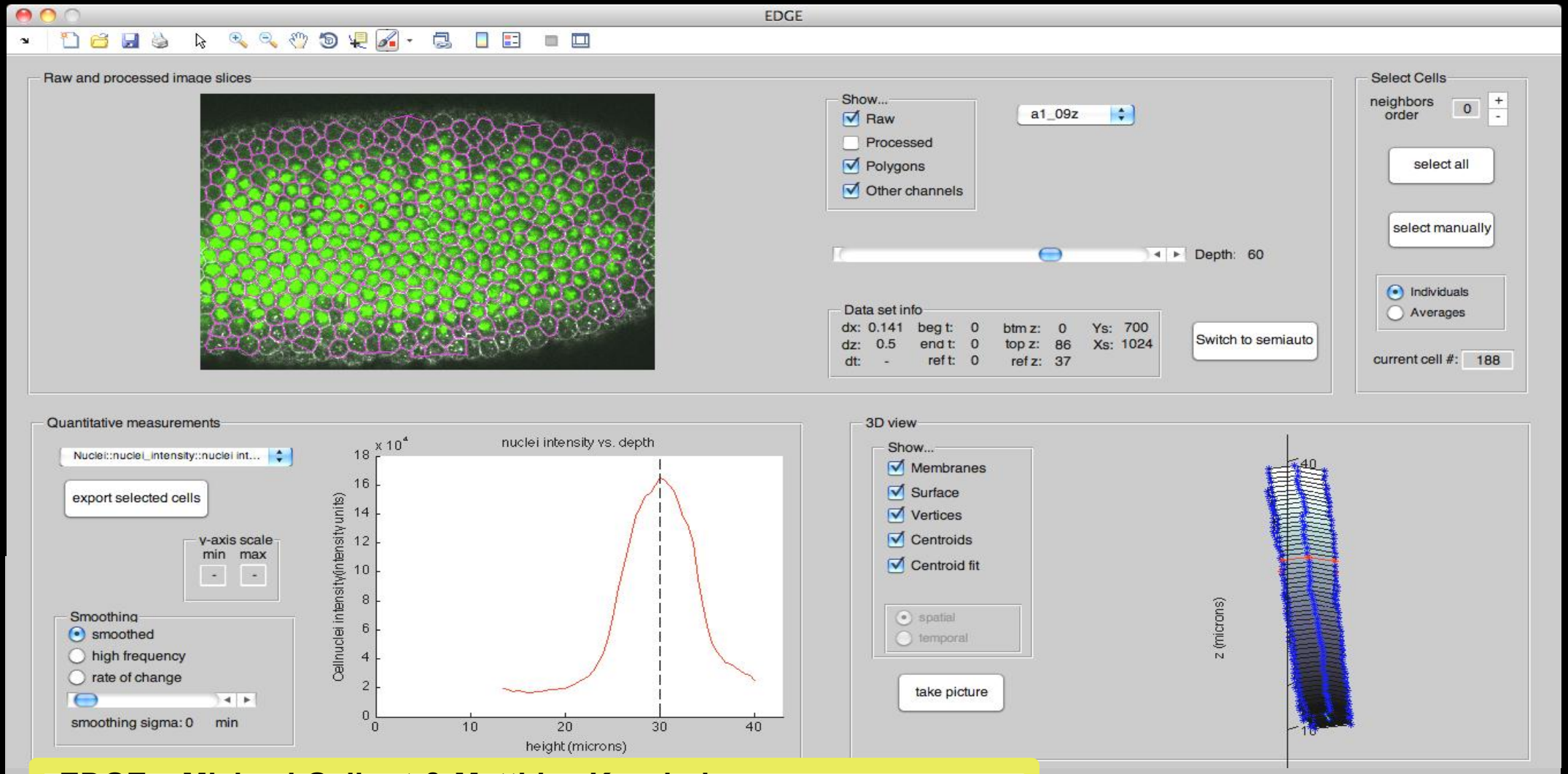
Membrane-GFP (Spider)

Testing cytoplasmic properties by injection of biologically inert fluorescent beads



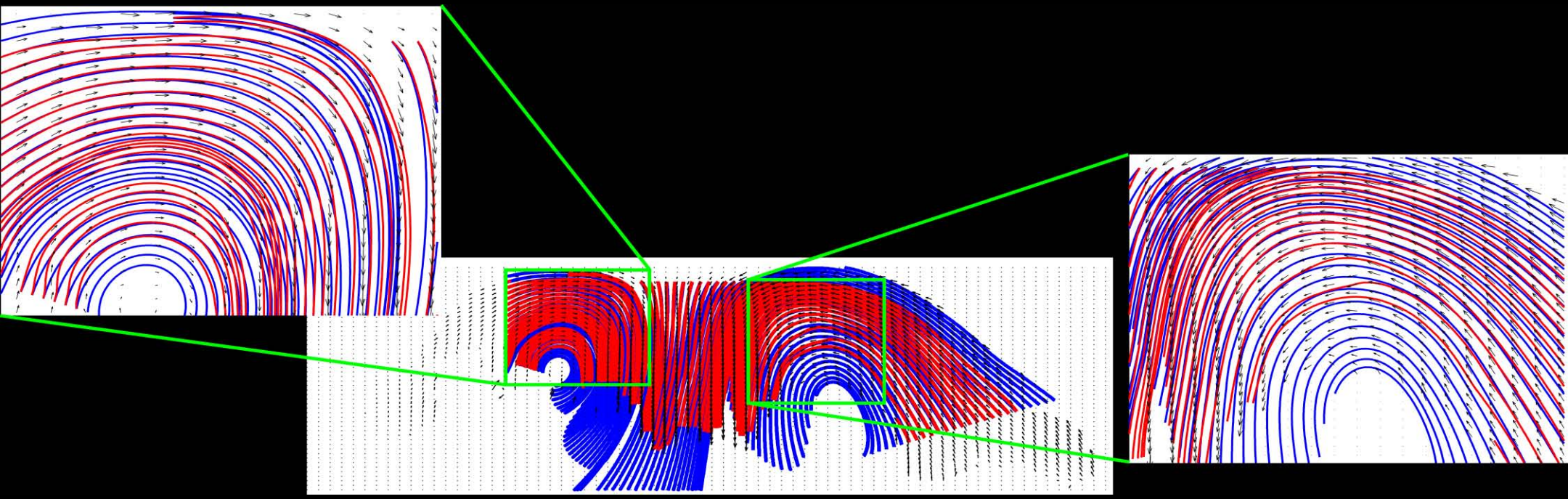
Bing He, Konstantin Doubrovinsky, Oleg Polyakov

Embryo Development Geometry Explorer (EDGE 1)



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!)

Molecular Biology Department

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Lewis Sigler Institute
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Thomas Gregor

William Bialek

Matthias Kashube

Michael Gelbart

Oleg Polyakov

Konstantin Doubovinski

Data and slides from labs
supported by NICHD

Anna-Katerina Hadjantonakis
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David McClay
Duke University

Eric Davidson
Cal Tech

Rebecca Burdine
Princeton University

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