



BENJAMIN R. PLUMRIDGE
DEPARTMENT OF MATHEMATICS
WEST CHESTER UNIVERSITY

DEVELOPMENT OF A MODEL OF DORSAL CLOSURE

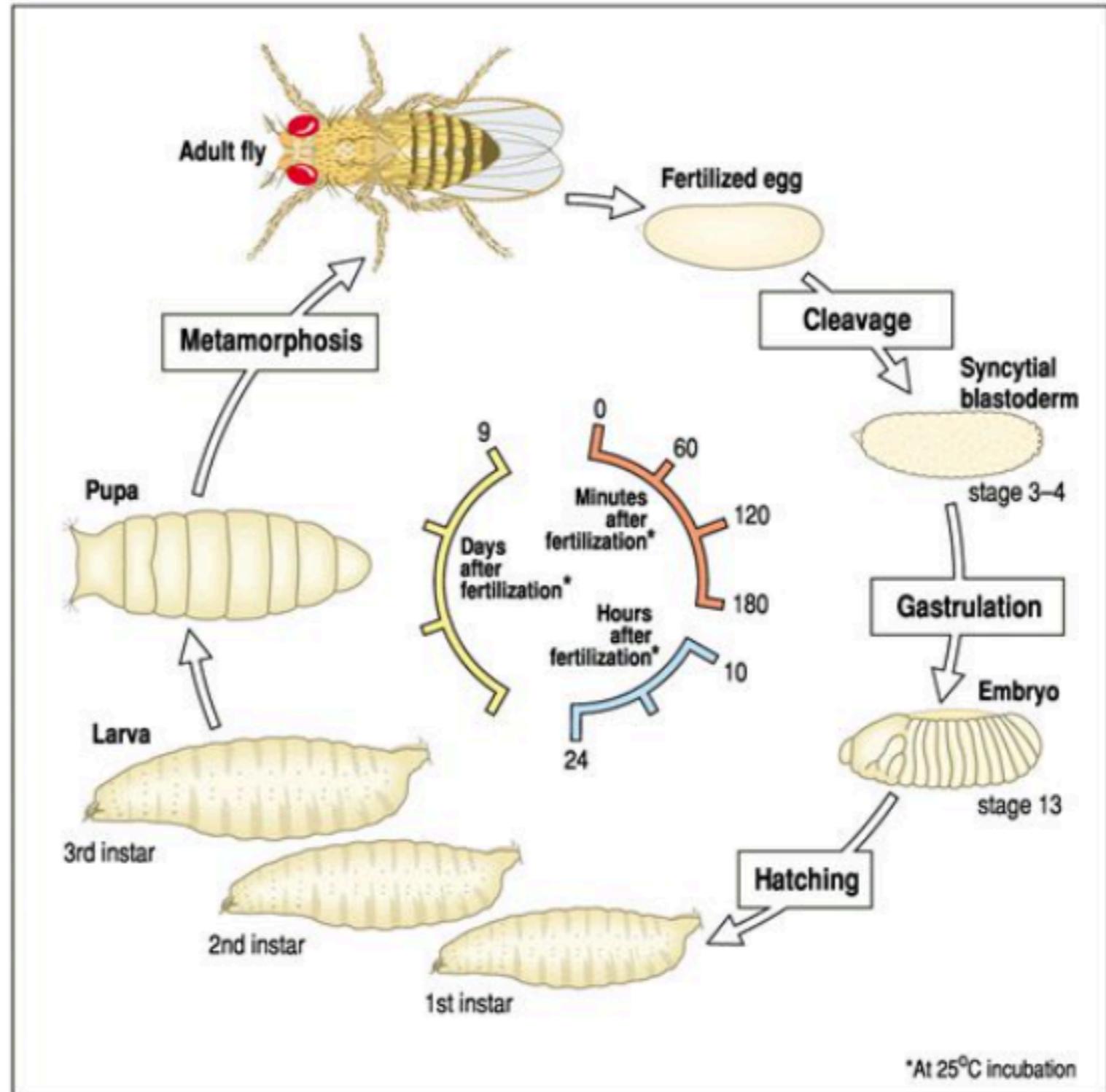
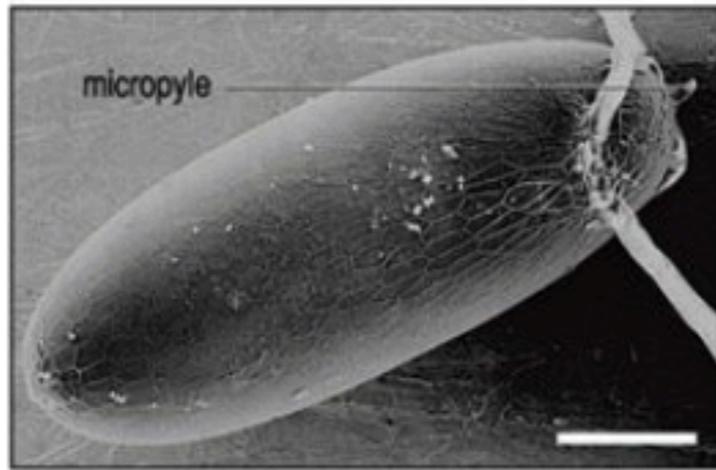
OUTLINE

- What is dorsal closure?
- Research goals
- Model development
- Simulation results and testing
- Ongoing work

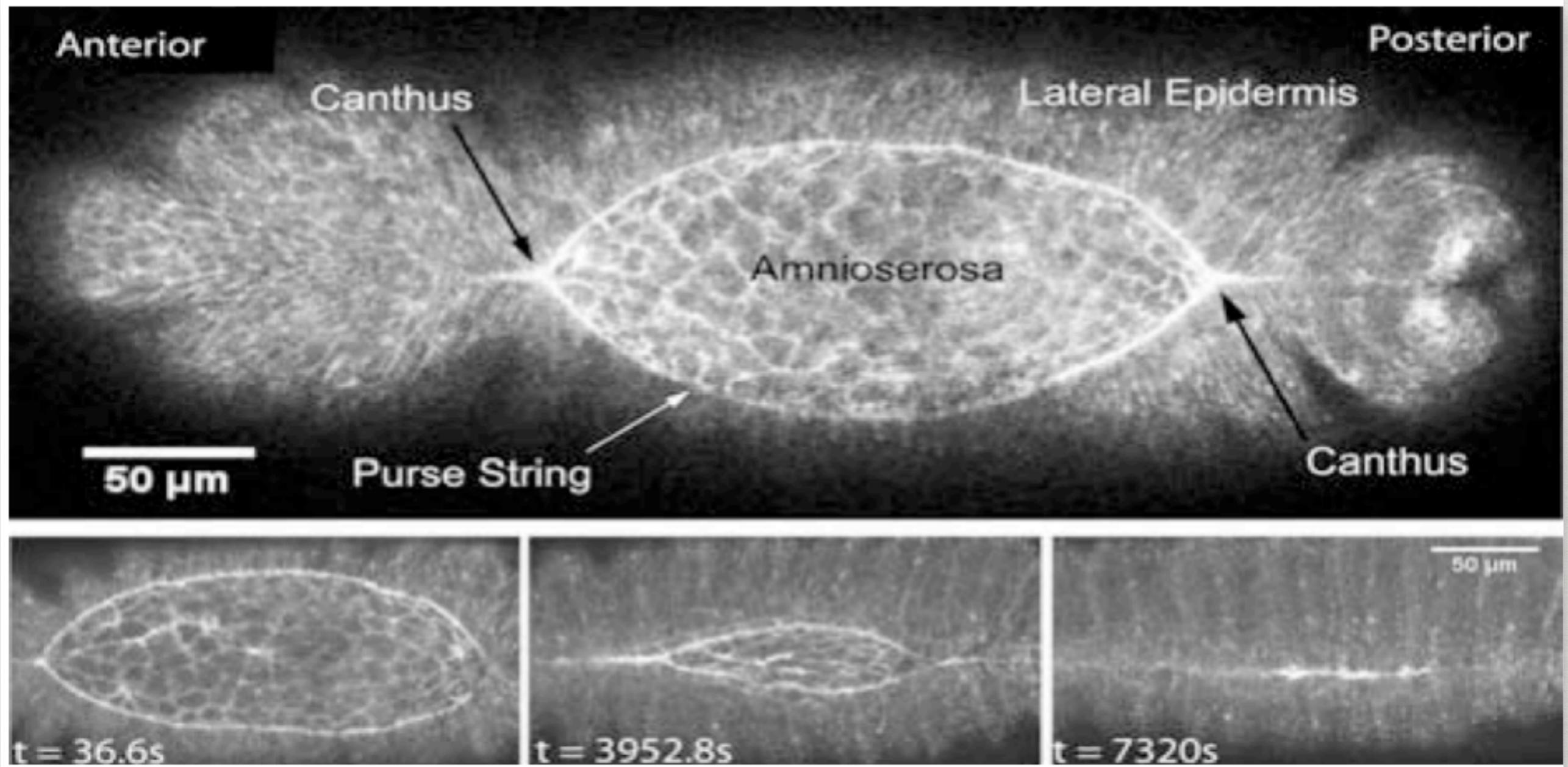
DROSOPHILA MORPHOGENESIS

- Morphogenesis- process causing an organism to develop its shape
- Stage of embryogenesis
- Wound-like region (amnioserosa) undergoes a closure process
- Apical constriction

DROSOPHILA MORPHOGENESIS

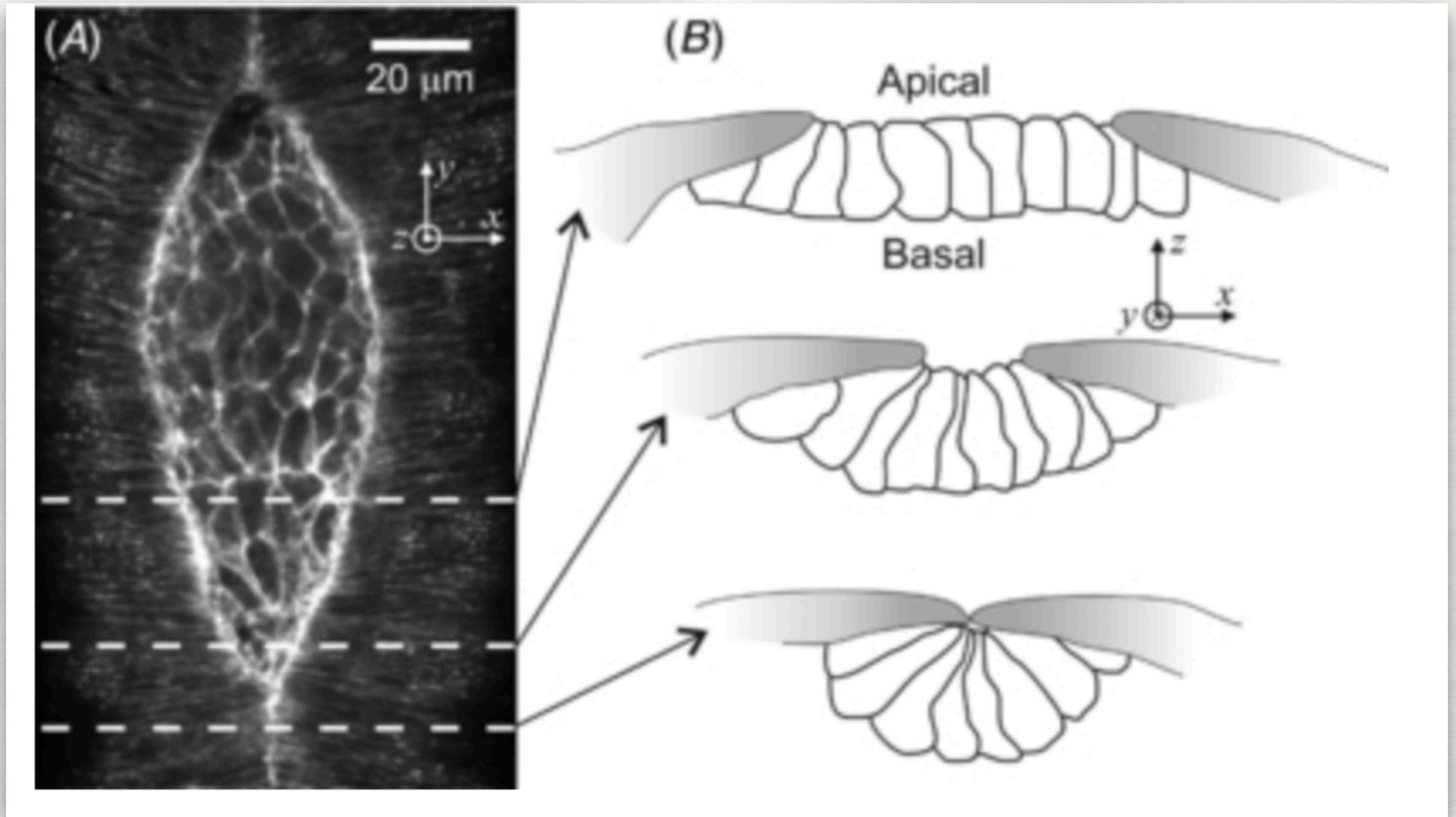


AMNIOSEROSA



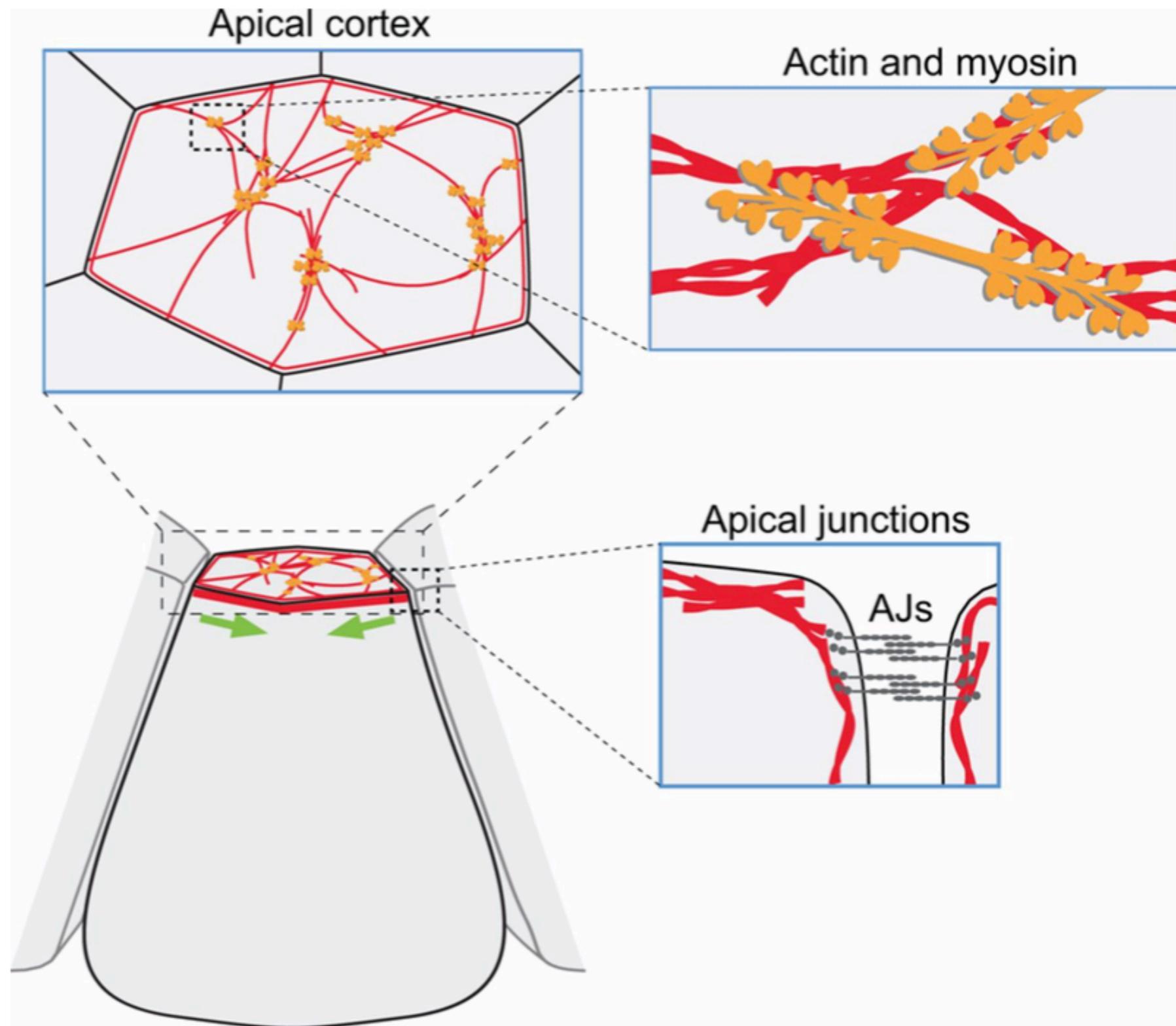
¹²Sokolow et. al, 2012

APICAL CONSTRICTION



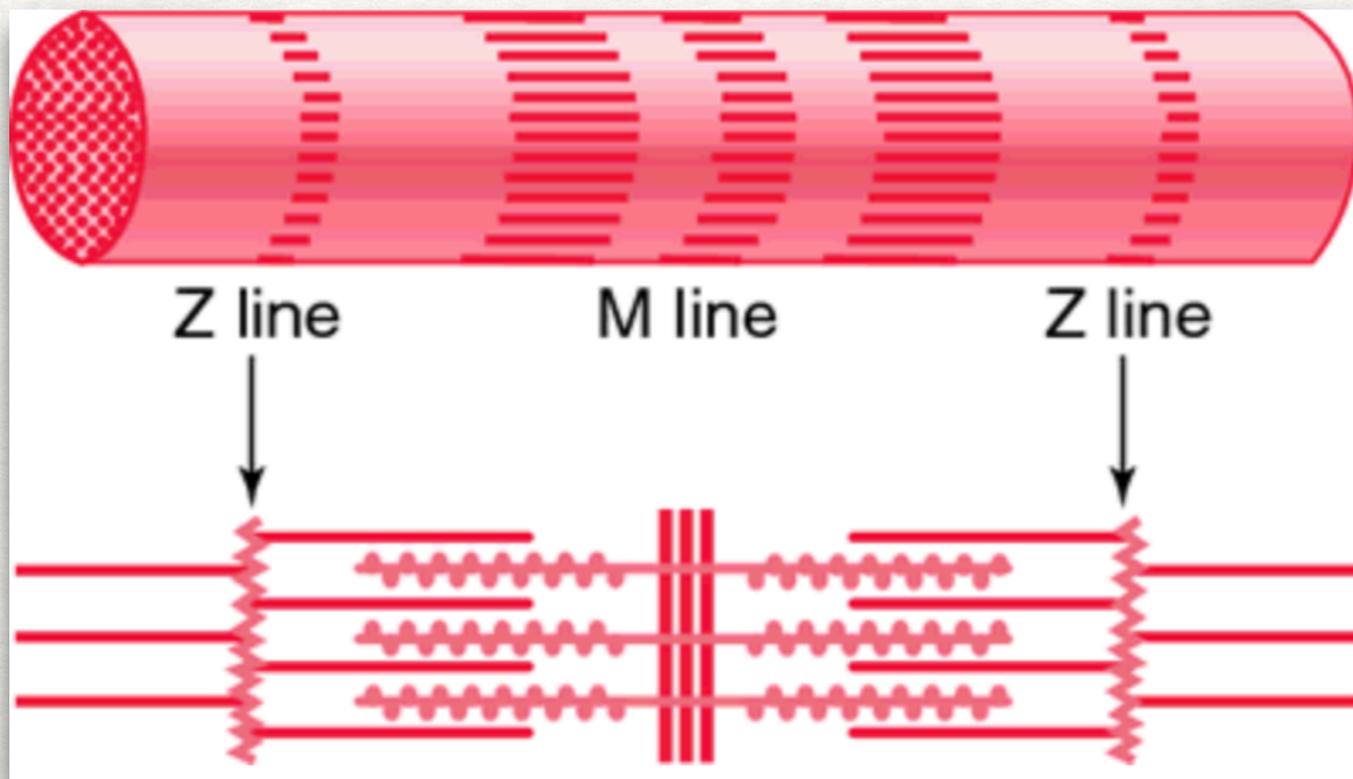
⁵Hutson and Xiaoyan, 2008

APICAL CONSTRICTION



SARCOMERES

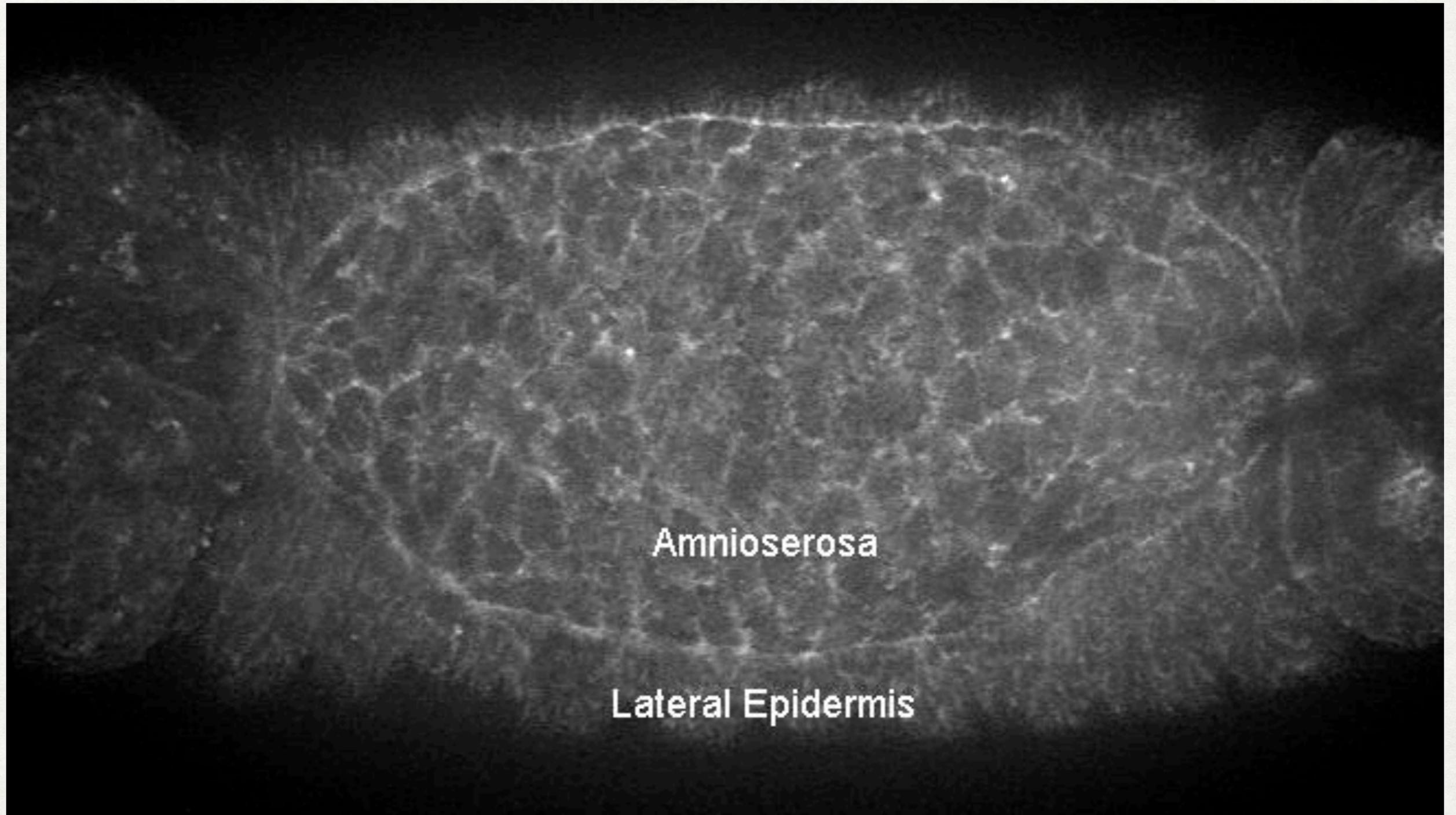
- Actin filaments
 - Essential for movement in cells
 - Associate with other proteins to form stable structures
 - Contractile apparatus of muscle
- Myosin
 - Actin-dependent motor protein
 - Produce mechanical energy in a cell



DORSAL CLOSURE

- Offers insights in understanding wound healing and morphogenetic processes
- Cell oscillations and other phenomenon
- Force producing biological elements (sarcomeres) drive the closure
- Process takes approximately 2.5 hours
- Can be separated into three stages: Early phase, Slow phase, and Fast phase

MOVIE



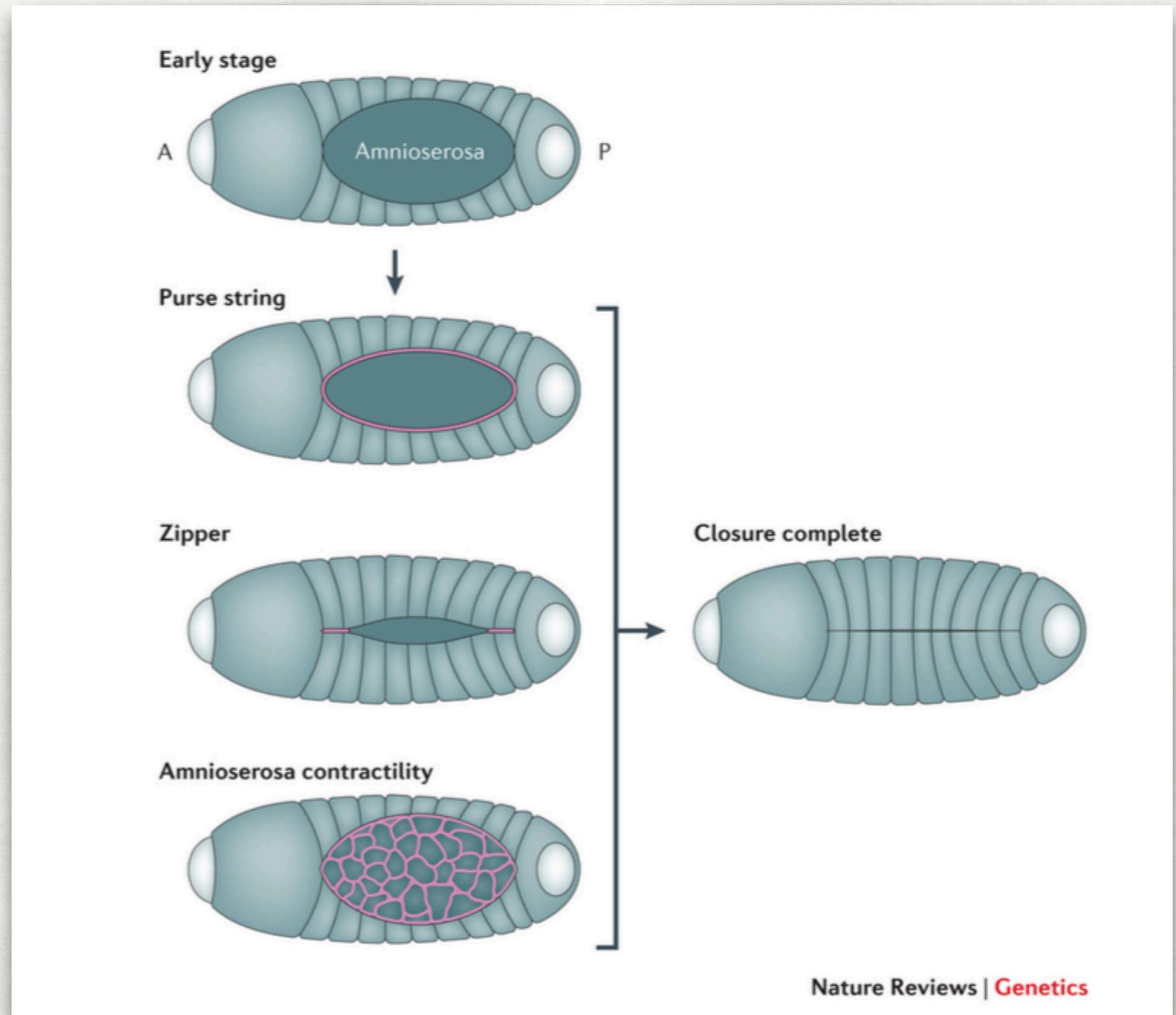
Provided by U. Serdar Tulu, Ph.D.

RESEARCH GOALS

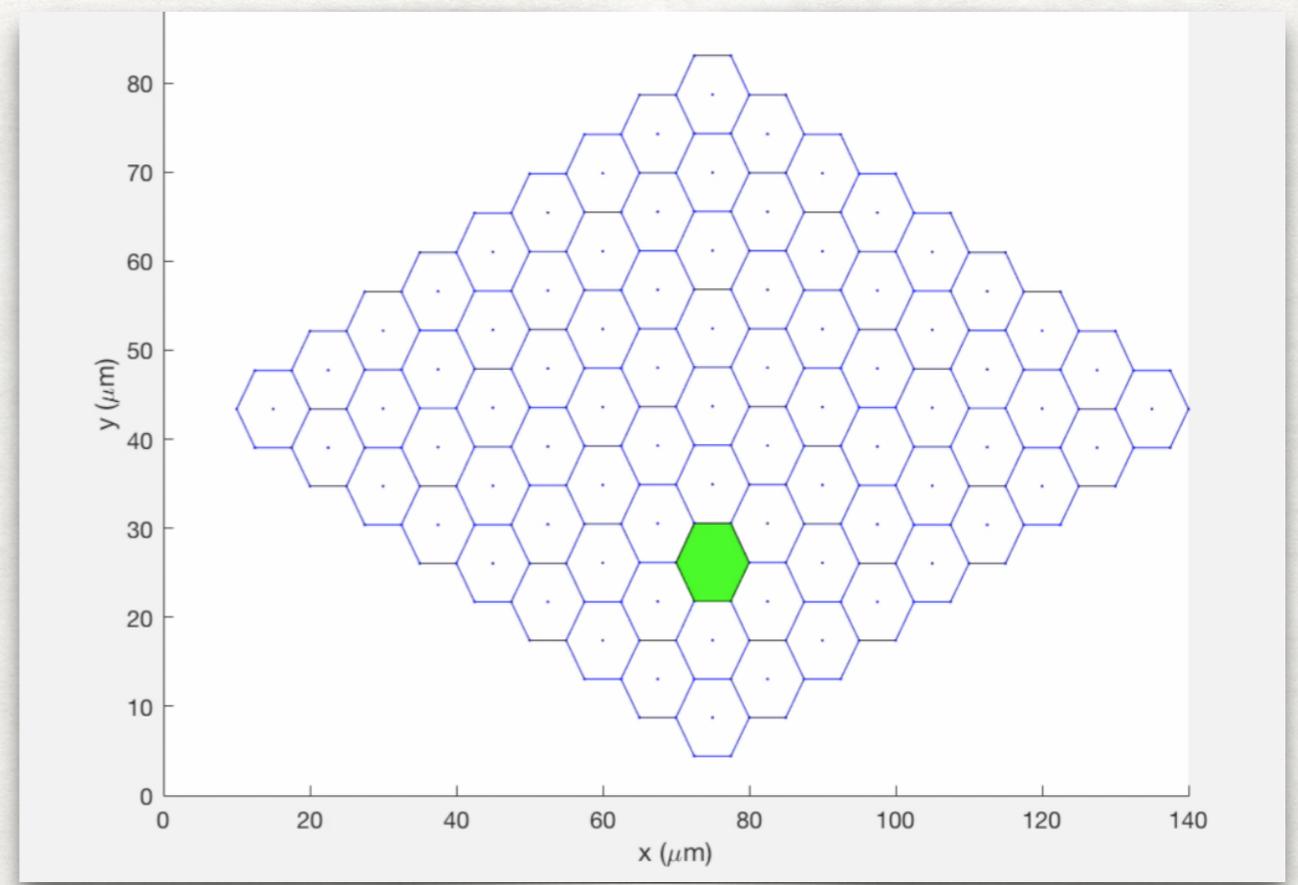
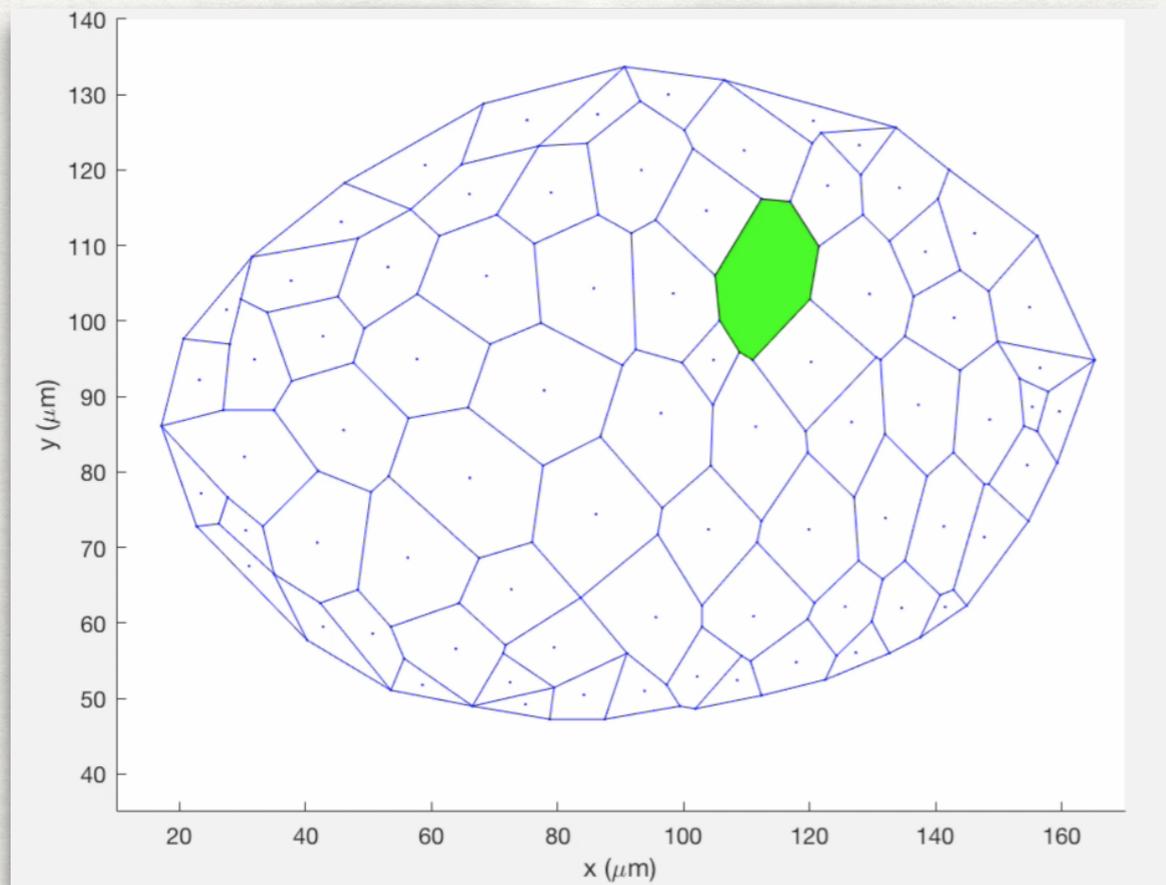
- develop a mechanical model of dorsal closure, testing various force equations
- test different cell geometries
- produce simulations that exhibit realistic behavior
- perform analysis on various aspects of the model, based on experimental findings

MECHANISMS OF DORSAL CLOSURE

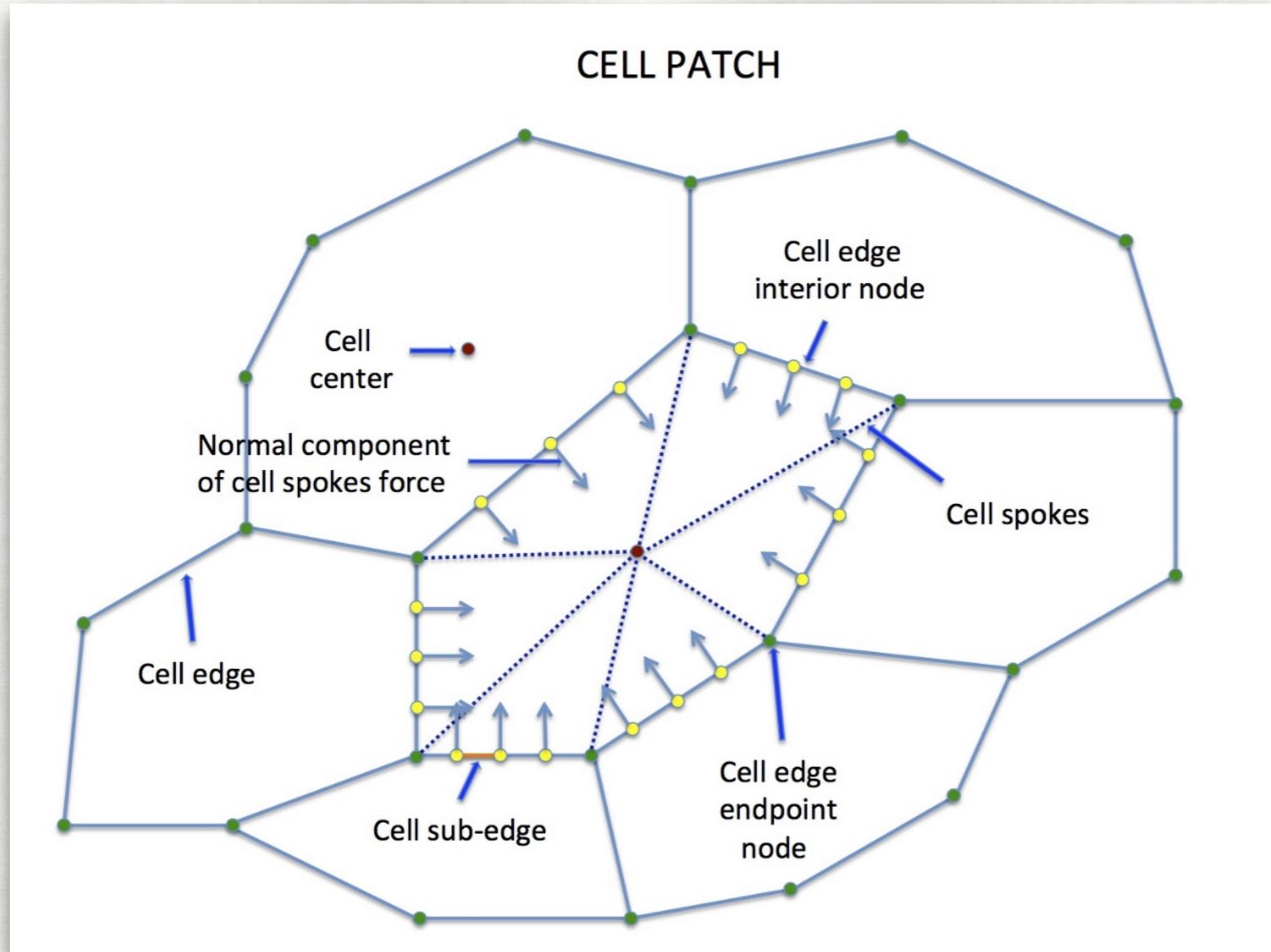
- Purse string or actin cable
- Zippering
- Amnioserosa contractility
- Lateral Epidermis



GEOMETRY



GEOMETRY



³Aristotelous, 2016

EQUATIONS

$$f_{i,j} = \underbrace{\mu (l_{i,j} - l_{0i,j})}_{\text{elastic}} + \underbrace{\beta m_{i,j}}_{\text{contractile}}$$

(Force on an edge)

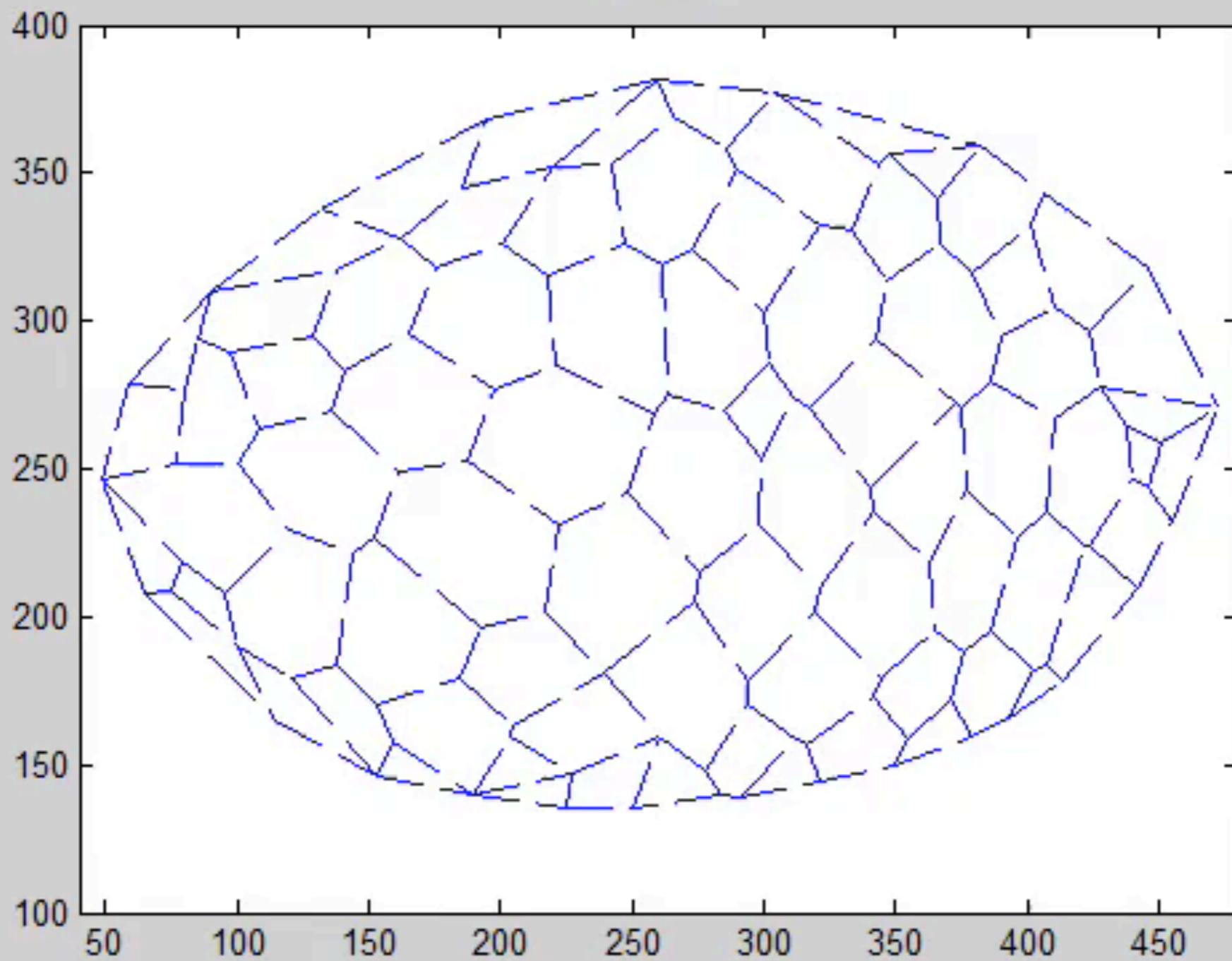
- elastic term is applied to all edges and spokes
- Contractile term is only applied to spokes

$$\eta \frac{d\vec{x}_i}{dt} = \vec{f}_i \quad \text{where } \vec{f}_i = \sum_j f_{i,j} = \frac{x_j - x_i}{|x_j - x_i|}$$

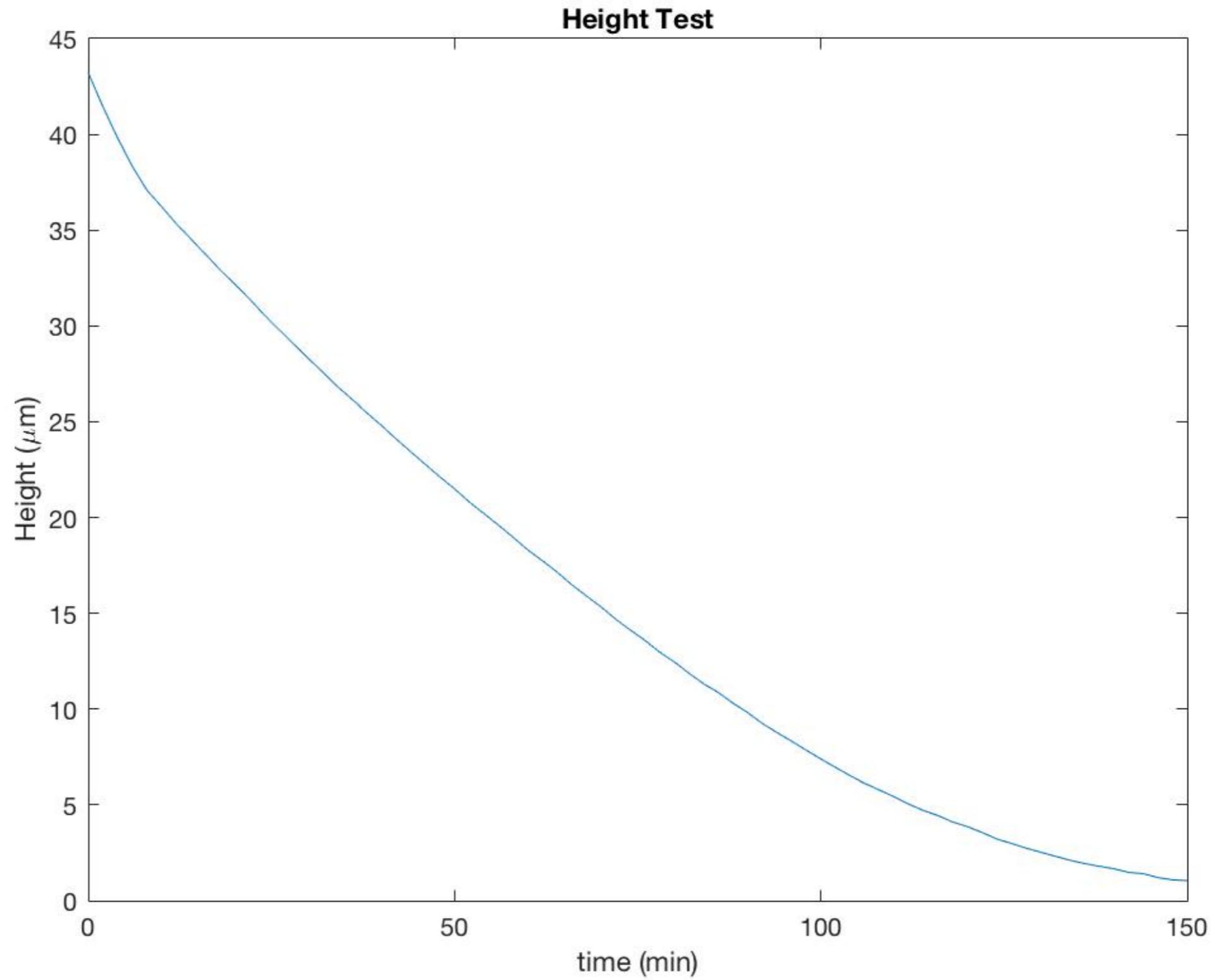
(Equation of motion)

SIMULATION

$t=0$



TESTING



MYOSIN AND SIGNALING EQUATIONS

$$\frac{dm_{k,j}}{dt} = k^+ s_k h_{kj} - k^- m_{k,j}$$

(myosin concentration)

$$k^- = k_1 e^{-k_2 f_{i,j}}$$

$$\frac{ds_k}{dt} = q - k_0 M_k$$

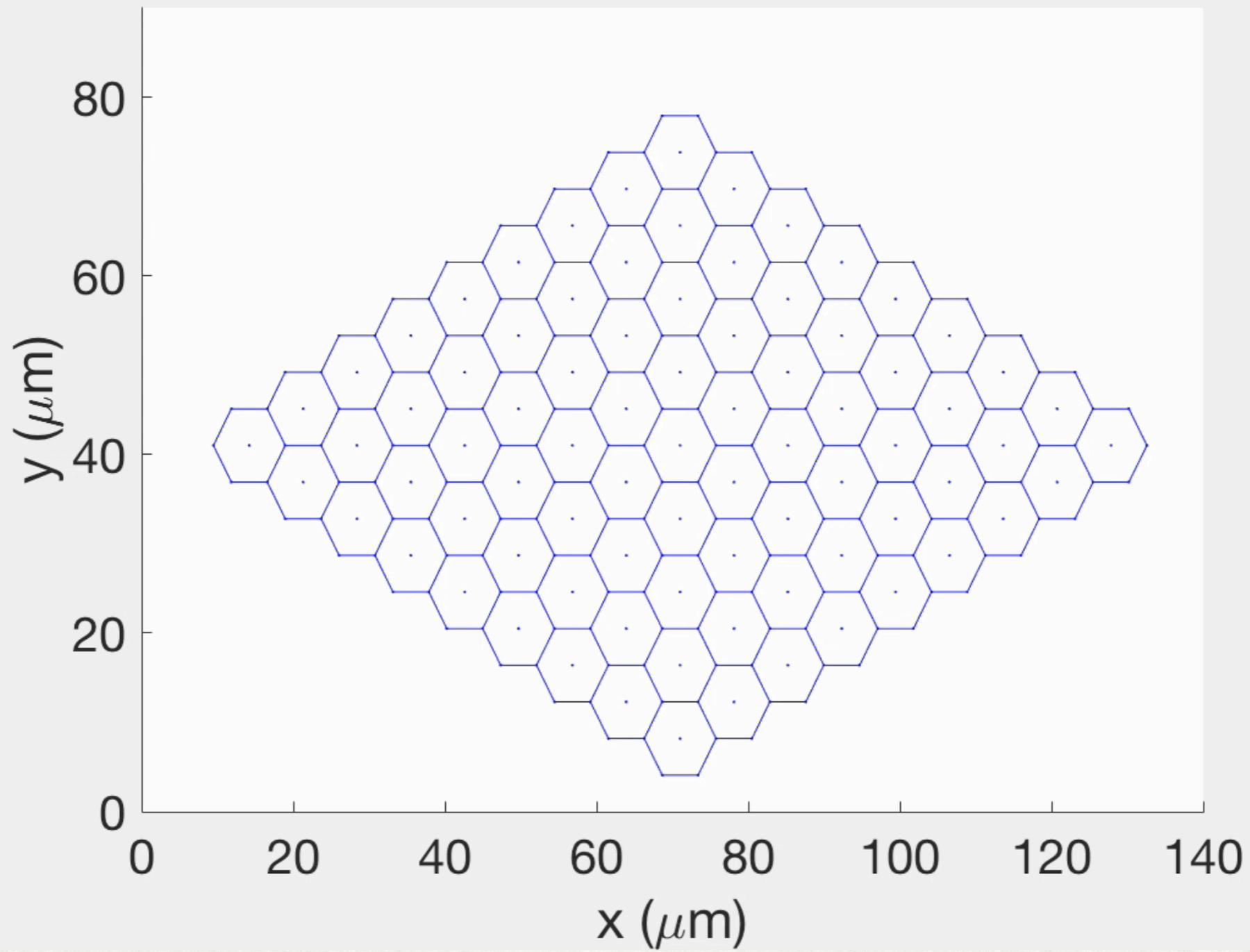
(signaling)

$$M_k = \sum_j m_{k,j}$$

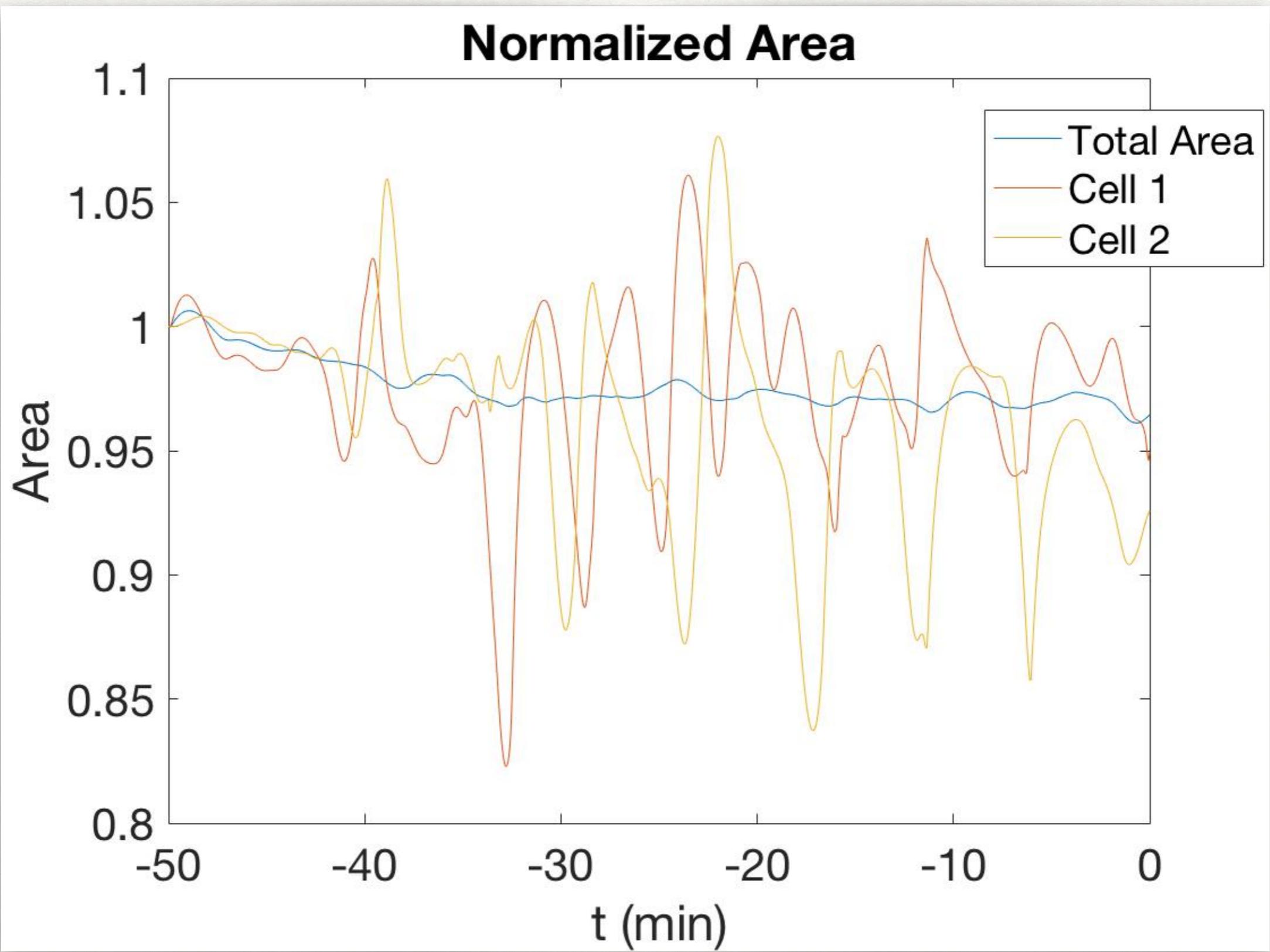
(myosin concentration in a cell)

SIMULATION

t=0

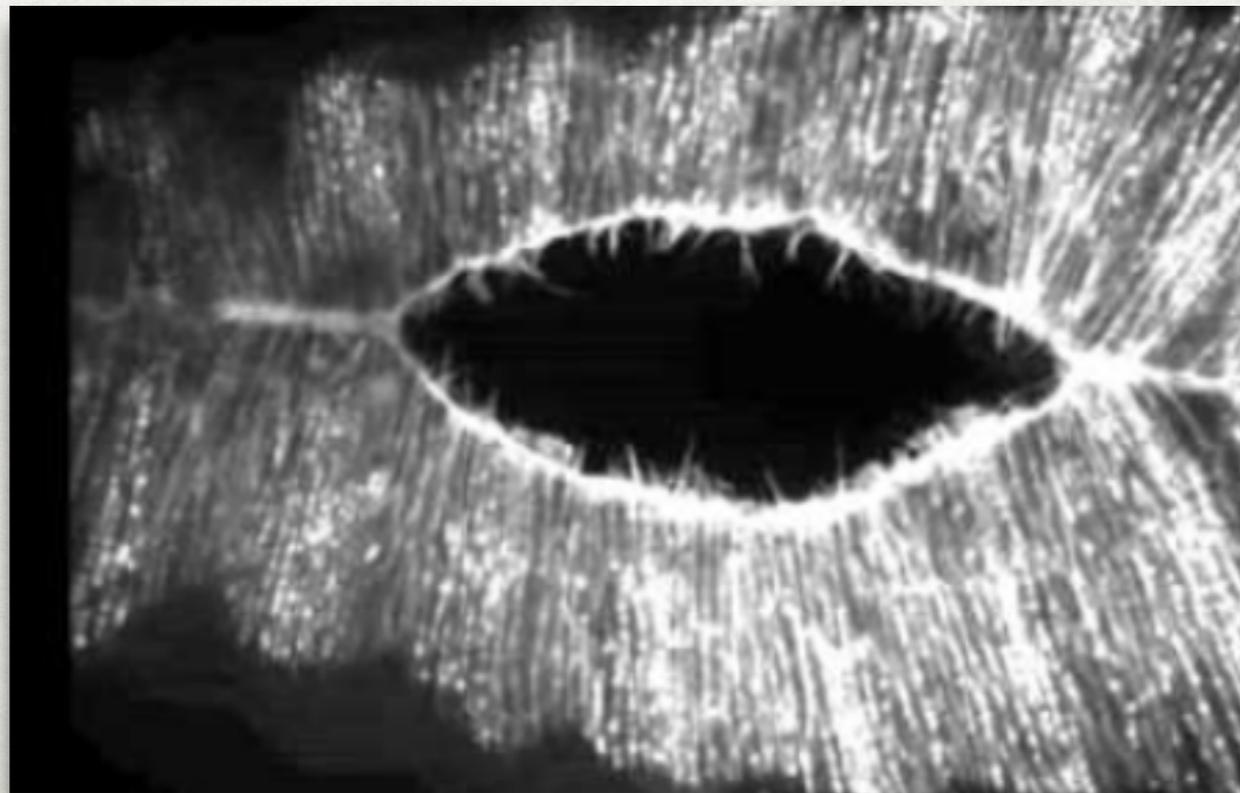


TESTING



ONGOING WORK

- Testing of lateral epidermis
- Testing of sub-edges
- Imitating cell ablation experiments
- Zippering →



³Aristotelous, 2016

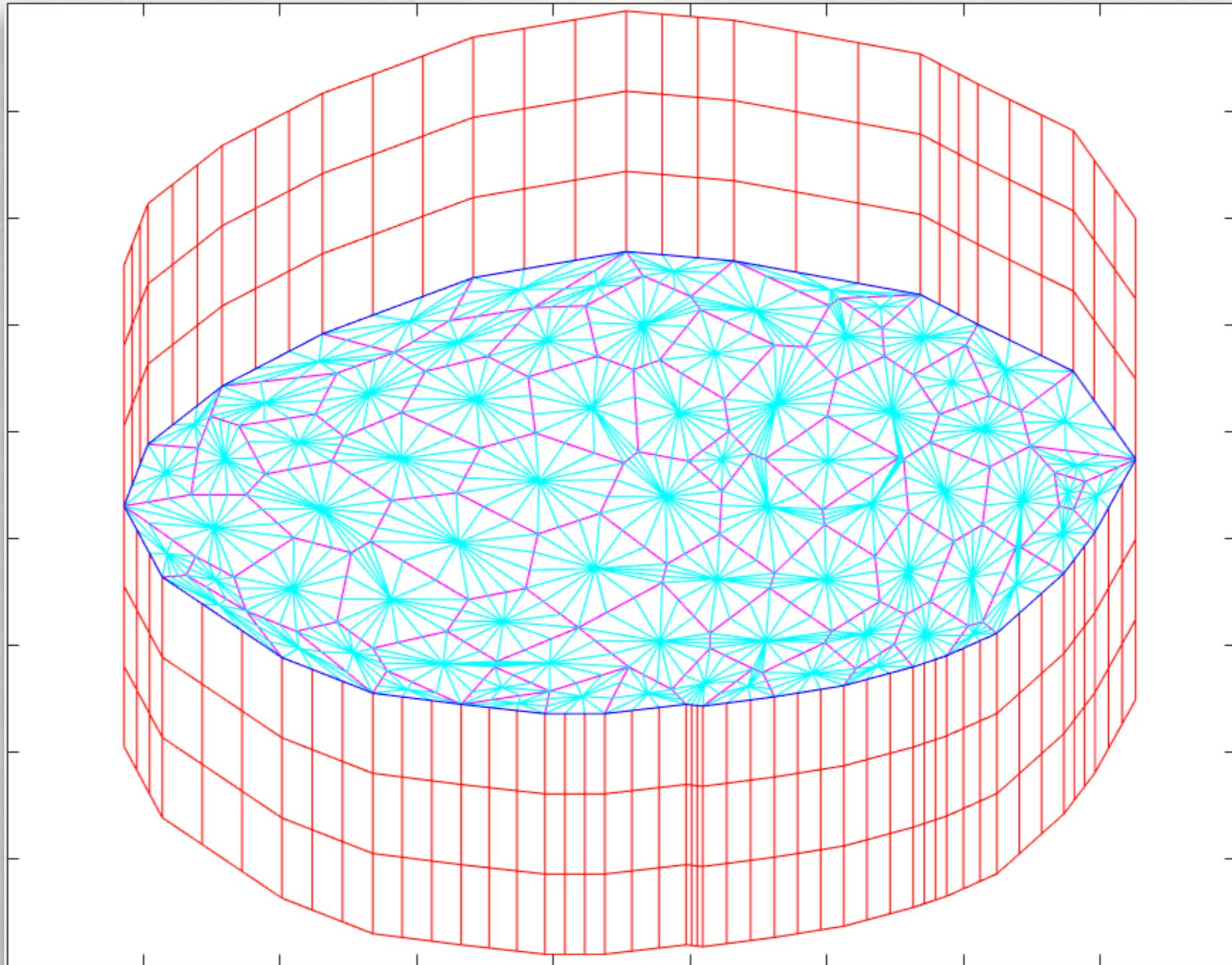
Lateral Epidermis

Sub-Edges

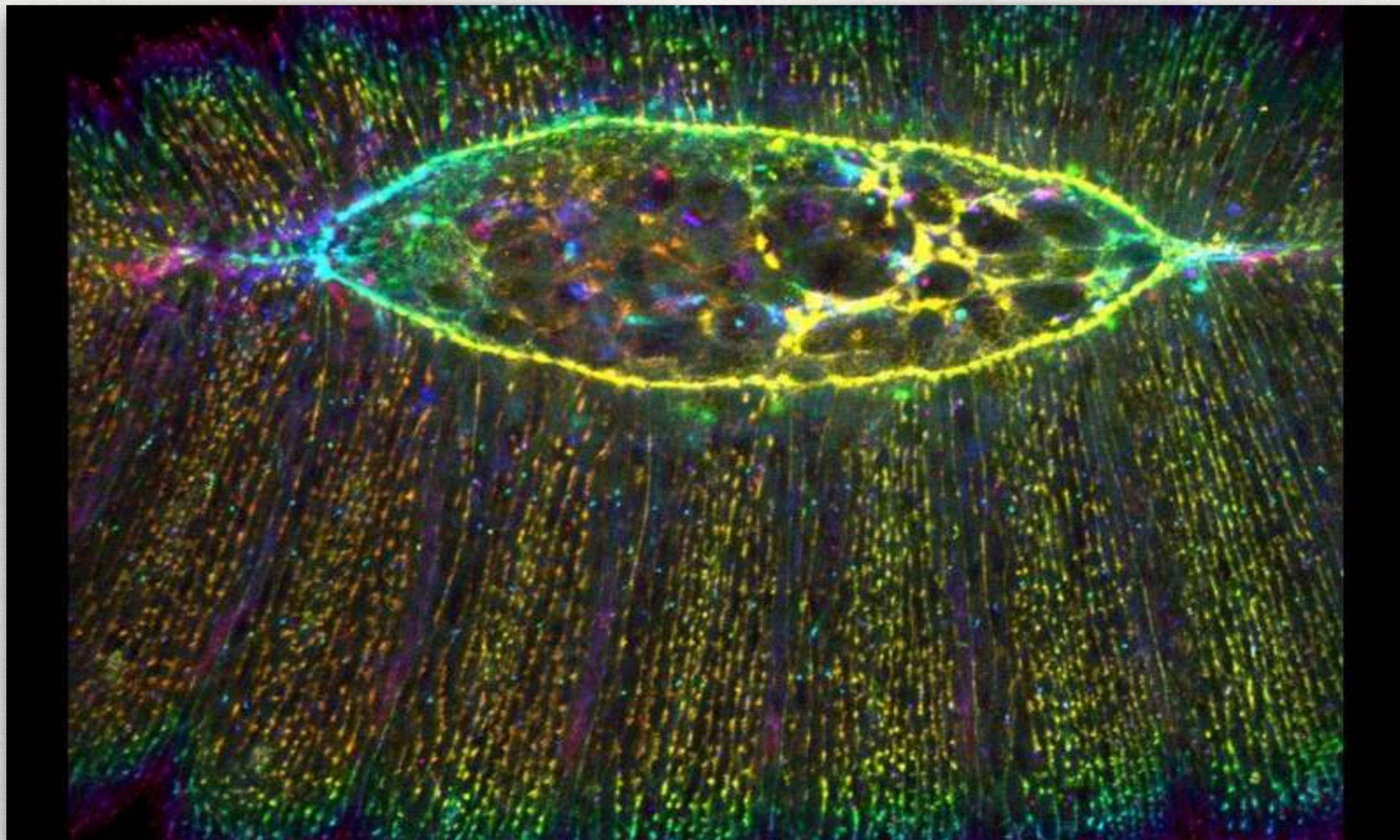
Spokes

Purse String

NEW GEOMETRY



THANK YOU!



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- Dr. Aristotelous
- Dr. Li
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