

# Intrinsic Chirality Properties of the *Xenopus* Egg Cortex and Left-Right Asymmetry

Presented in the Embryo Physics Course <http://www.embryophysics.org>  
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By

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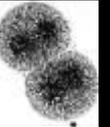
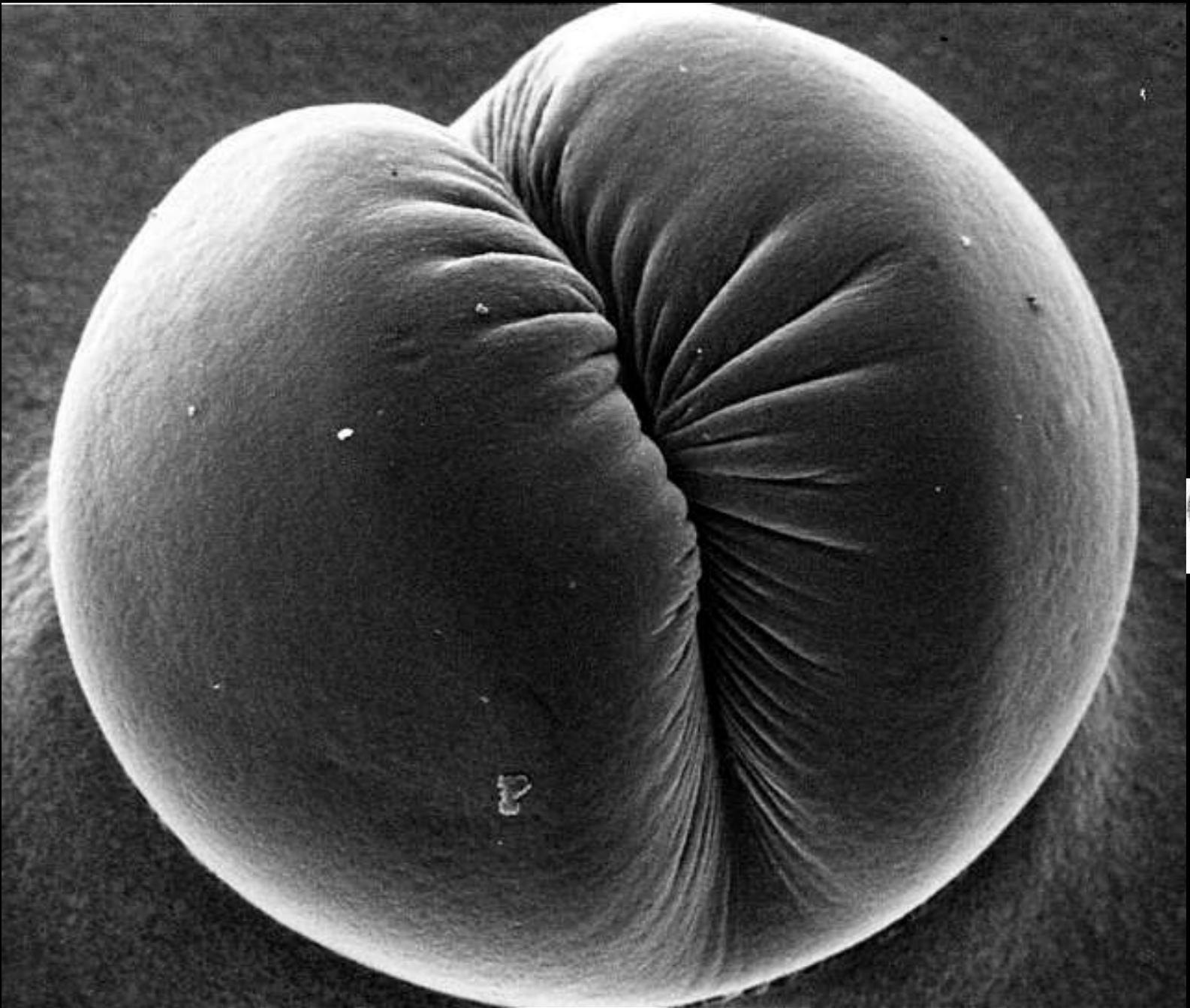


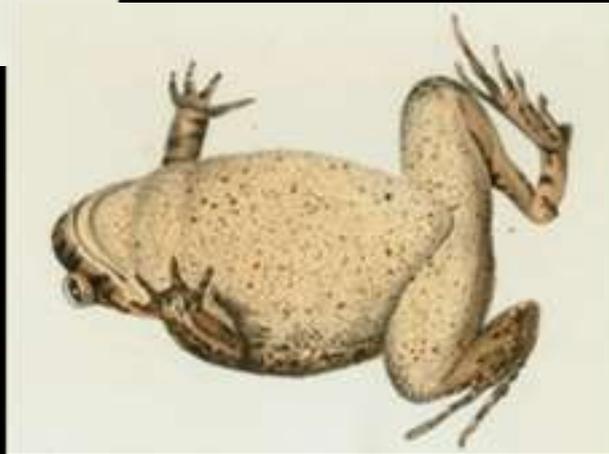
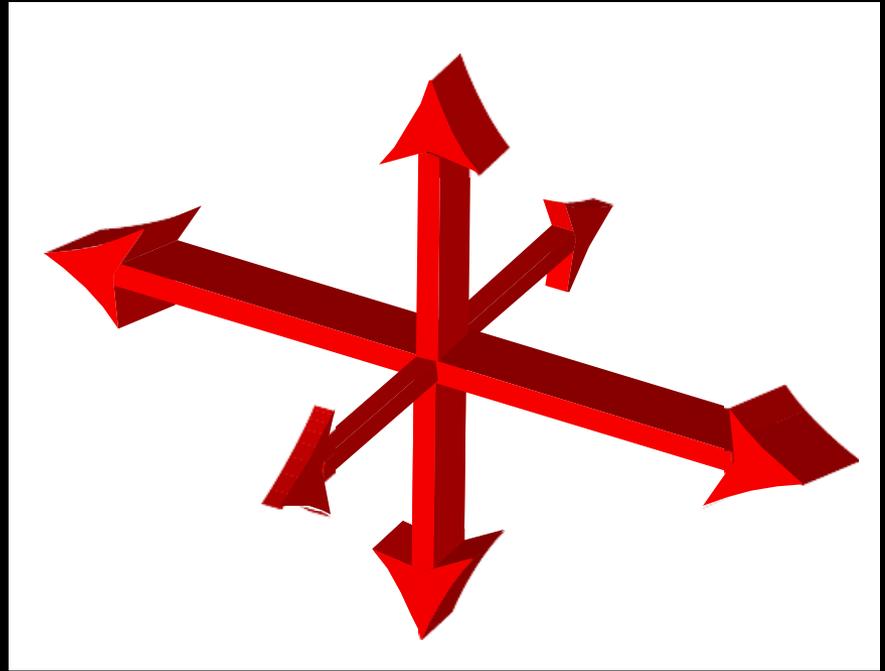
Intrinsic chirality of the *Xenopus*  
egg's actomyosin cortex--

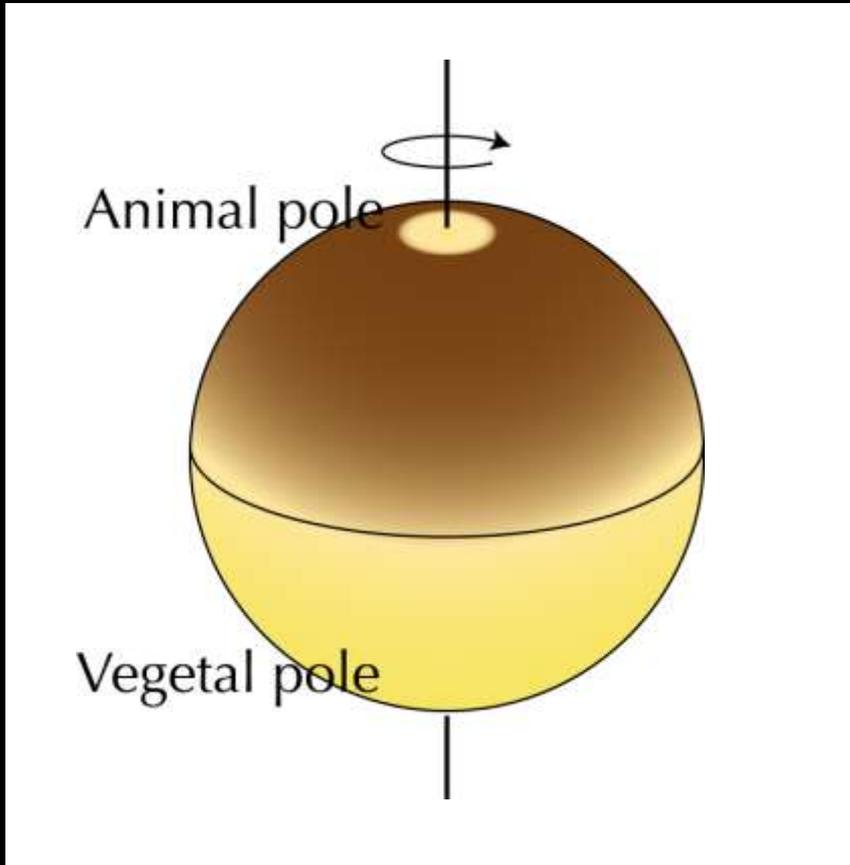
¿ cleavage-stage embryonic patterning?

¿ contractile ring organization &  
function during cytokinesis?

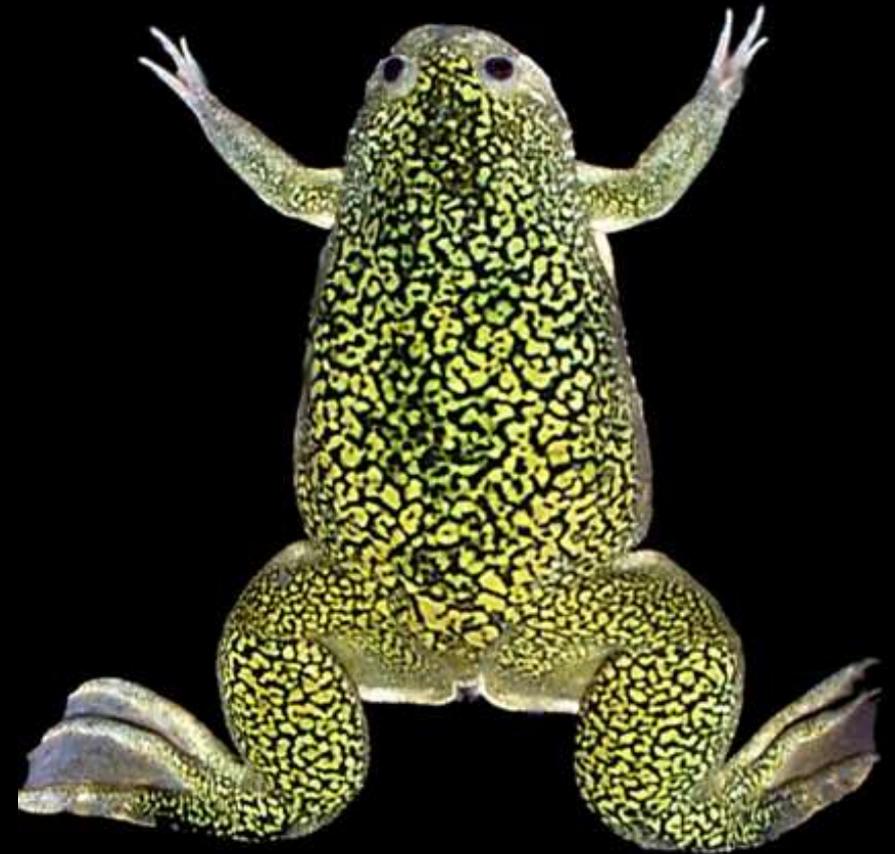
Mike Danilchik  
danilchi@ohsu.edu







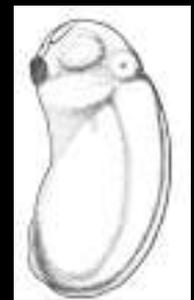
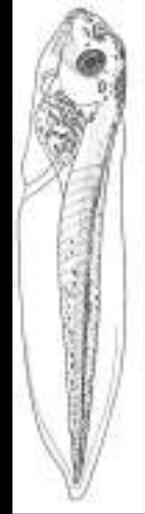
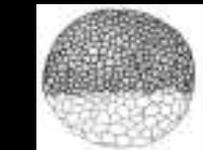
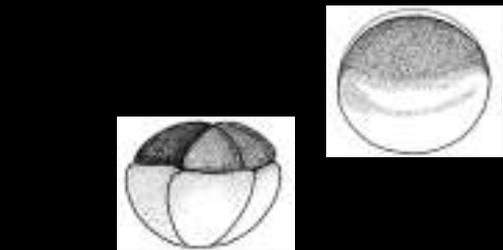
Unfertilized egg is radially symmetric and has only a single (cellular) axis ...



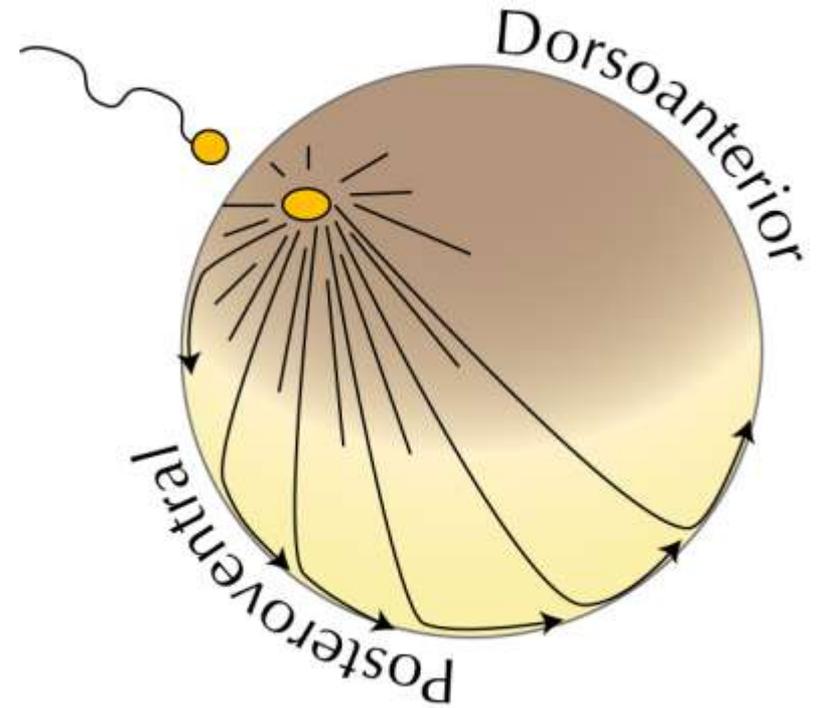
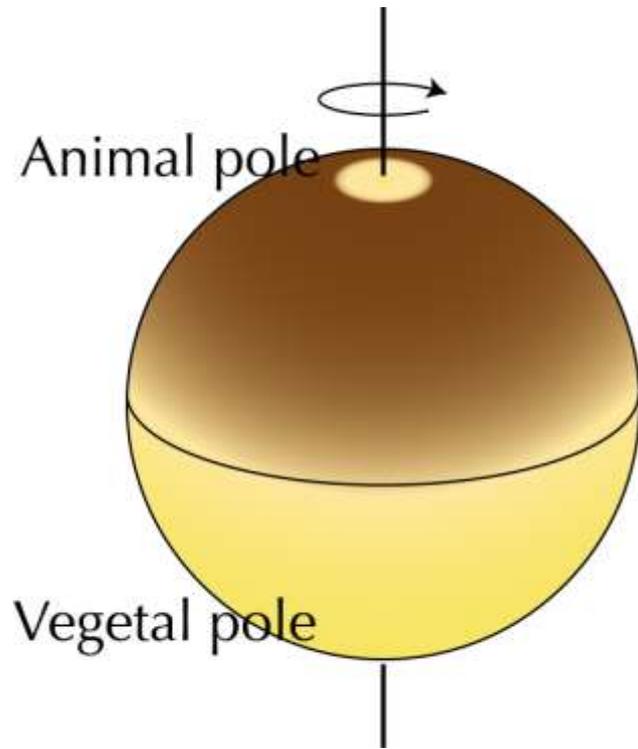
How does the more complex body plan arise?



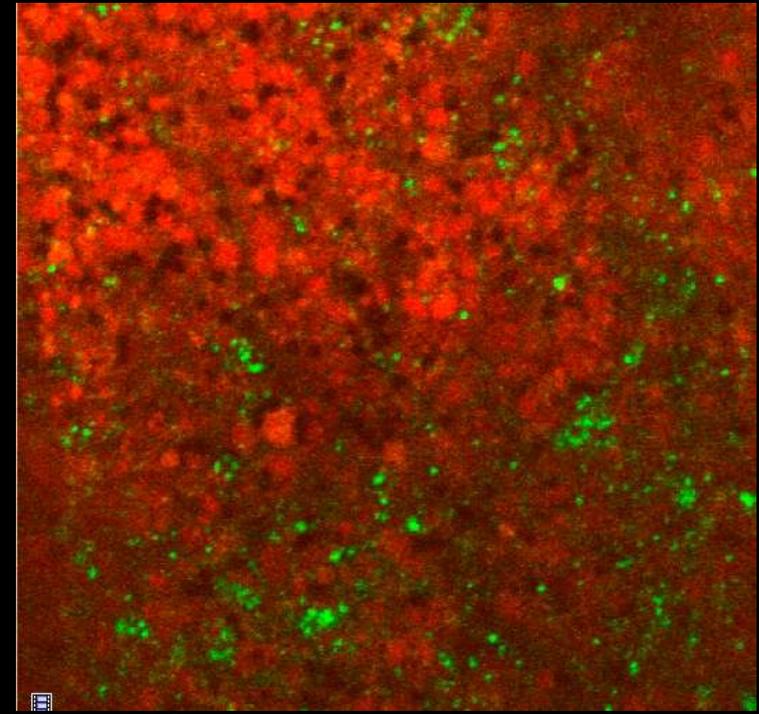
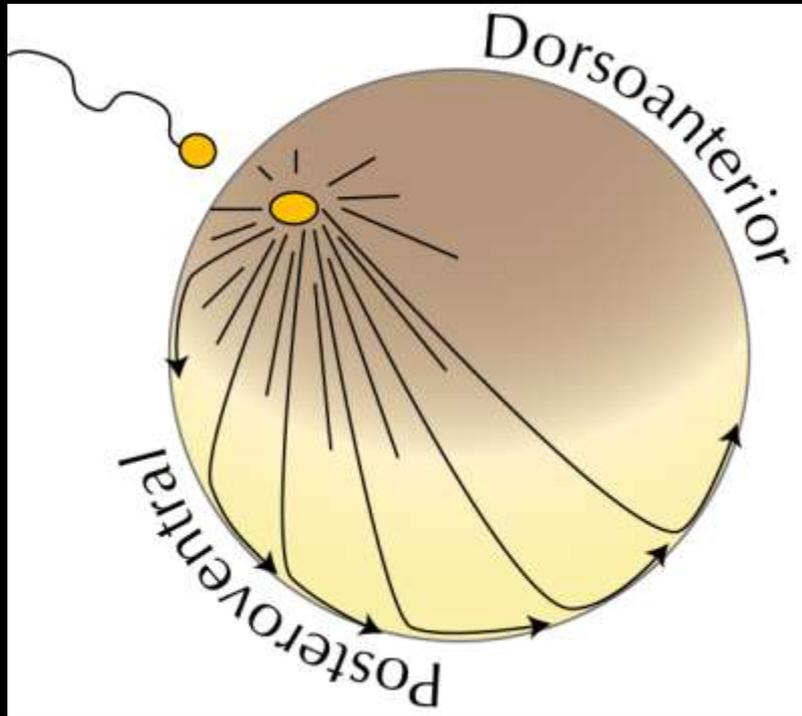
Play “movie1.mov”



Stage figs from Nieuwkoop & Faber (1956)

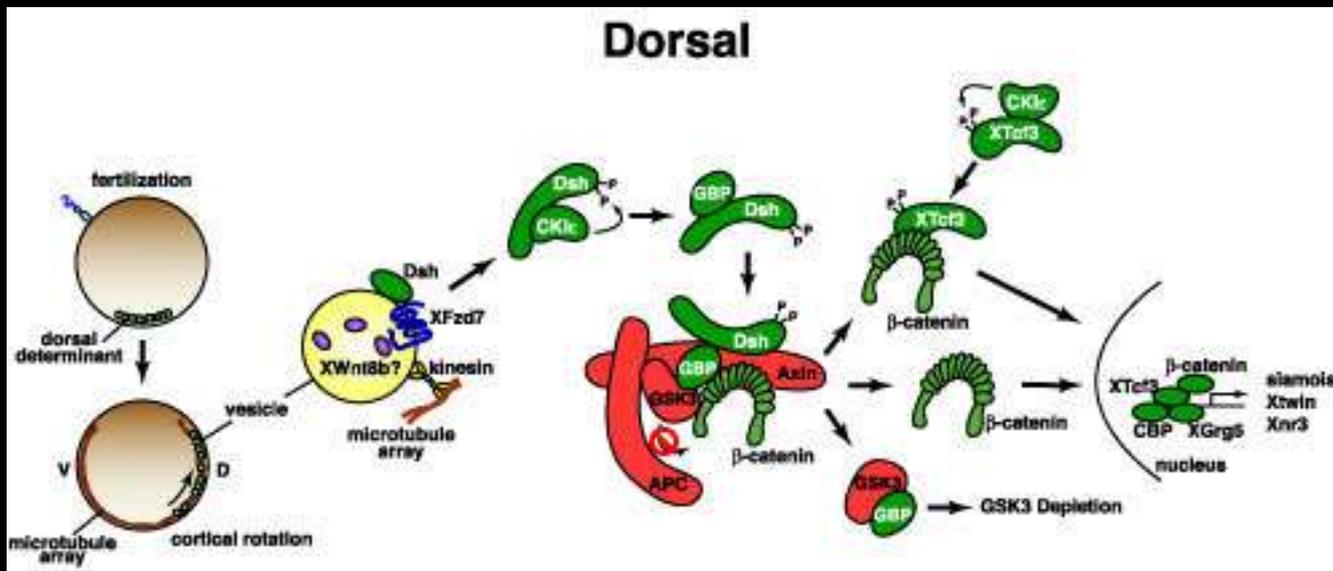


# Localization of maternal determinants is microtubule-dependent

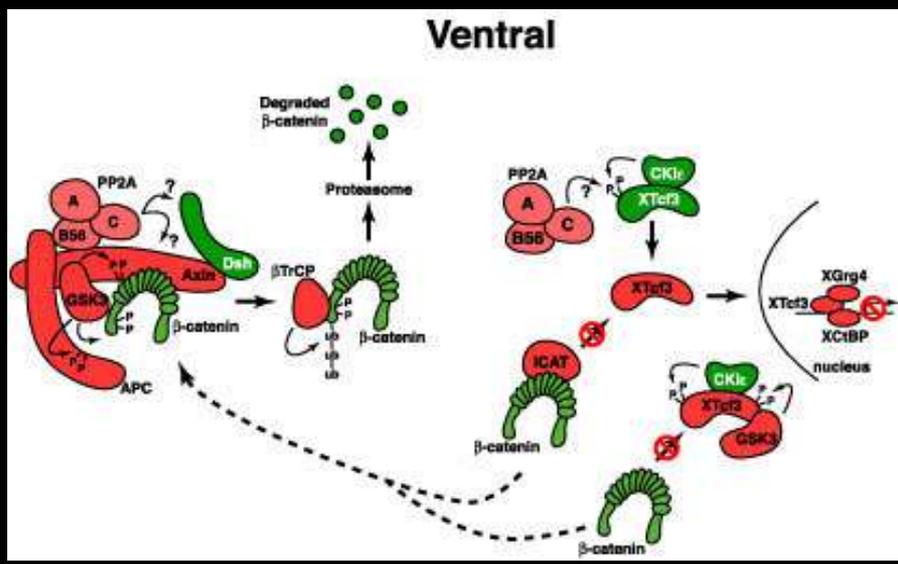
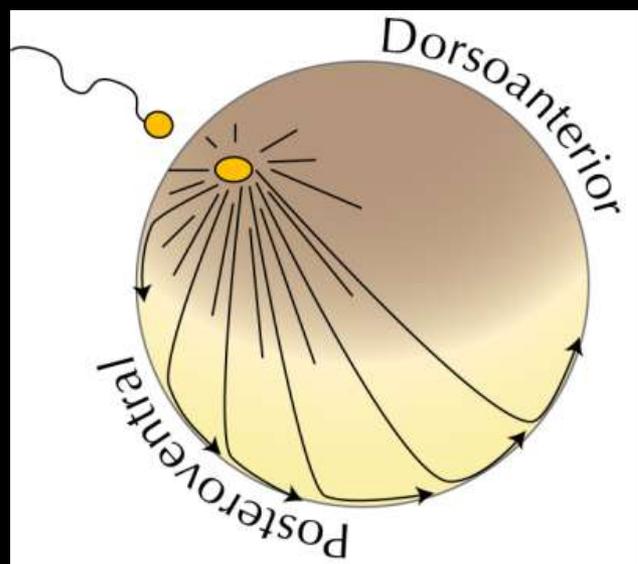
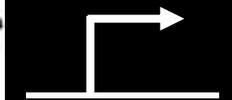


yolk GFP-kinesin Weaver & Kimelman 2003

Play "movieWK"

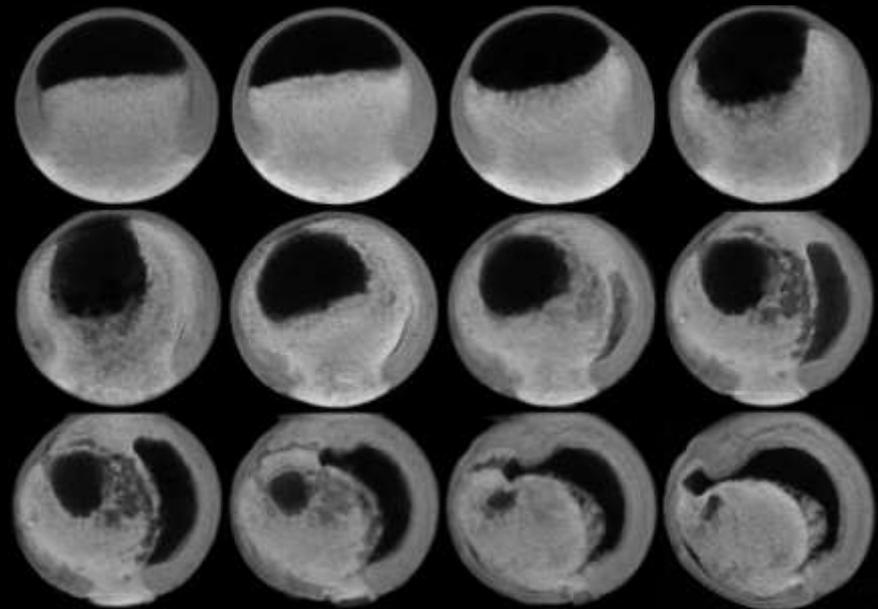
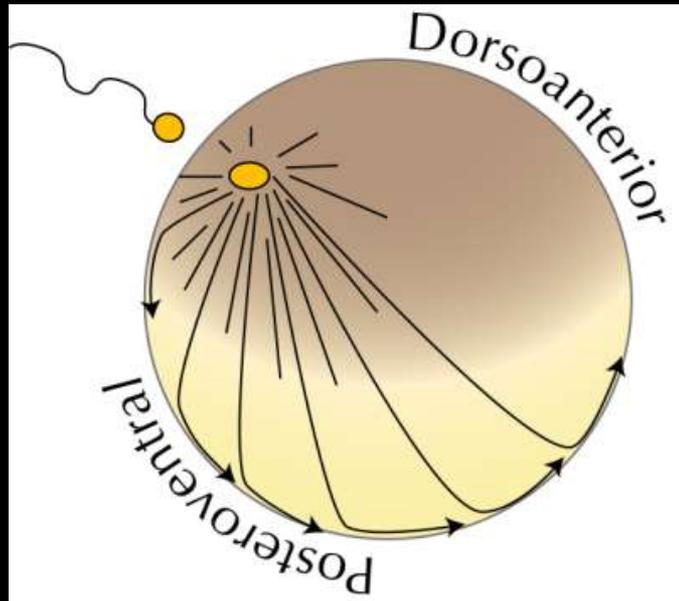


dorsal-specific genes



... so, in *Xenopus*, vegetal rotation specifies the dorsal-ventral axis...

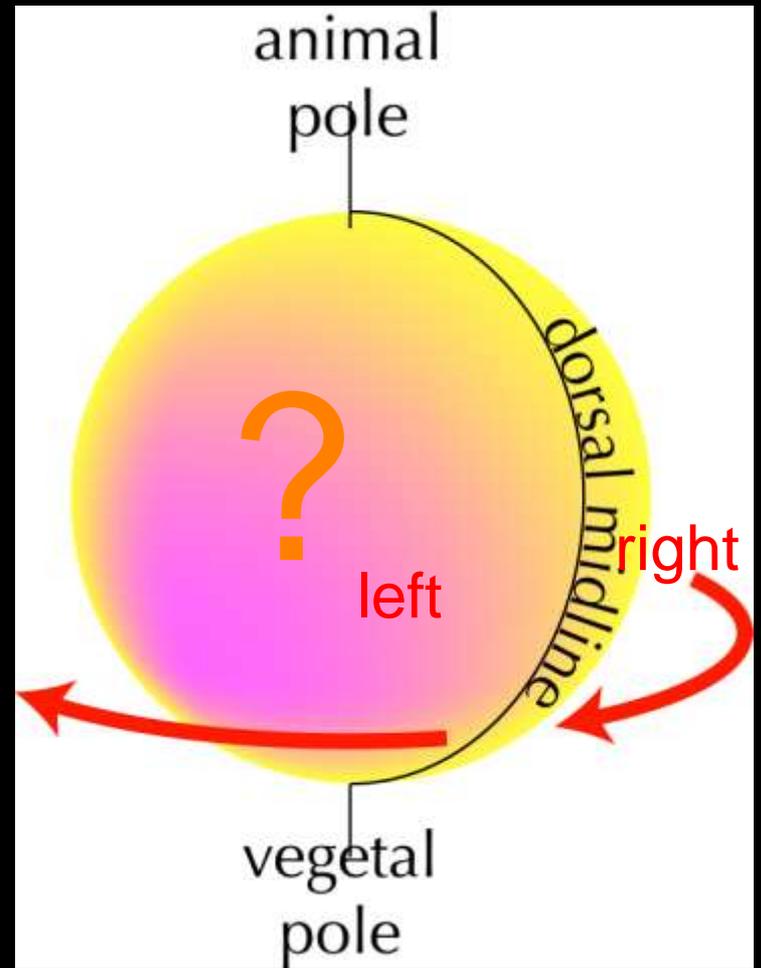
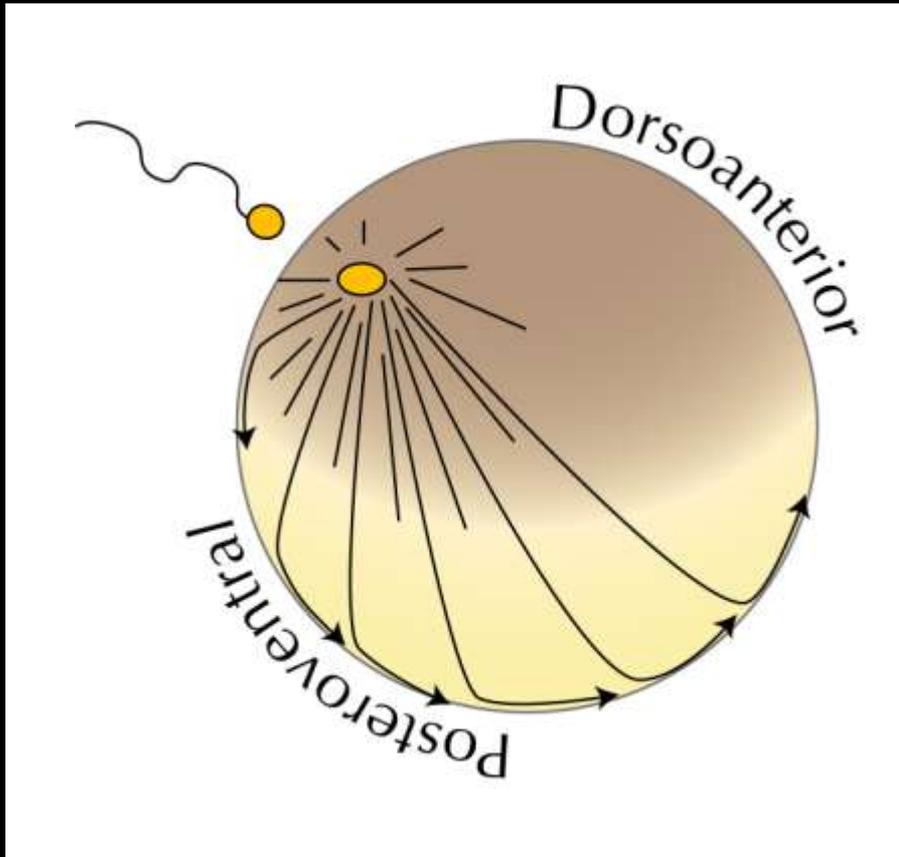
... the plane of mirror-image (bilateral) symmetry emerges directly from this specification; first manifested during gastrulation.



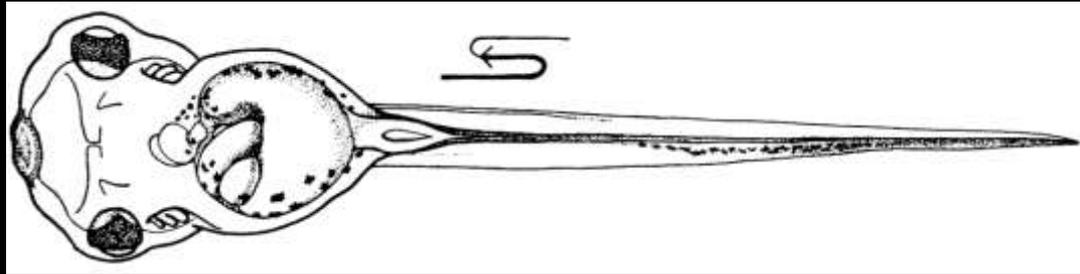
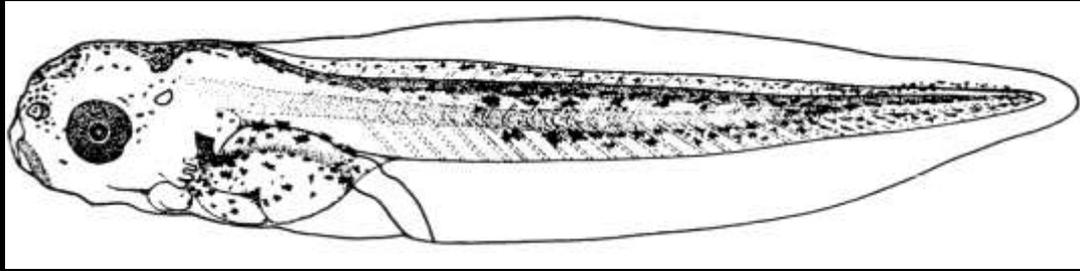
Play Amaya, Danilchik, Keller, or Williams' gastrulation/neurulation movies, located at:

<http://www.xenbase.org/xenbase/original/atlas/movies.html>

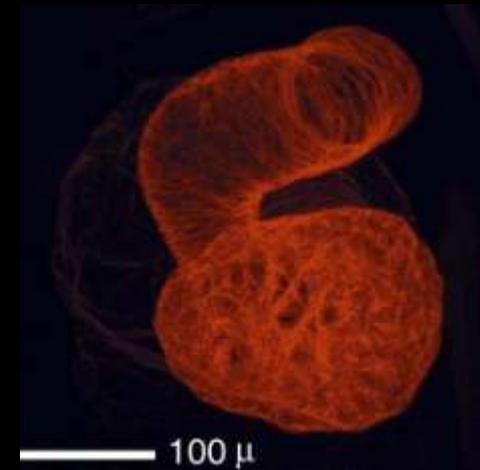
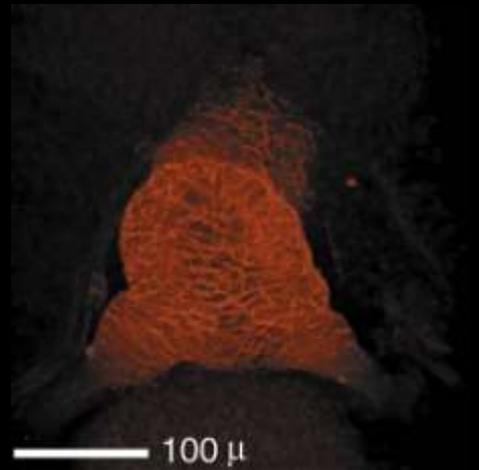
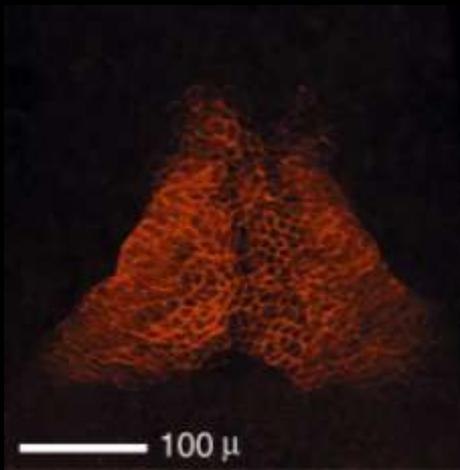
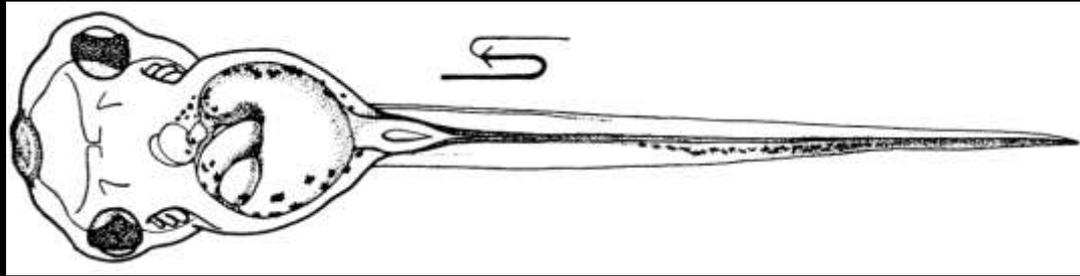
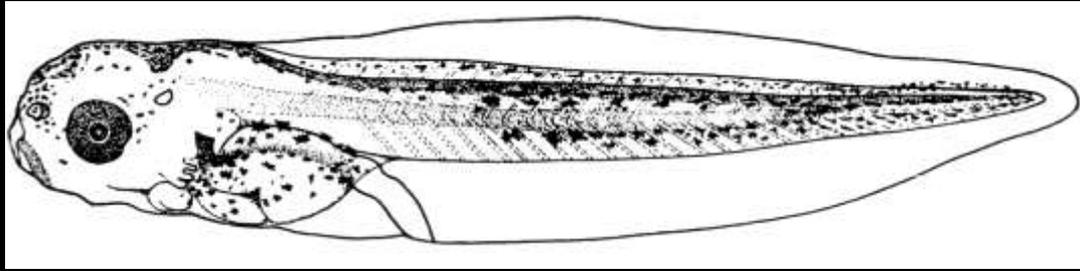
DV and AP are fixed early, and thus define the mediolateral plane ...



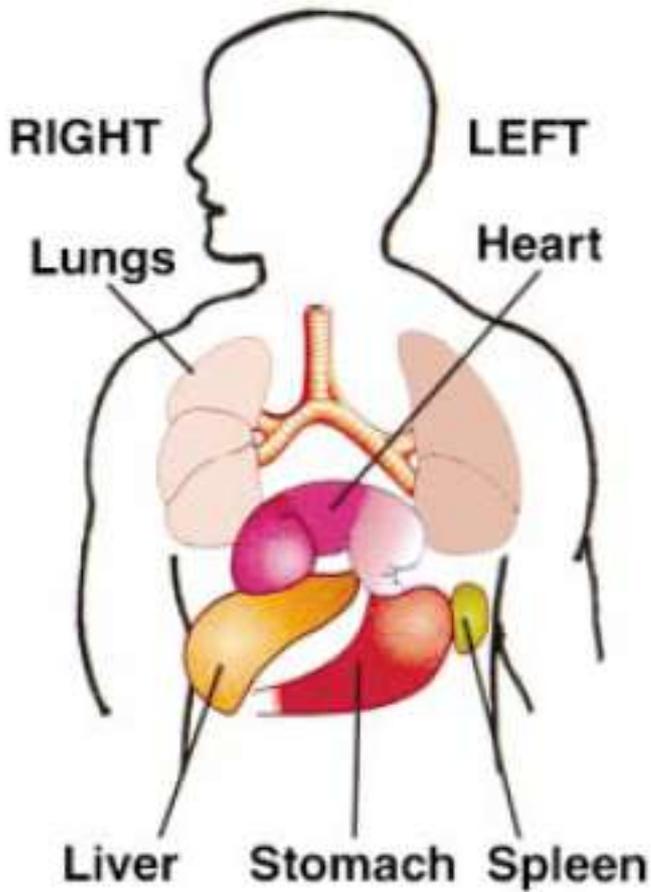
What about L-R?



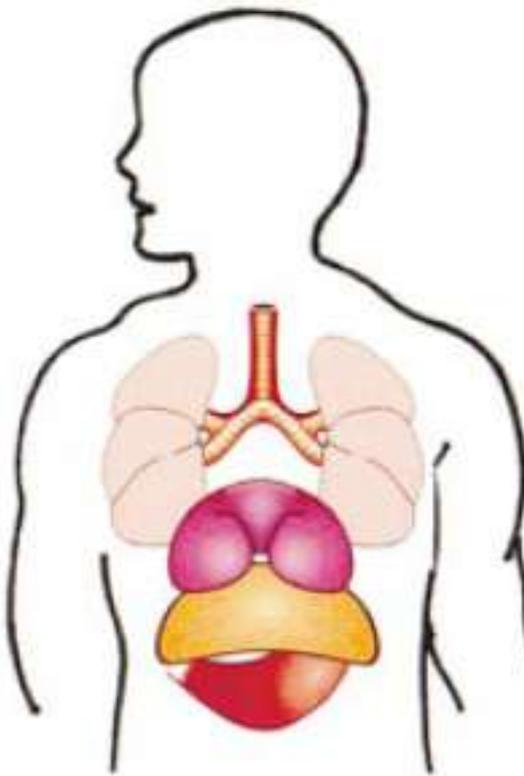
Visceral organization isn't  
mirror-image symmetrical



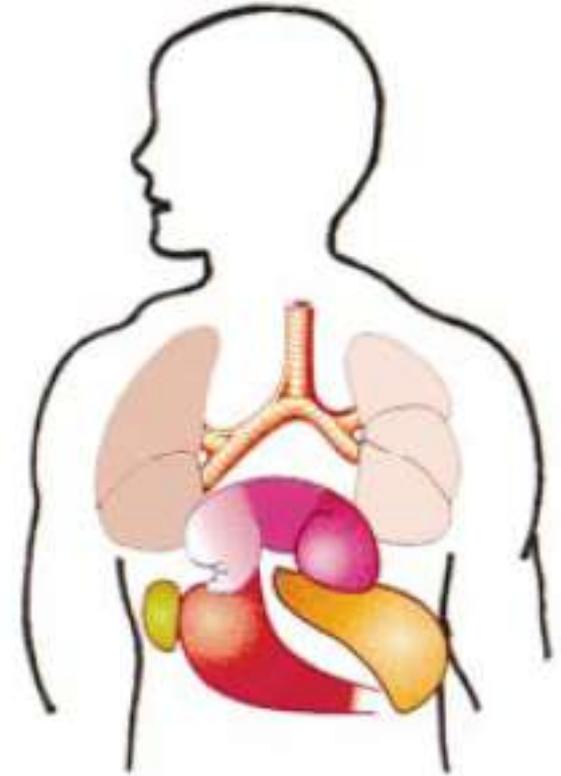
Sandra Kolker & Dan Weeks, [www.xenbase.org/atlas/organs/heart/](http://www.xenbase.org/atlas/organs/heart/)



**SITUS SOLITUS**



**RIGHT ISOMERISM**



**SITUS INVERSUS**

Capdevila et al., *Cell* 2000

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# Julius No

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Dr. **Julius No** is a fictional character and the main antagonist in the *James Bond* film and novel *Dr. No*. He was the first James Bond villain in the film series, where he was portrayed by actor *Joseph Wiseman*.

## Contents [hide]

- 1 Novel biography
  - 1.1 Novel henchmen
- 2 Film biography
  - 2.1 Film henchmen
- 3 Other appearances

## Novel biography [[edit](#)]

Although the film and novel are similar in plot, the backgrounds for Julius No carry certain differences. An individual of unique, Sino-Germanic cultural heritage Dr. No was born in [Peking](#) to a German [Methodist](#) missionary and a Chinese girl, but was raised by his aunt. When older, he went to [Shanghai](#), where he became involved with the [Tongs](#), a Chinese crime syndicate. Later he was smuggled to the [United States](#) and settled in [New York City](#), where he became a clerk and eventually Treasurer for a Tong in America, called the "Hip-Sings."

In the late 1920s, a mob war broke out in New York, forcing the police to crack down on them. No stole a million dollars in [gold](#) from the Tongs and disappeared. But the Tongs tracked him down and [tortured](#) him to find the location of the gold. When No did not tell them, the Tongs cut off his hands, shot him through the left side of the chest and left him for dead. No survived, due to a condition called [dextrocardia](#), in which his heart was on the right side of the body.

No spent a long time in hospital, then enrolled in medical school in [Milwaukee, Wisconsin](#). It is unclear if he completed his studies, but he adopted the title Doctor and changed his name (his birth name is unknown) to Julius No, symbolic of his rejection of his father, whose given name was Julius. As in the film, No fitted himself with metal manual prostheses, but the book describes them as simple pincers (apparently similar to those of Tee-Hee in *Live and Let Die*) and judging by the lack of descriptive detail, they presumably lack the articulation of human hands. With the million dollars from the Tong, he purchased rare stamps in order to preserve his money against inflation; he later purchased the island of Crab Key, off the coast of Jamaica, where he re-started a defunct [guano](#) business as a cover for his proposed criminal operations. He employs Jamaican and Cuban labourers on good wages for the guano works, brutally

## Dr. Julius No

Character from the *James Bond* franchise



<b>Affiliation</b>	<a href="#">Soviet Union</a> (novel) <a href="#">SPECTRE</a> (film) <a href="#">Independent/OCTOPUS</a> (video games)
<b>Portrayed by</b>	<a href="#">Joseph Wiseman</a>



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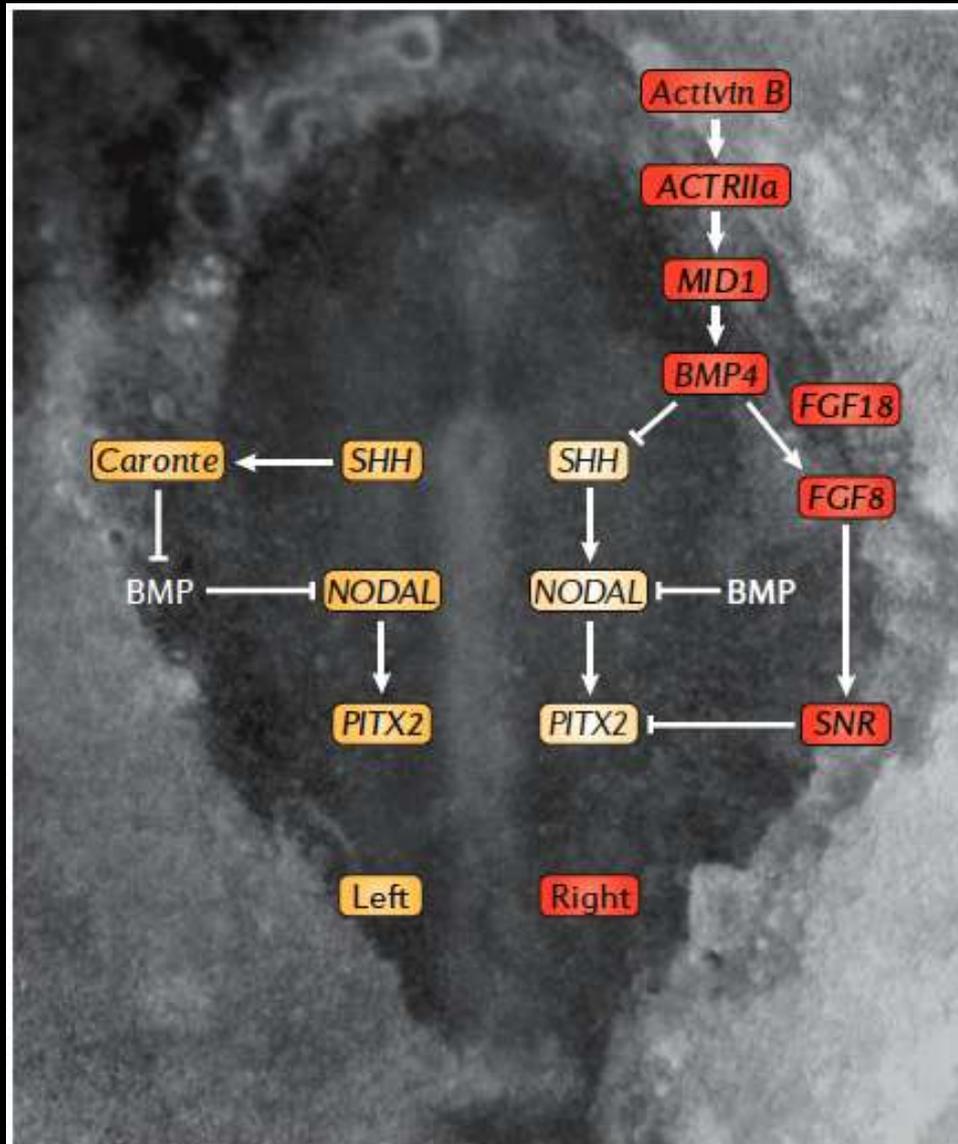
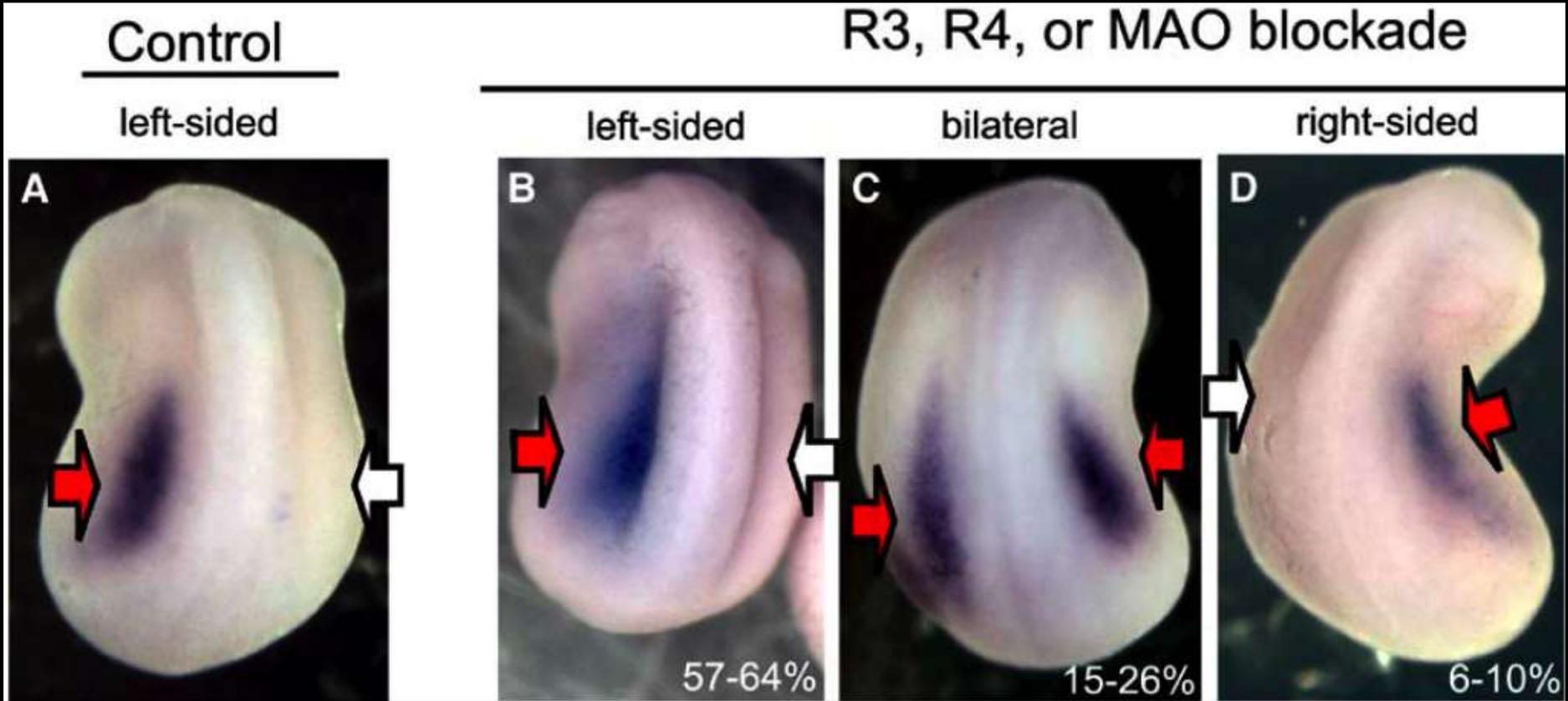
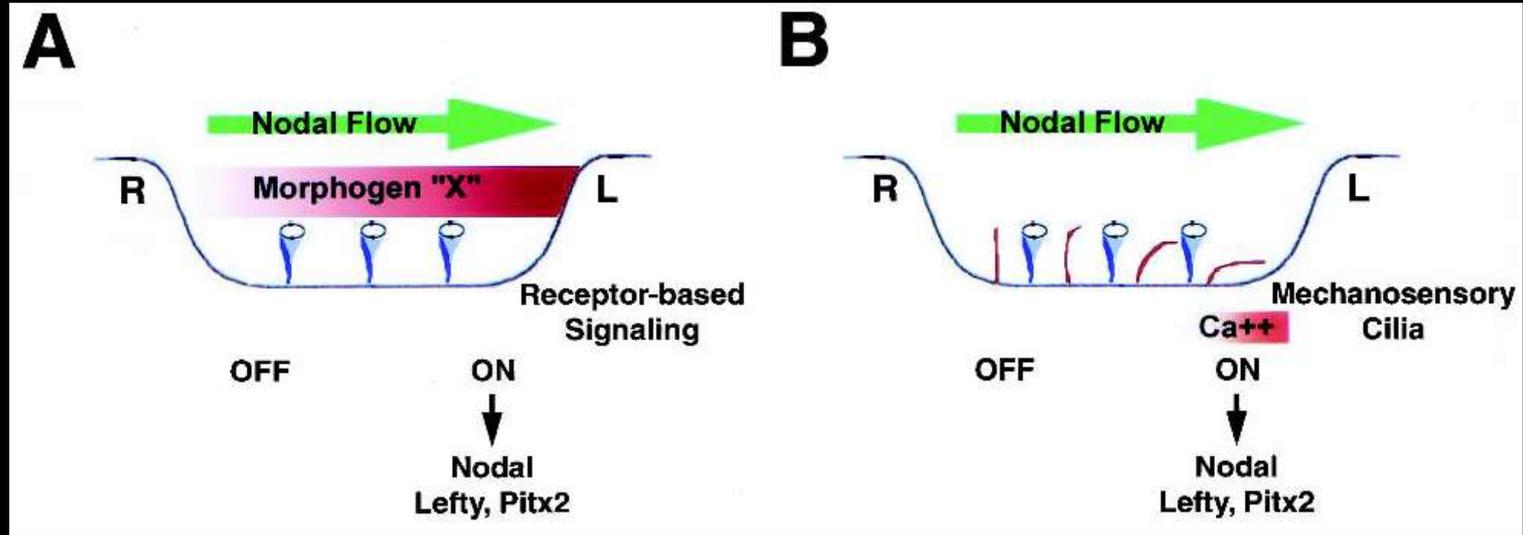


Figure 2 | Early left-right asymmetrical genetic cascades in the chick embryo. A cascade of side-

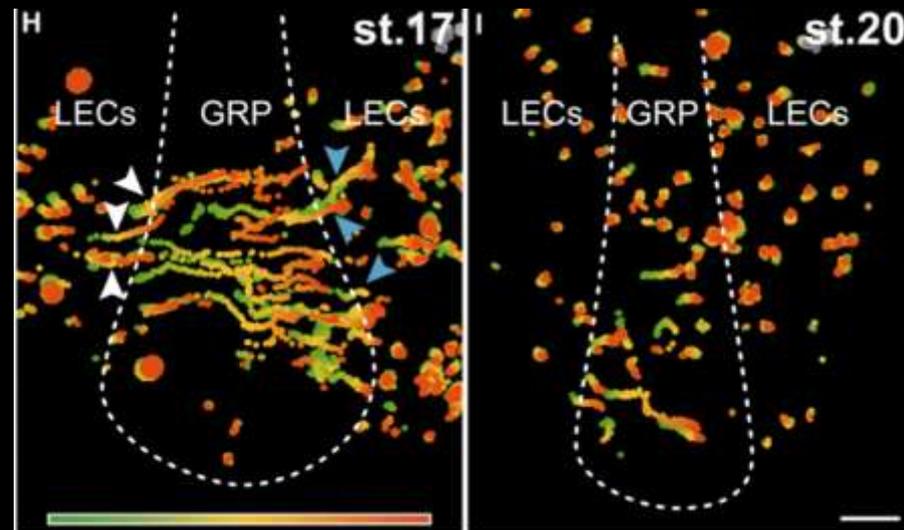
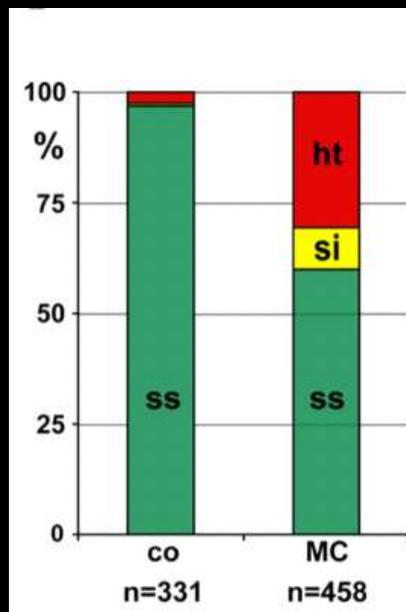
# early Xnr2 (nodal) expression



Fukumoto et al., *Curr. Biol.* 2005



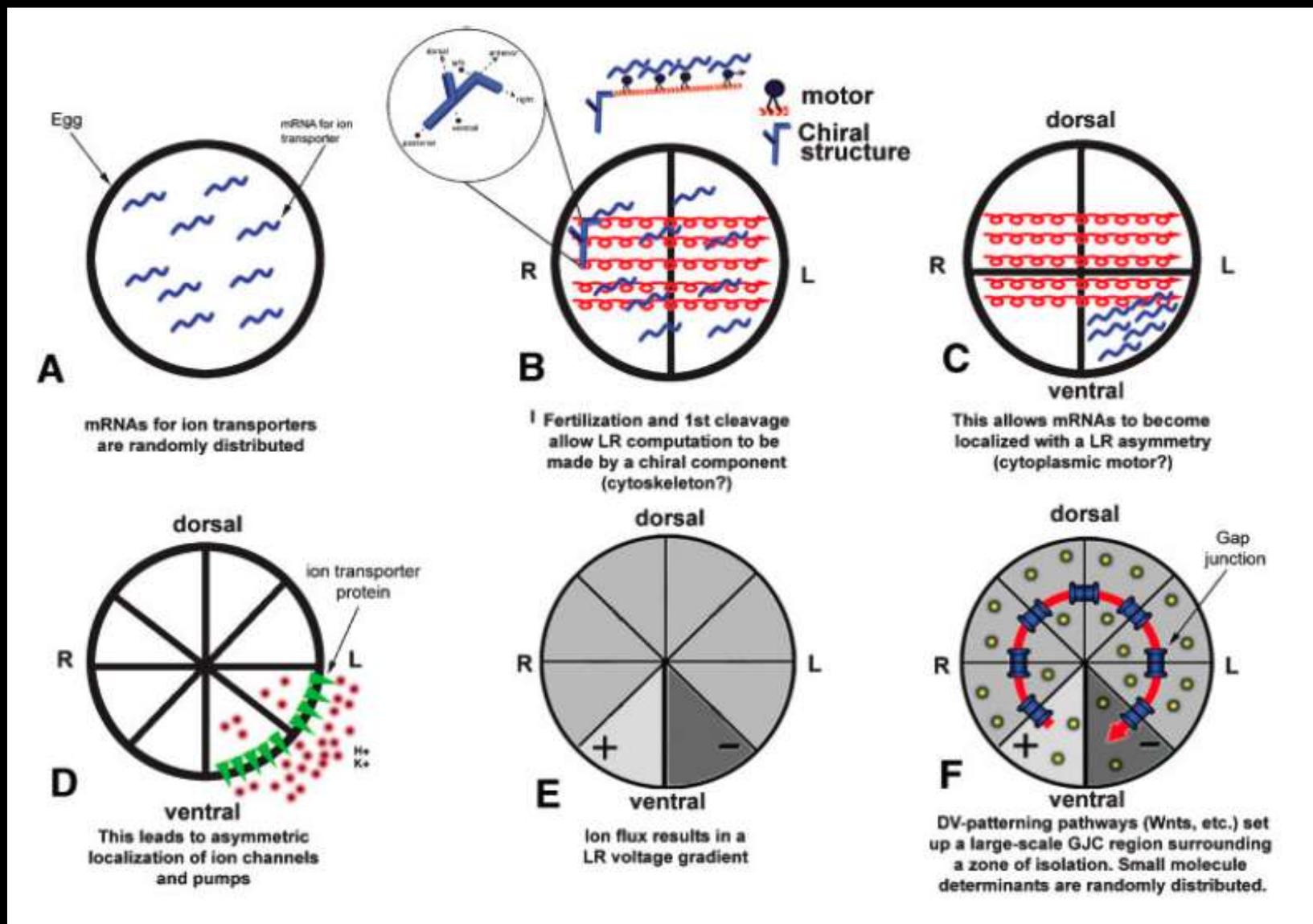
Capdevila et al., *Cell* 2000



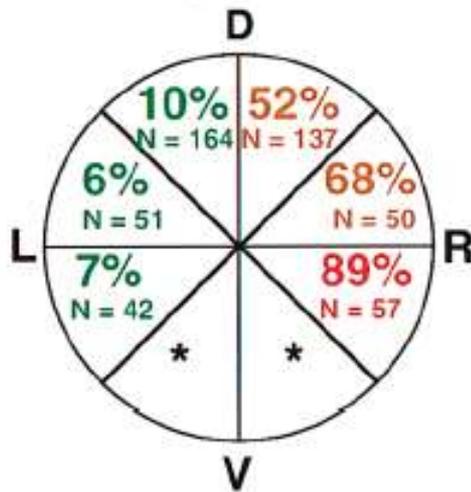
Cilia-Driven Leftward Flow Determines Laterality in *Xenopus*

Schweickert et al 2007. *Current Biology* 19

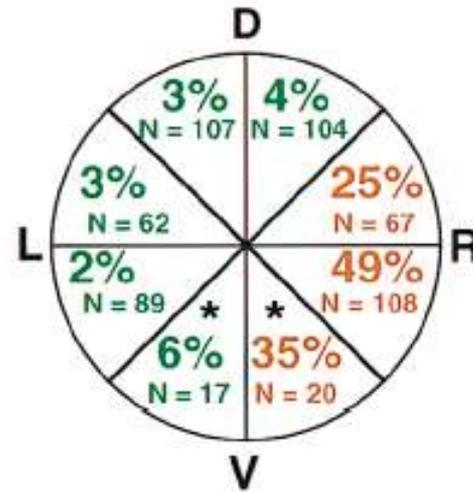
... but other LR asymmetries exist before nodal cilia appear



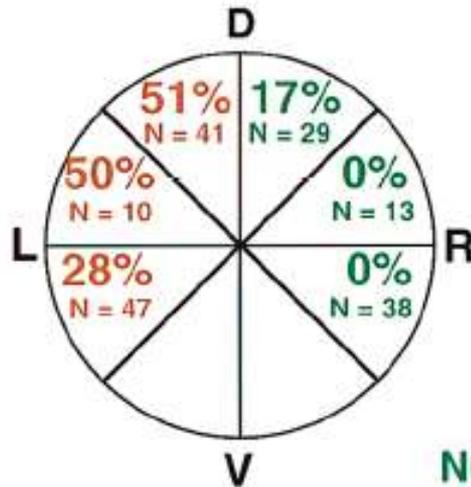
### A. BVg1



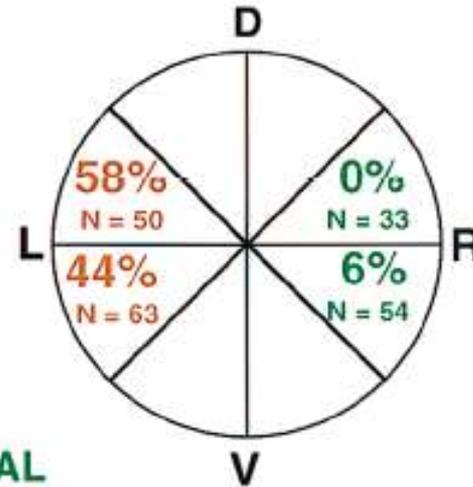
### B. Activin



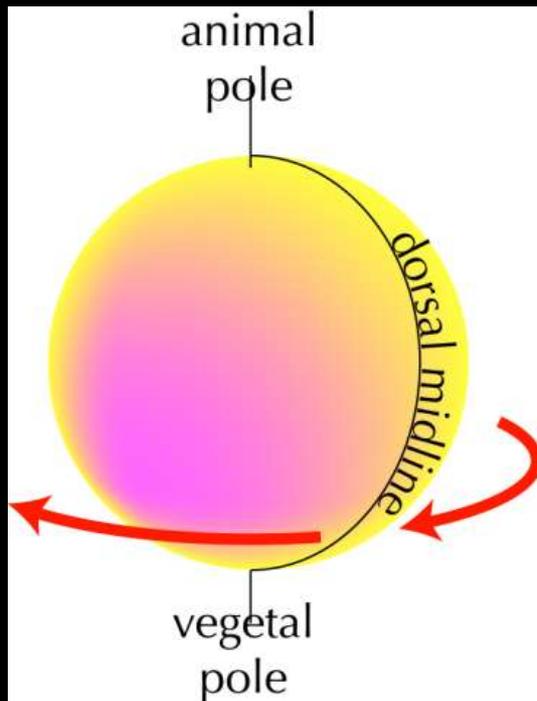
### C. tAR



### D. BMP2, 4

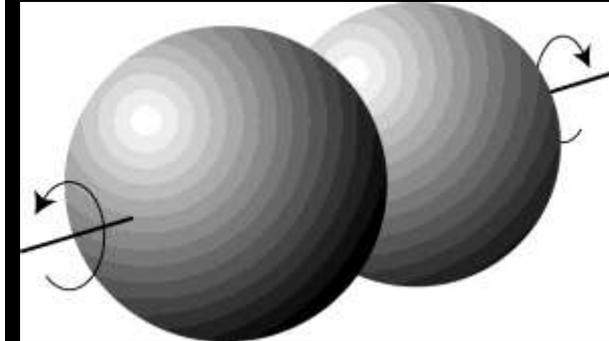
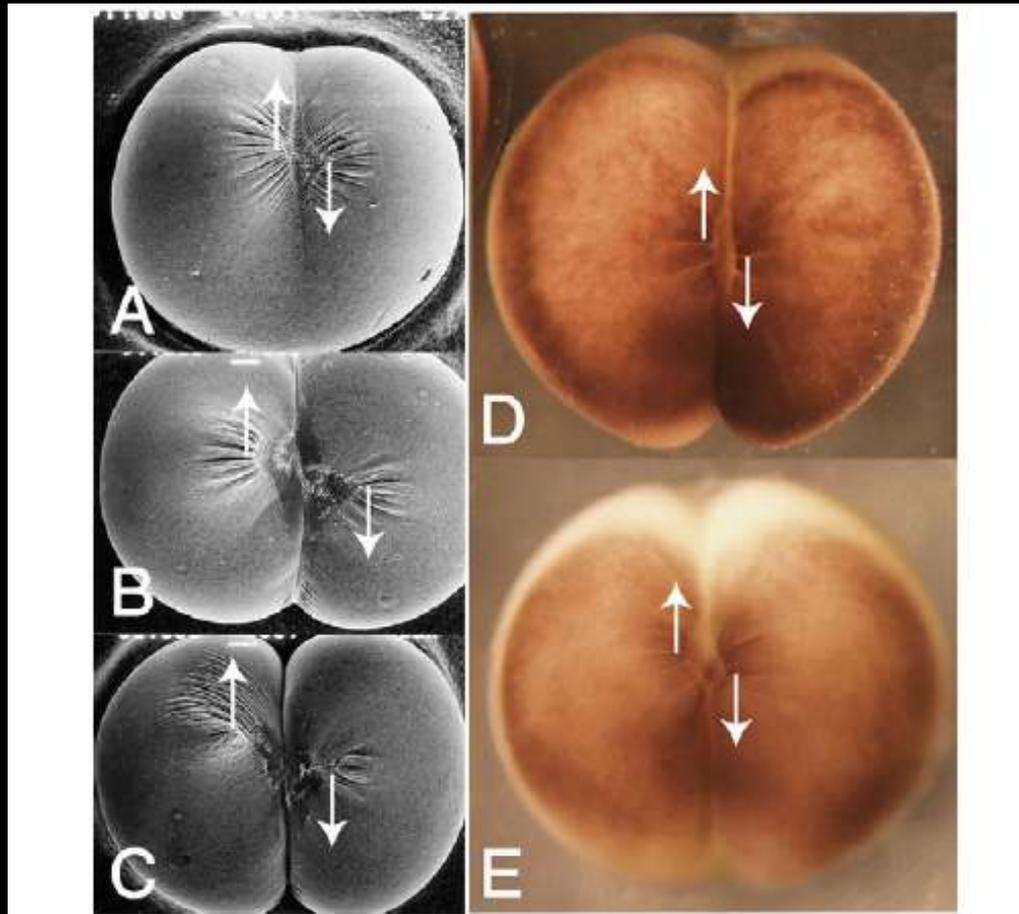


**NORMAL**  
**RANDOM**  
**INVERTED**



How do cleavage-stage asymmetries develop across the embryonic midline?

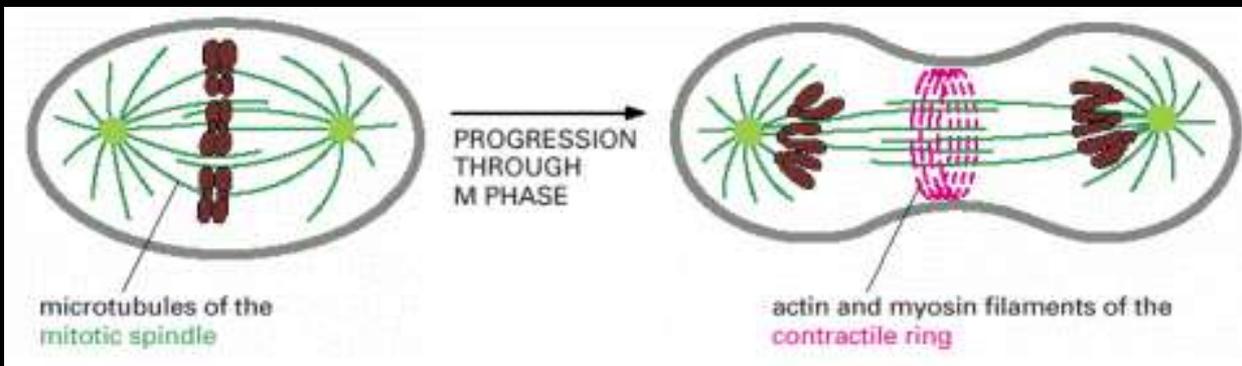
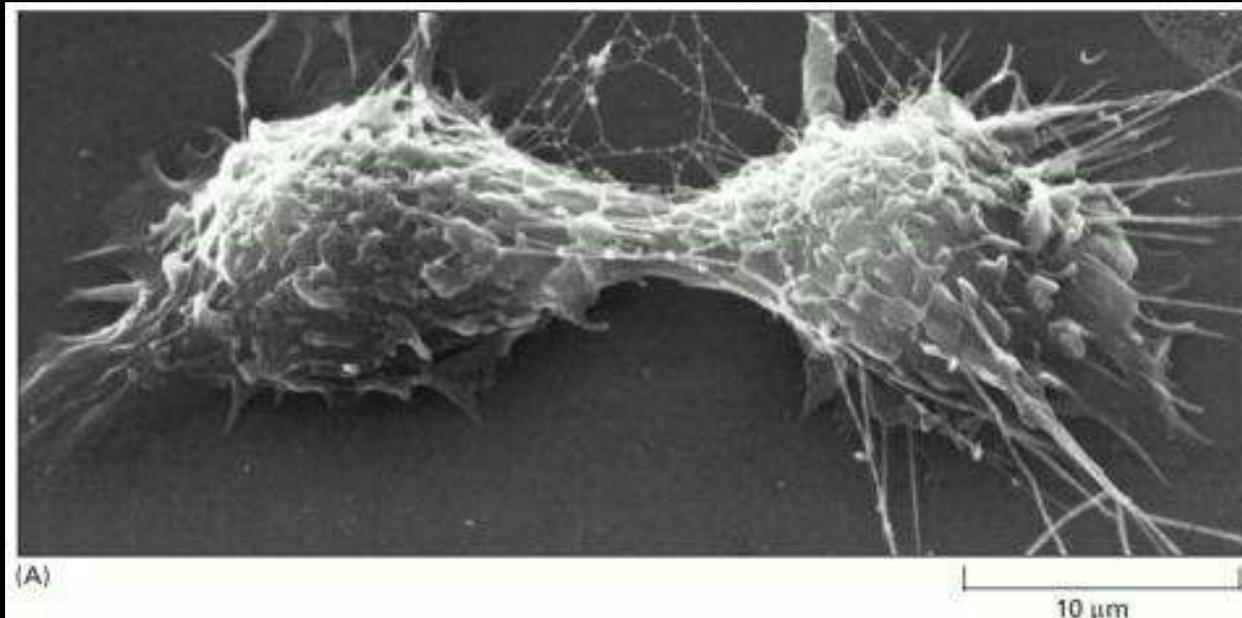
# Normal *X. laevis* cleavage exhibits slight chiral torsion



**Fig. 2. Normal first cleavage in *Xenopus* is chiral and not mirror-image symmetric.** Both fixed (A-C) and live (D-E) embryos, untreated, reveal a slight counterclockwise torsion of the two blastomeres during cleavage furrow advance. The apex of each furrow margin, i.e., the site

Danilchik, Brown, Riegert, 2006

# Cytokinesis



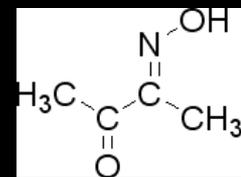
Molecular Biology of the Cell © 2002 Alberts et al.



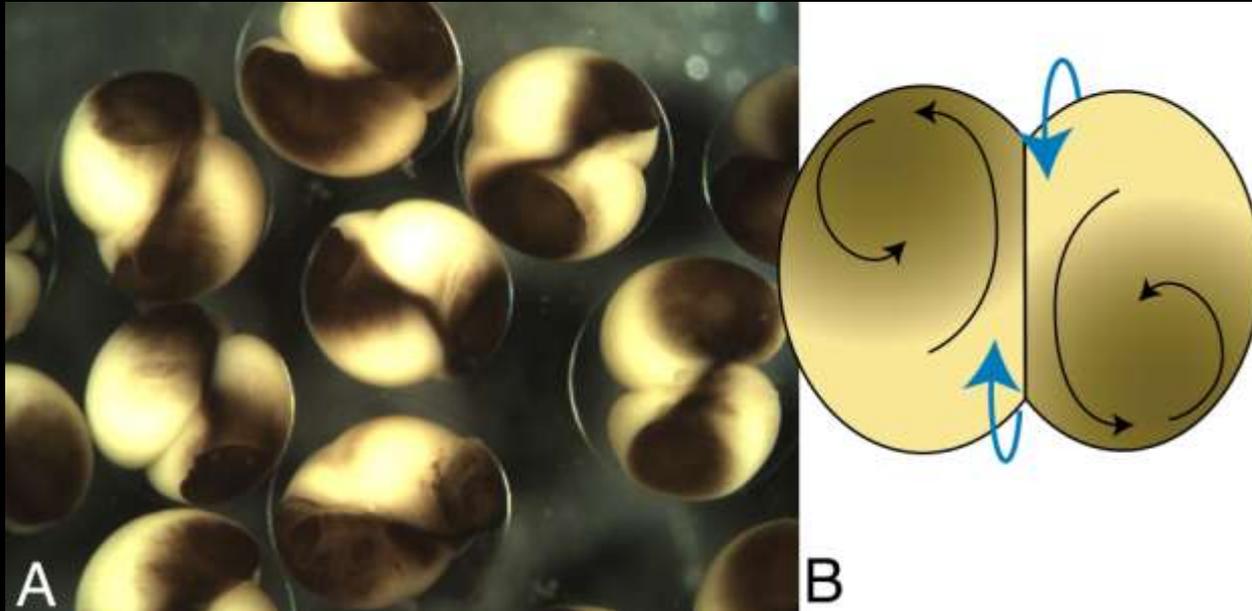
Untreated



BDM



# Response always (100%) CCW



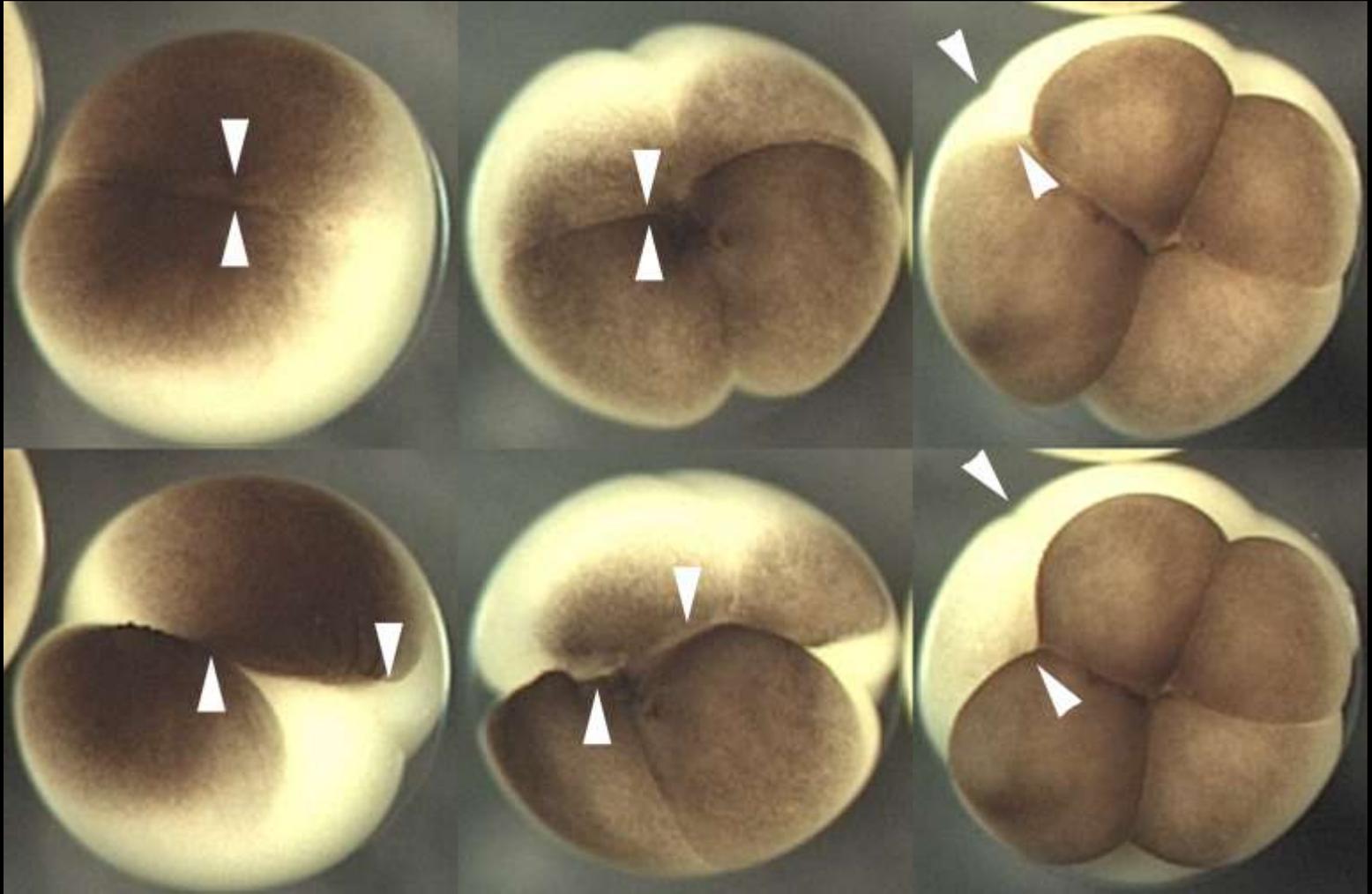
CCW  
every time

first

second

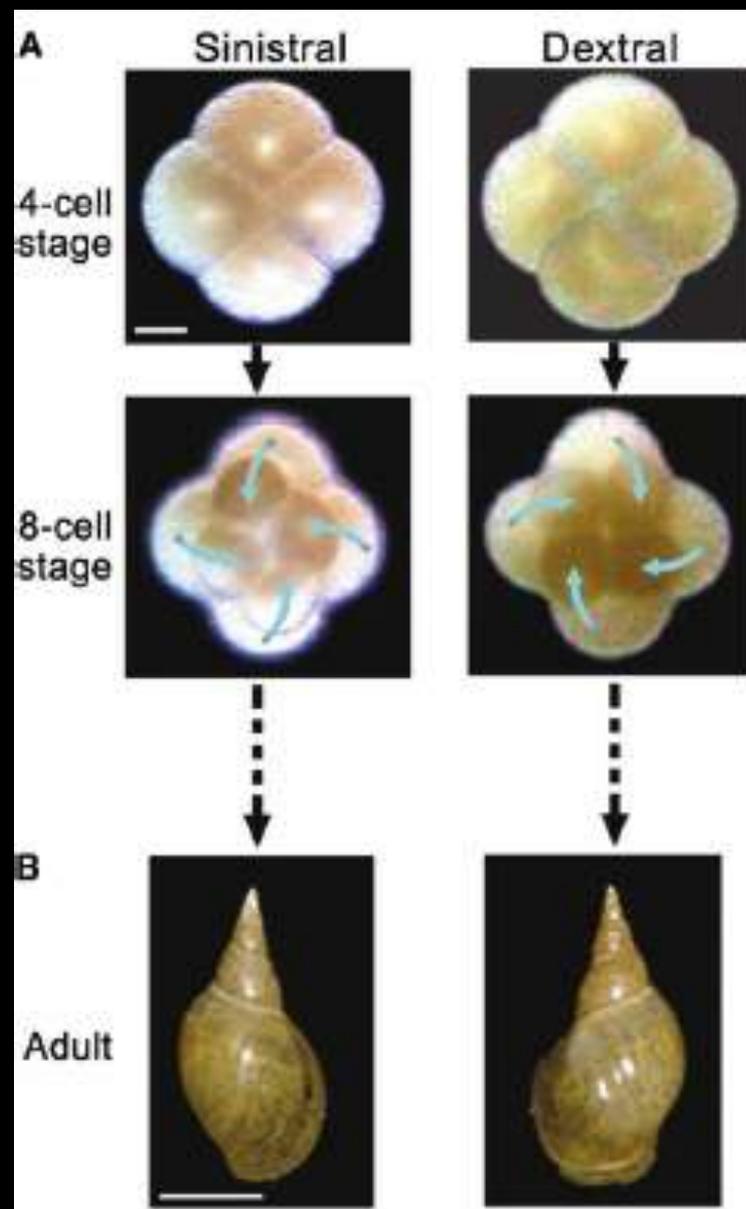
third

before



after

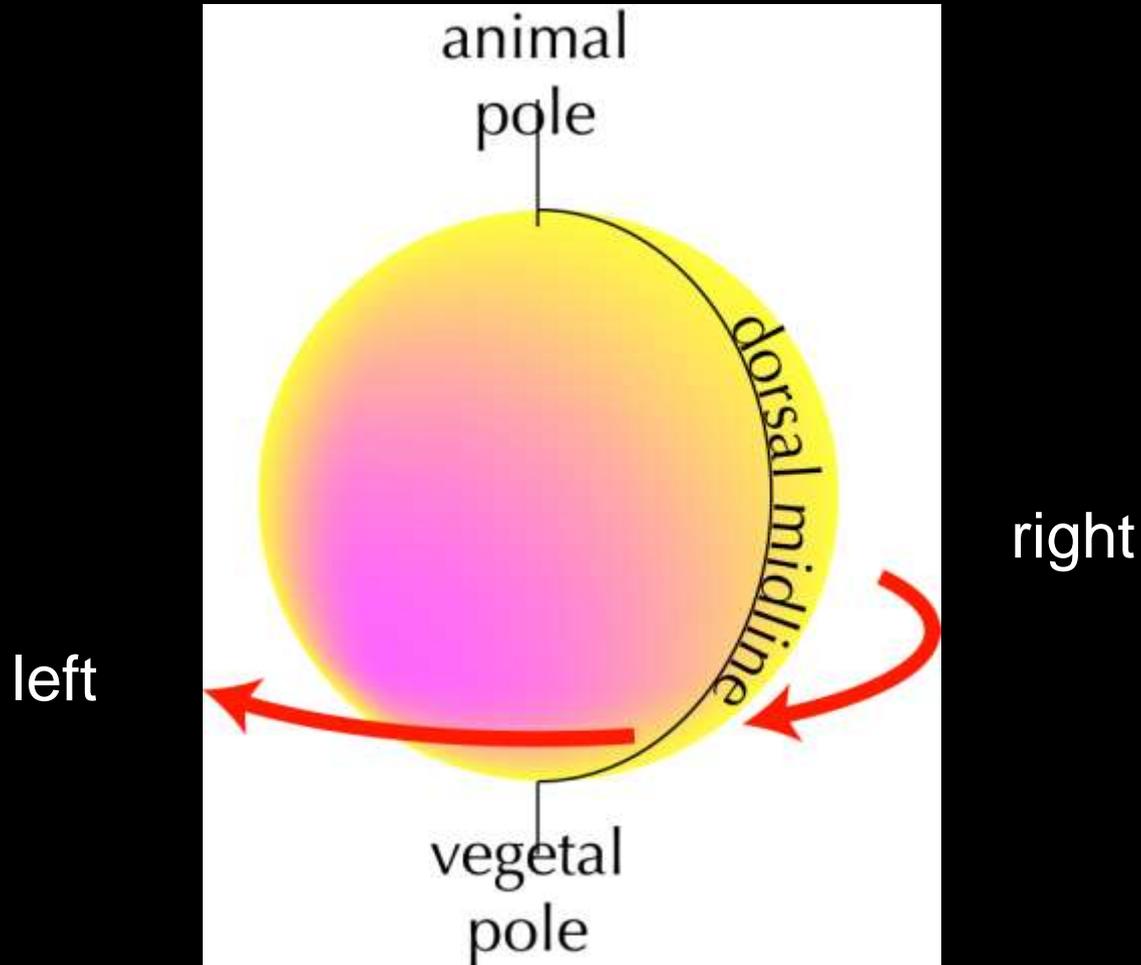
Play "movie2,3,4.mov"



Yuichiro Shibazaki,<sup>1,3</sup> Miho Shimizu,<sup>2</sup>  
and Reiko Kuroda<sup>1,2,3,\*</sup>

Current Biology, Vol. 14, 1462–1467, August 24, 2004,

# When?





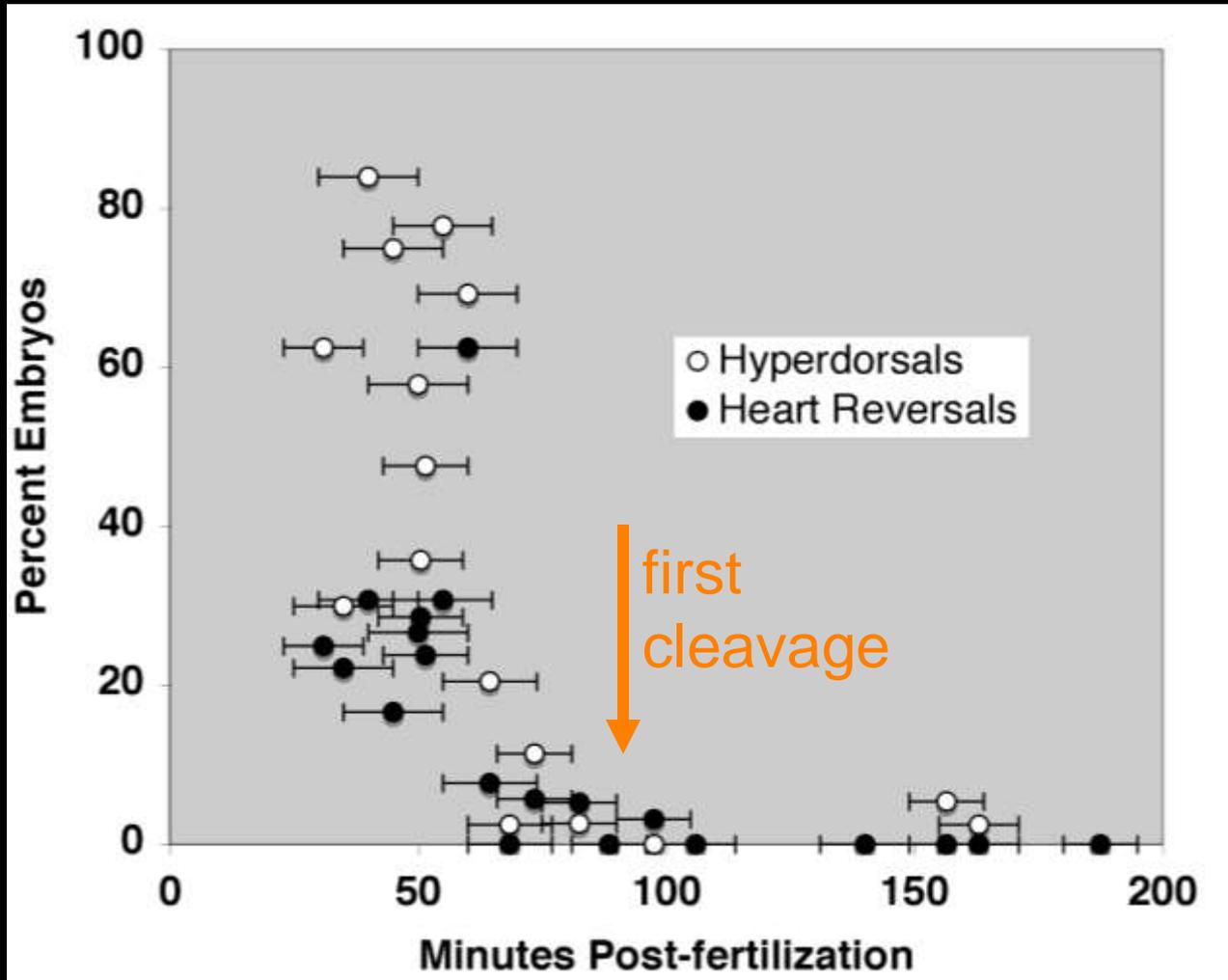
normal heart and  
gut arrangement



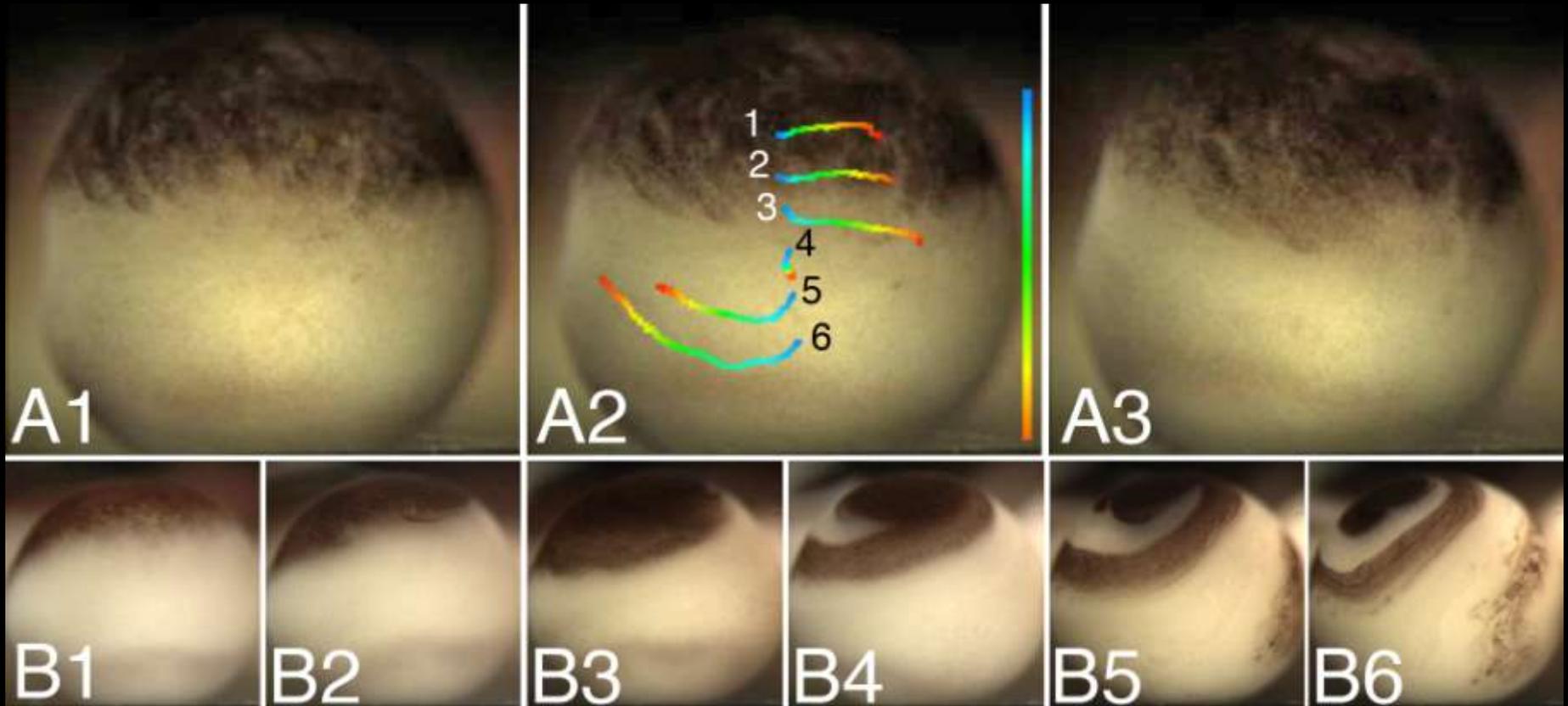
situs inversus  
(heart and gut reversed)

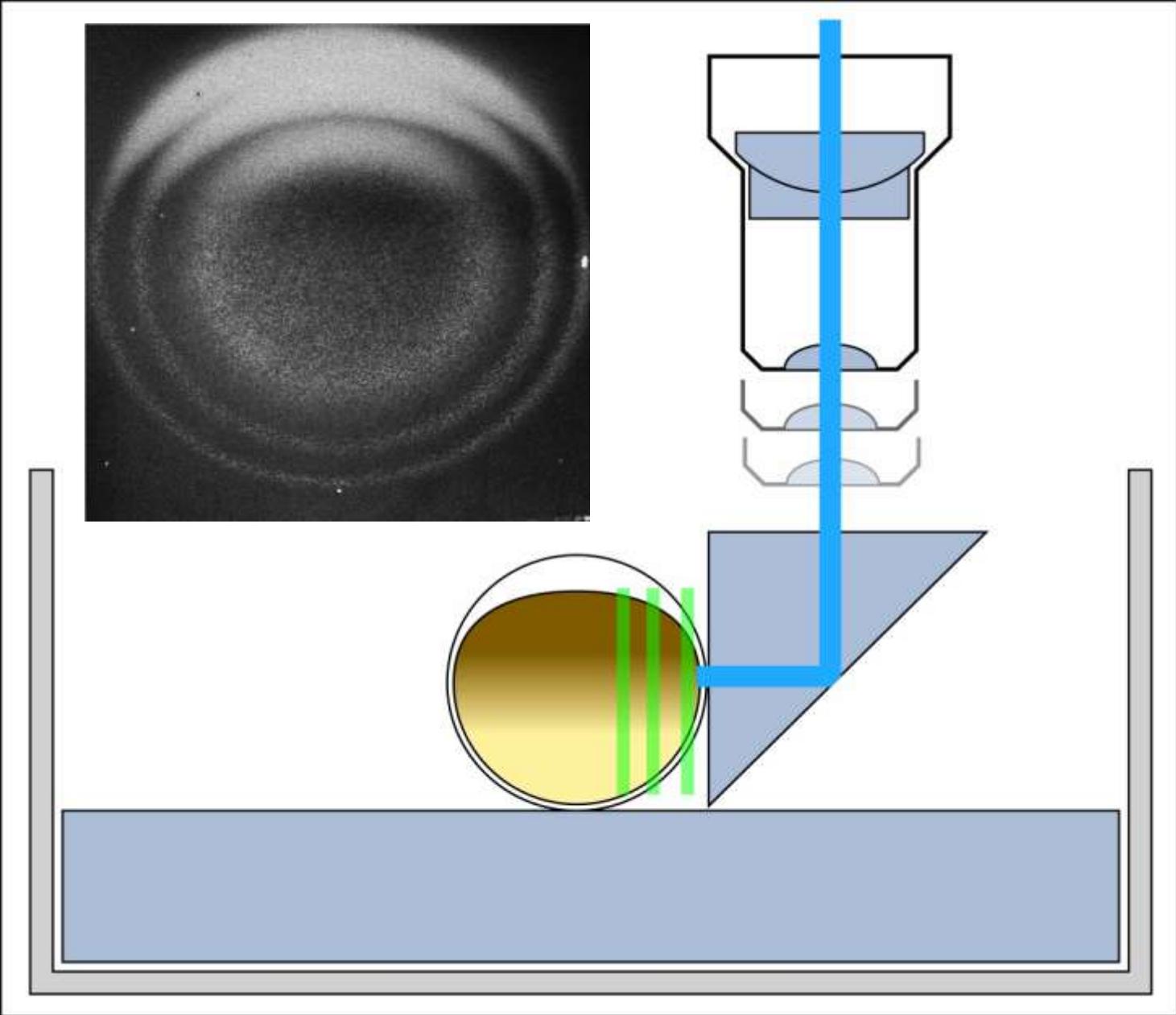


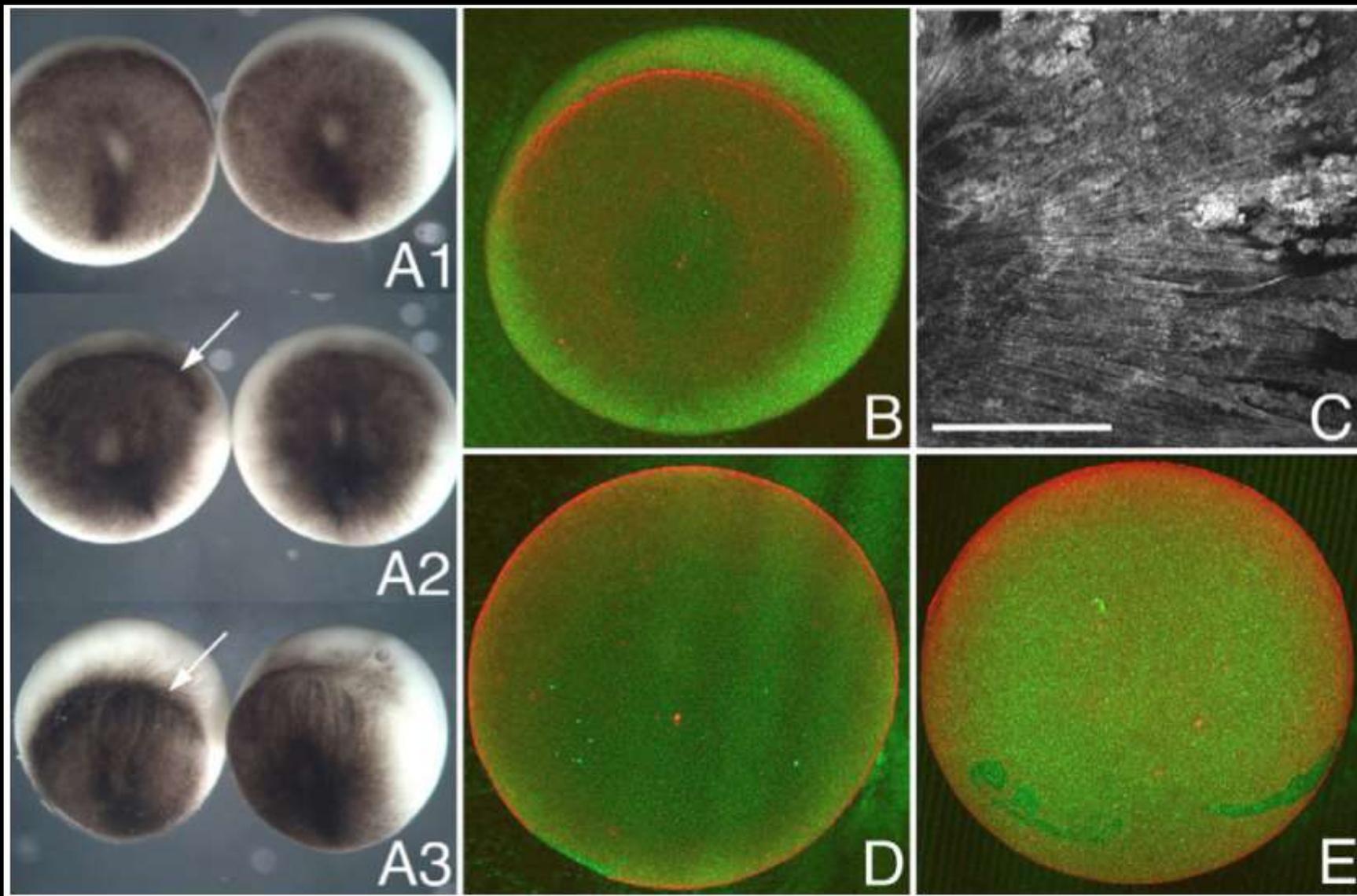
conjoined  
twinning



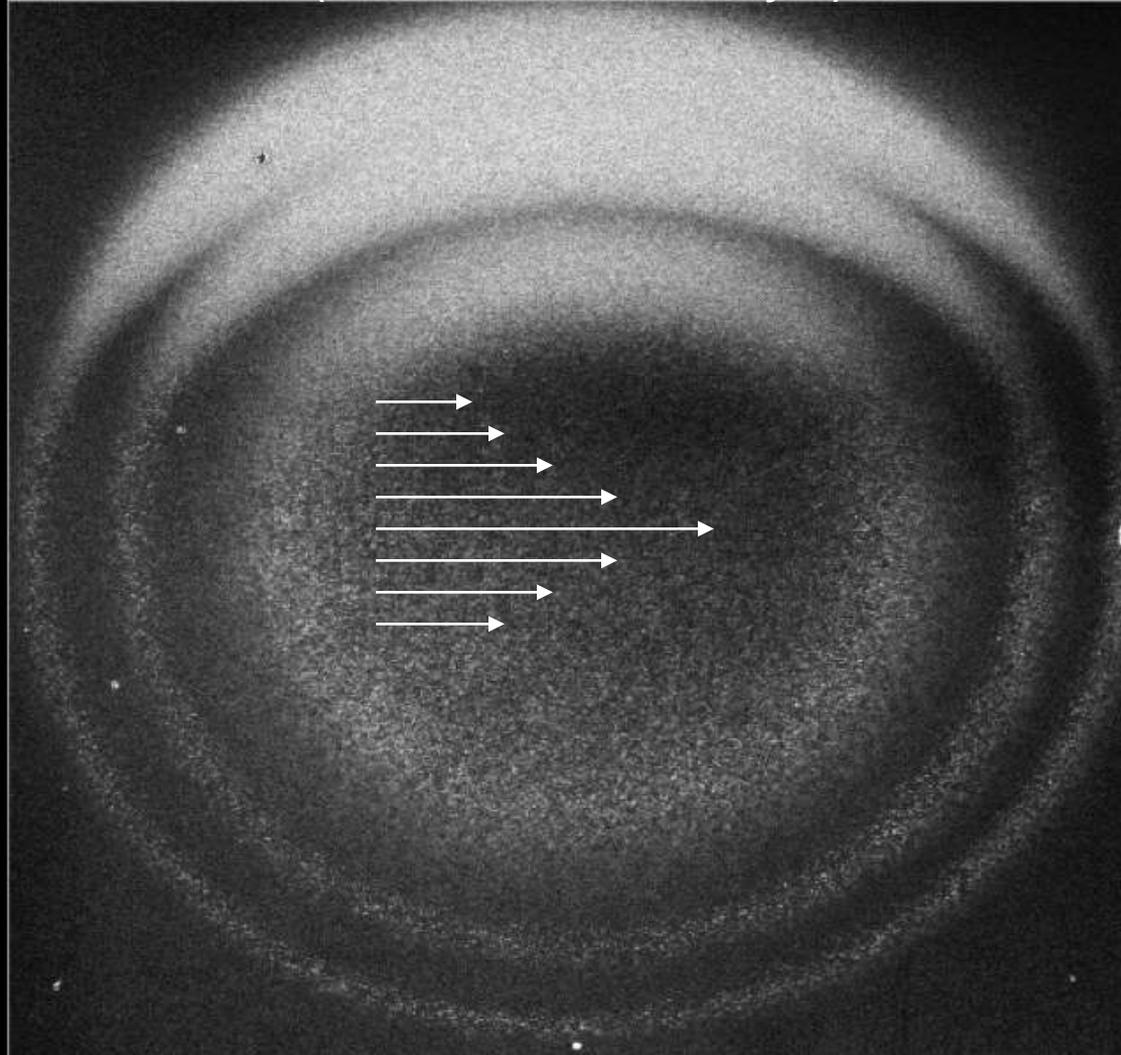
# Unidirectional shear @ equator during first cell cycle (BDM-treated embryo)

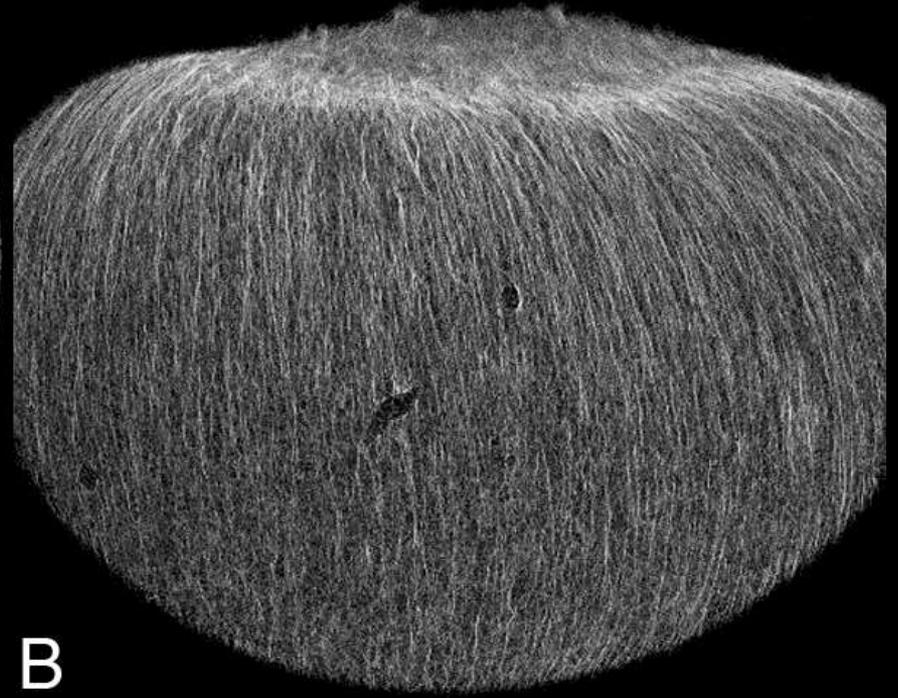
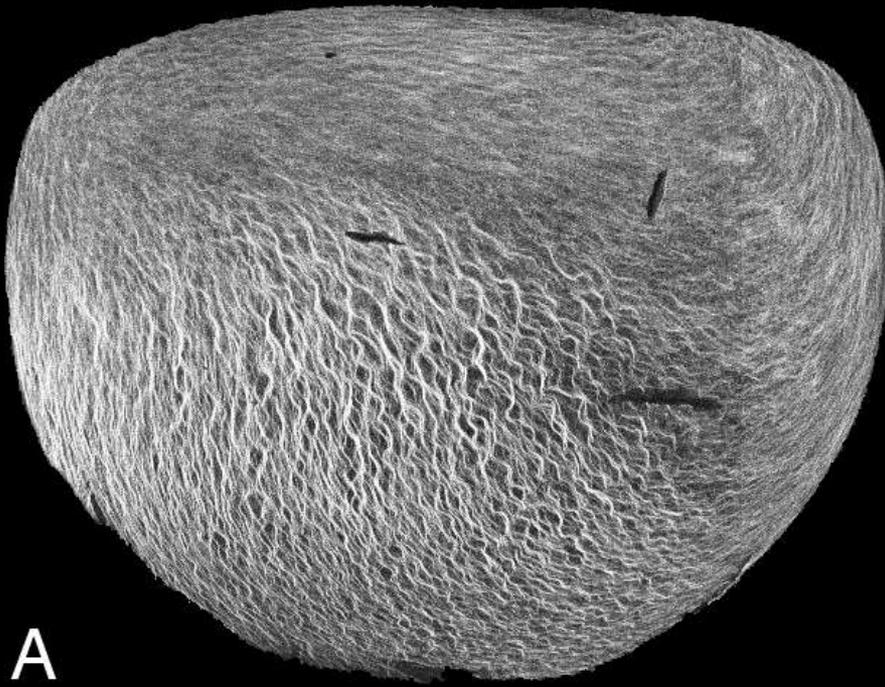
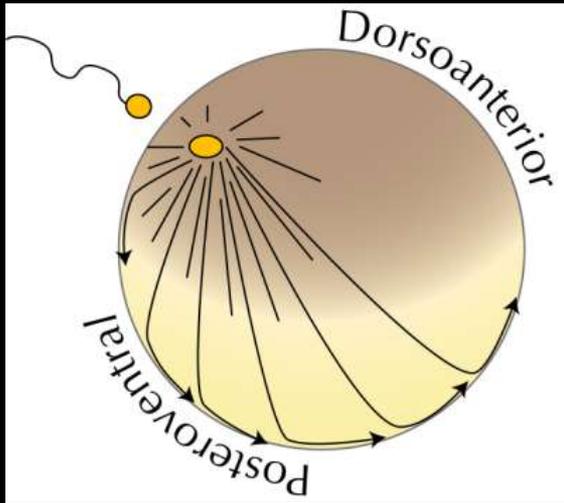


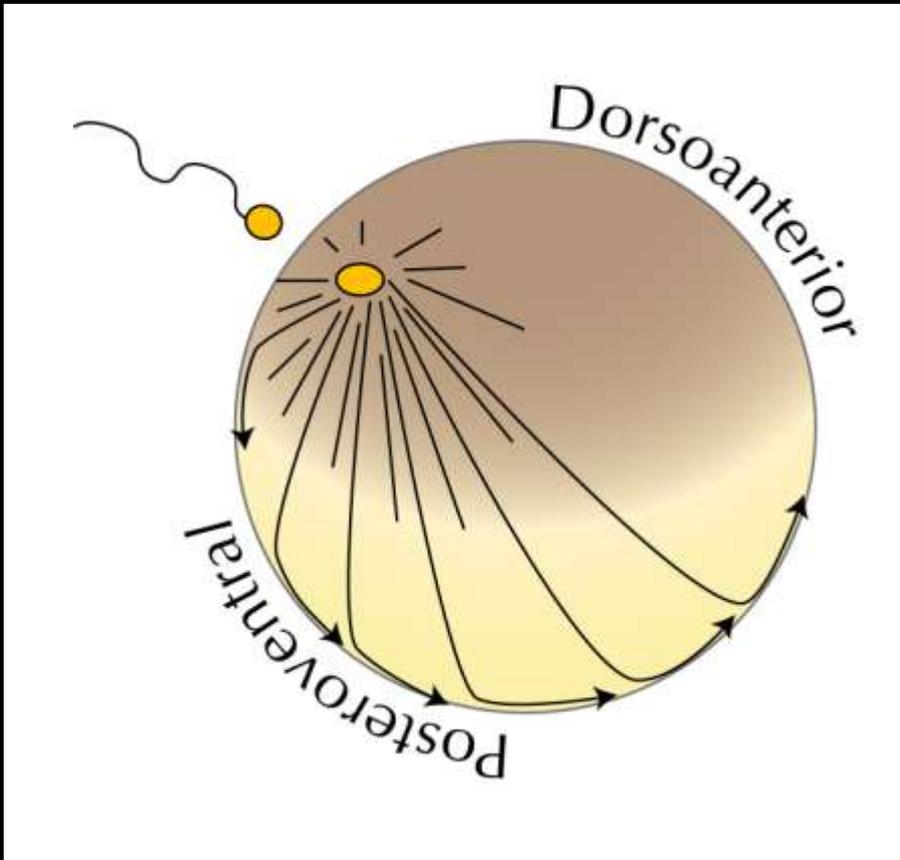




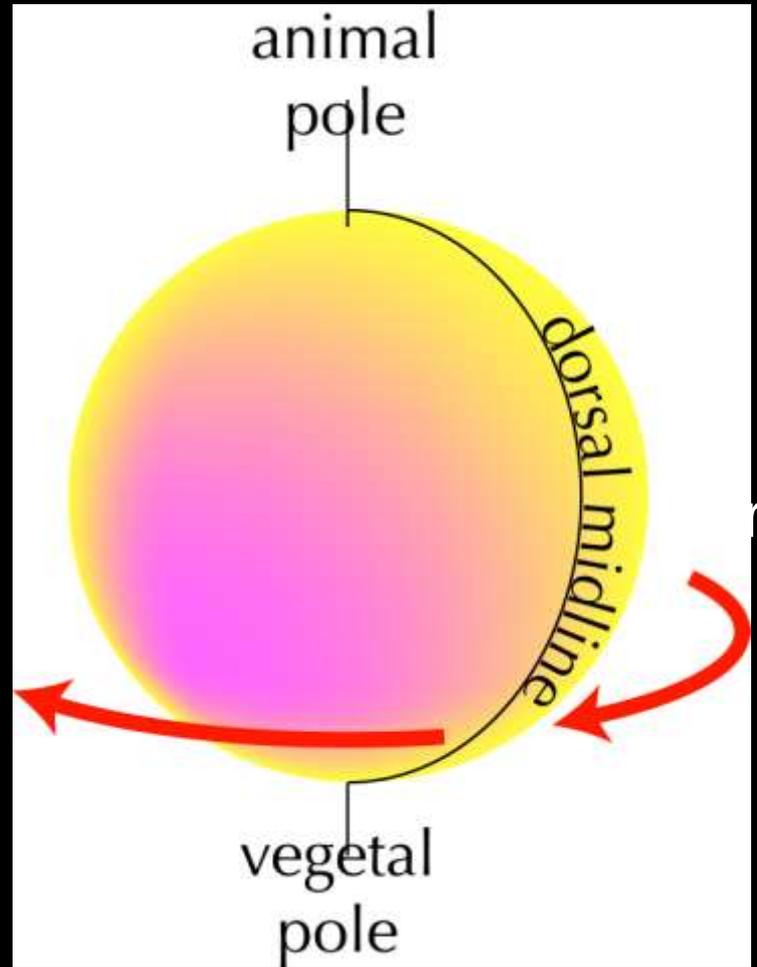
# Unidirectional shear @ equator during first cell cycle (untreated embryo)



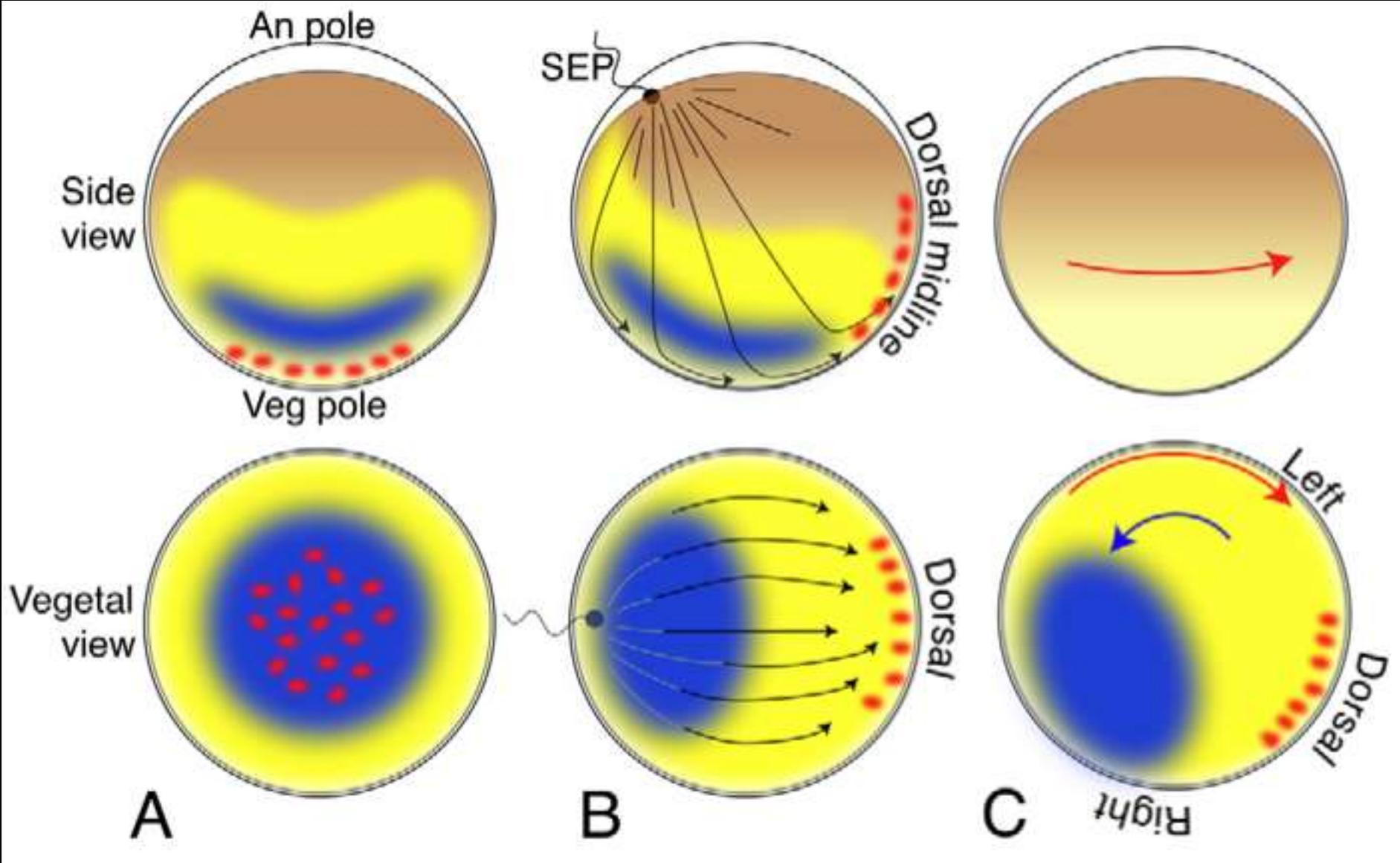




left

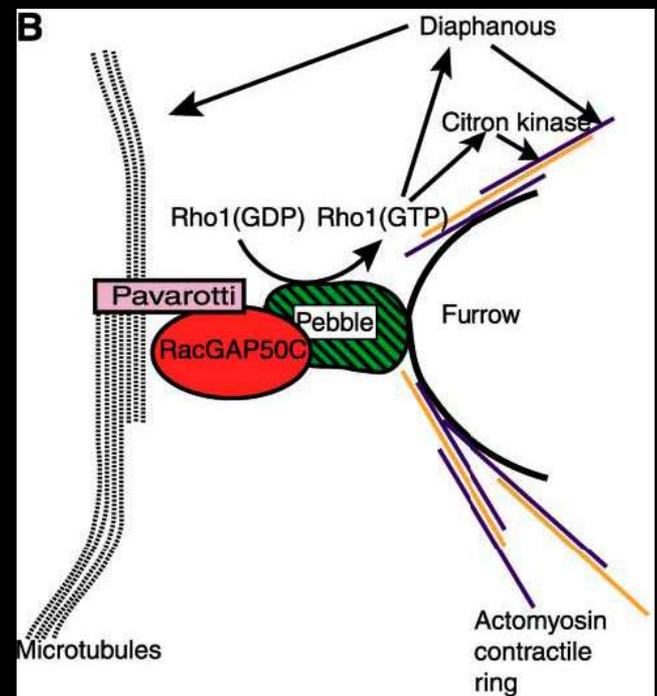
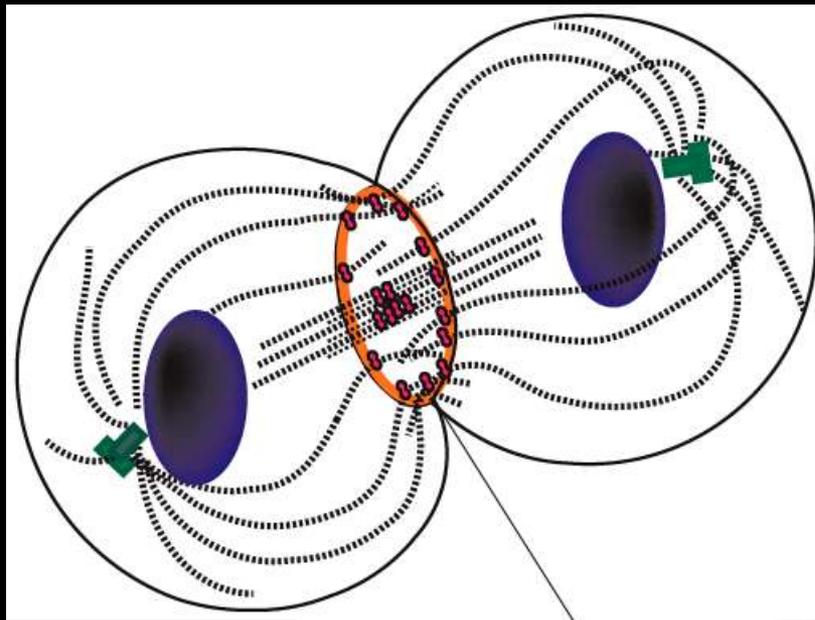


right

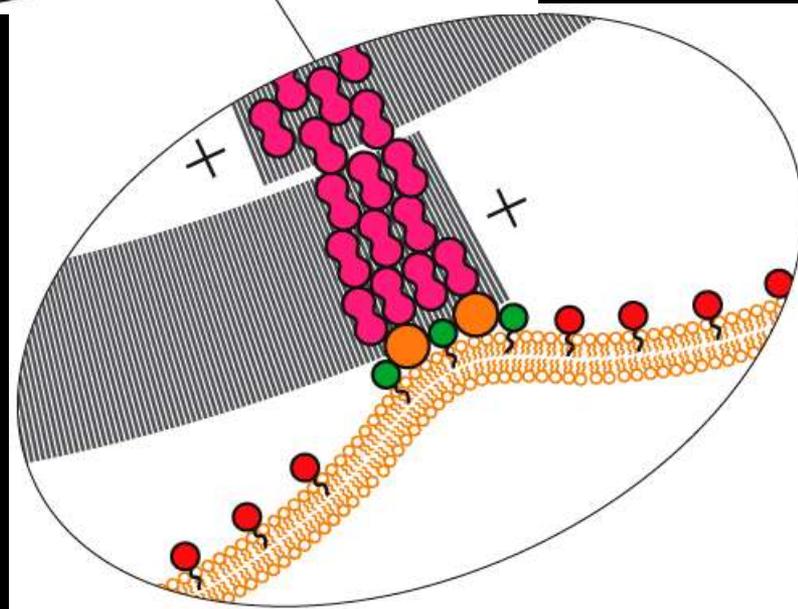


# Contractile ring organization & function during cytokinesis

DRUG	CSK FX	FX ON TORSION
nocodazole (10 $\mu\text{g/ml}$ )	depolymerize MTs	none
jasplakinolide (0.4 $\mu\text{g/ml}$ )	block actin assembly	none
cytochalasin B (10 $\mu\text{g/ml}$ )	block actin assembly	none
latrunculin B (1 $\mu\text{g/ml}$ )	depolymerize actin	blocks



- Microtubules
- RhoGTP
- RhoGDP
- centralspindlin (RacGAP/PAV-KLP)
- PBLRhoGEF



Microtubules not necessary for chiral response to BDM: parthenogenetically activated eggs also exhibit CCW torsion.

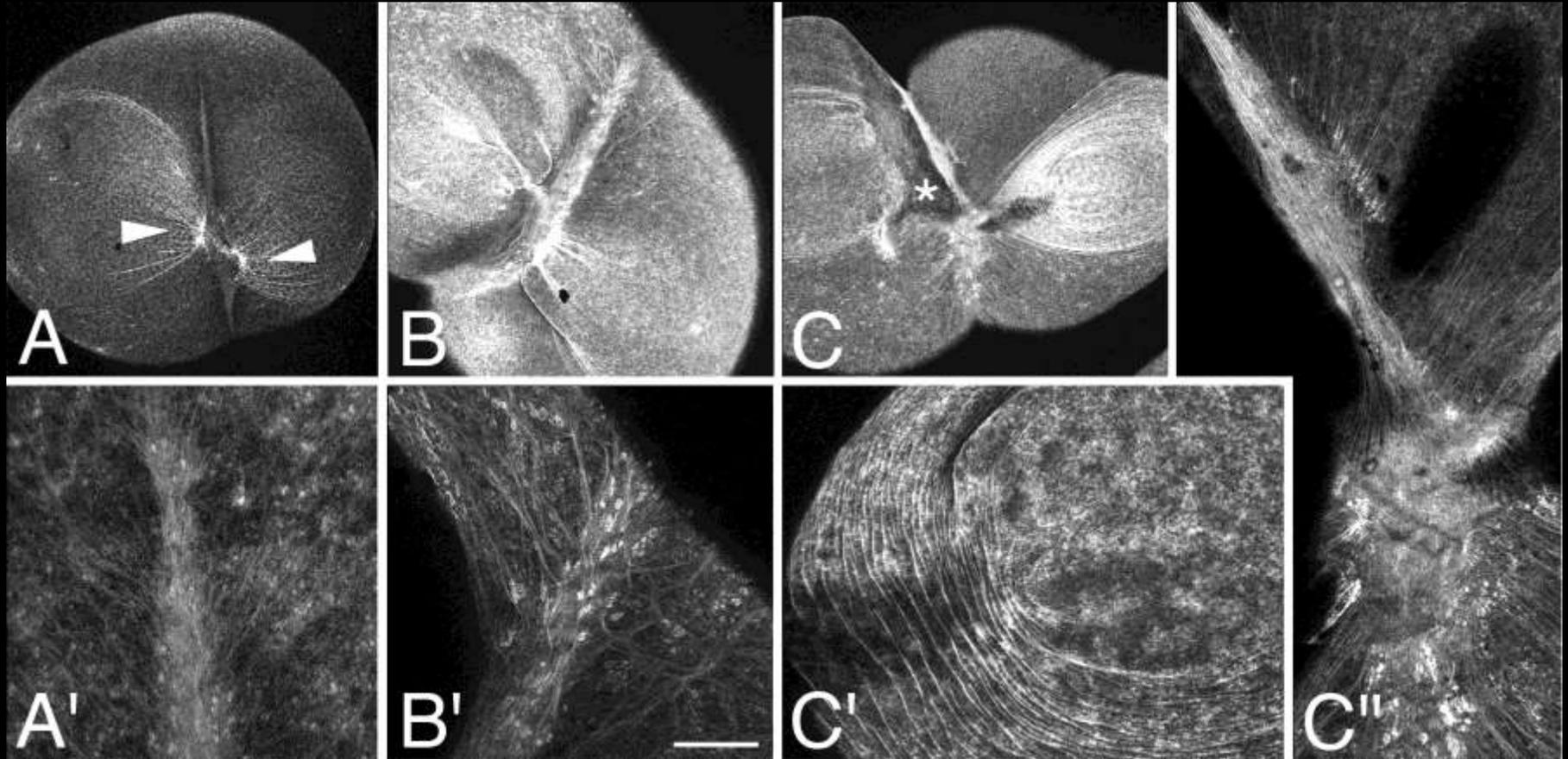


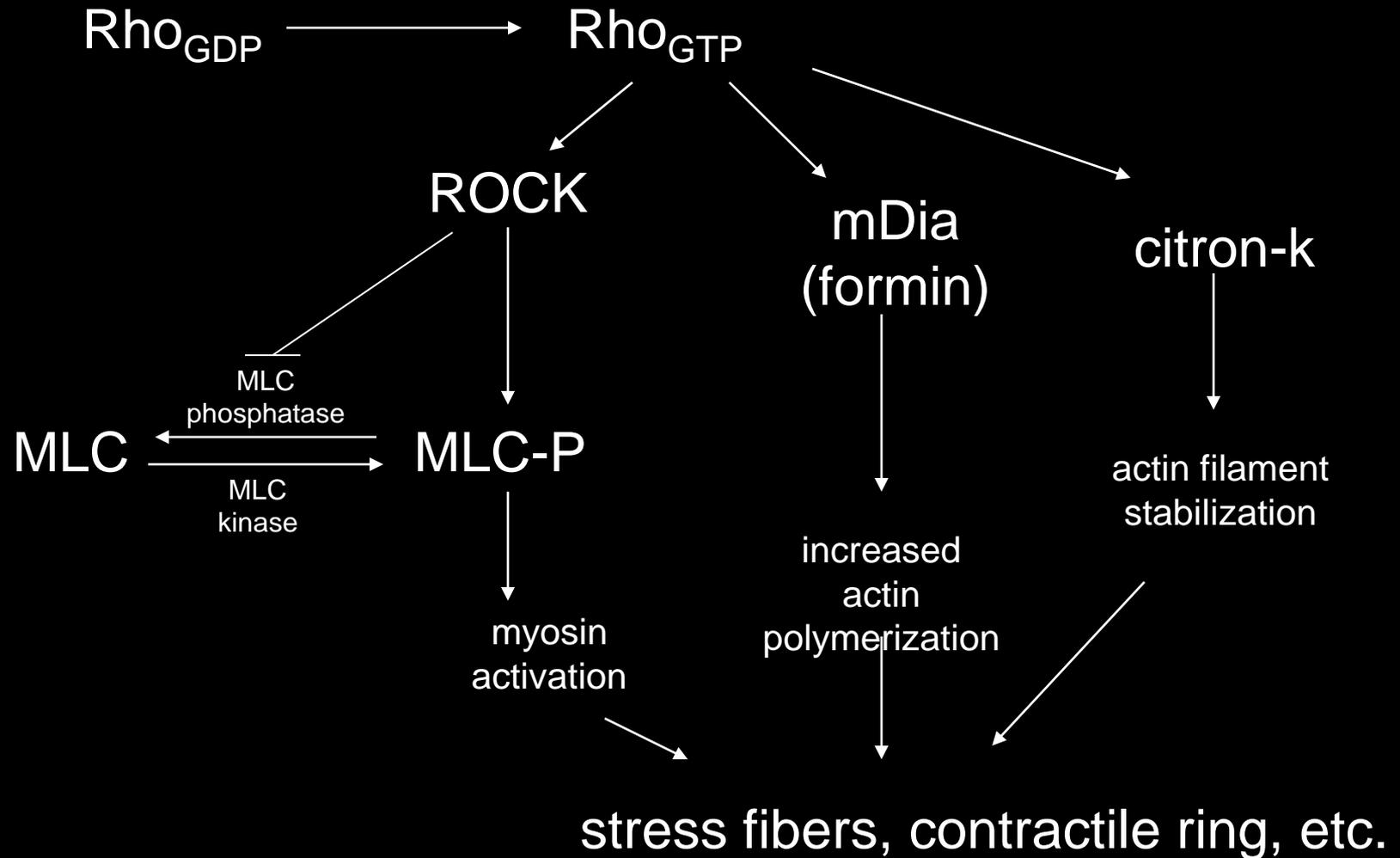
Prick activated in presence of BDM plus the microtubule-depolymerizing drug nocodazole

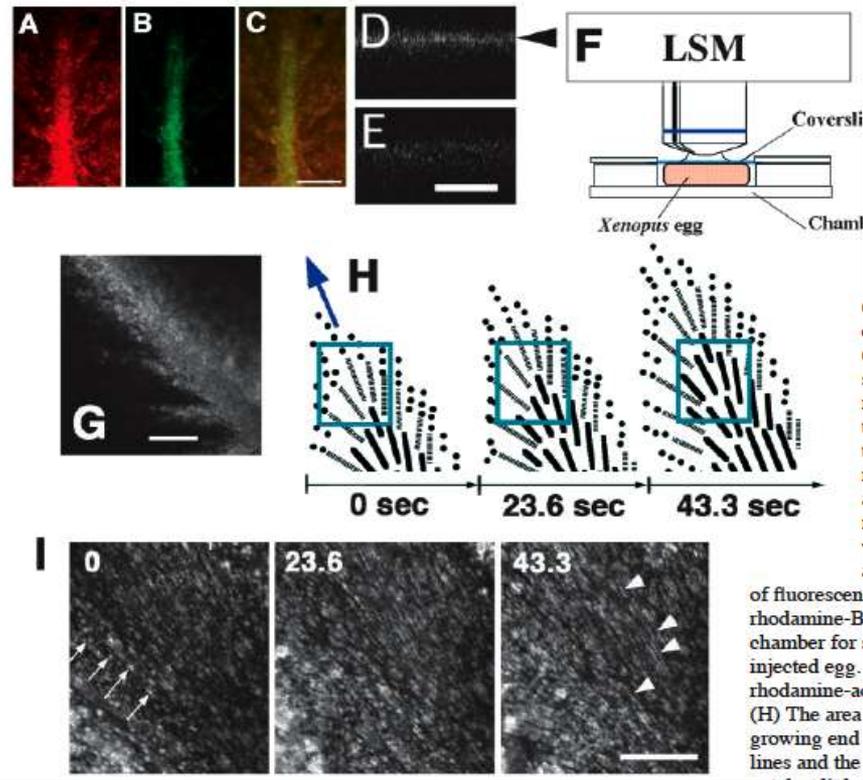
Play movie7.mov!



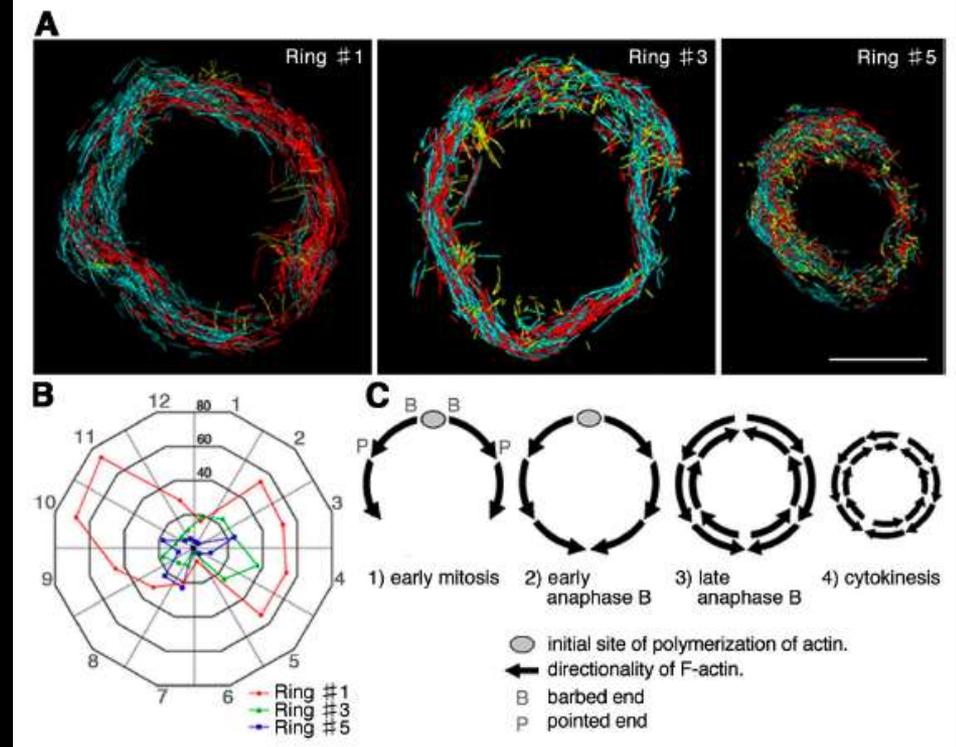
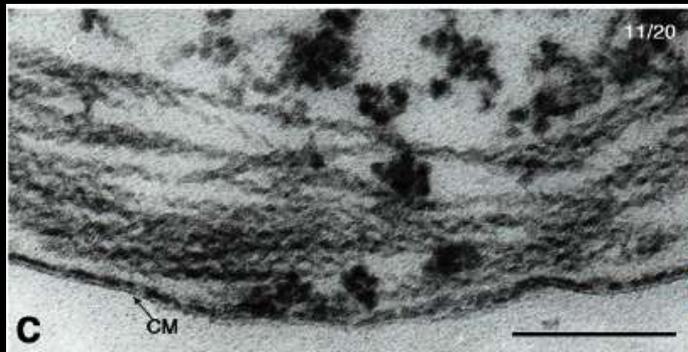
# BDM enhances microfilament bundling







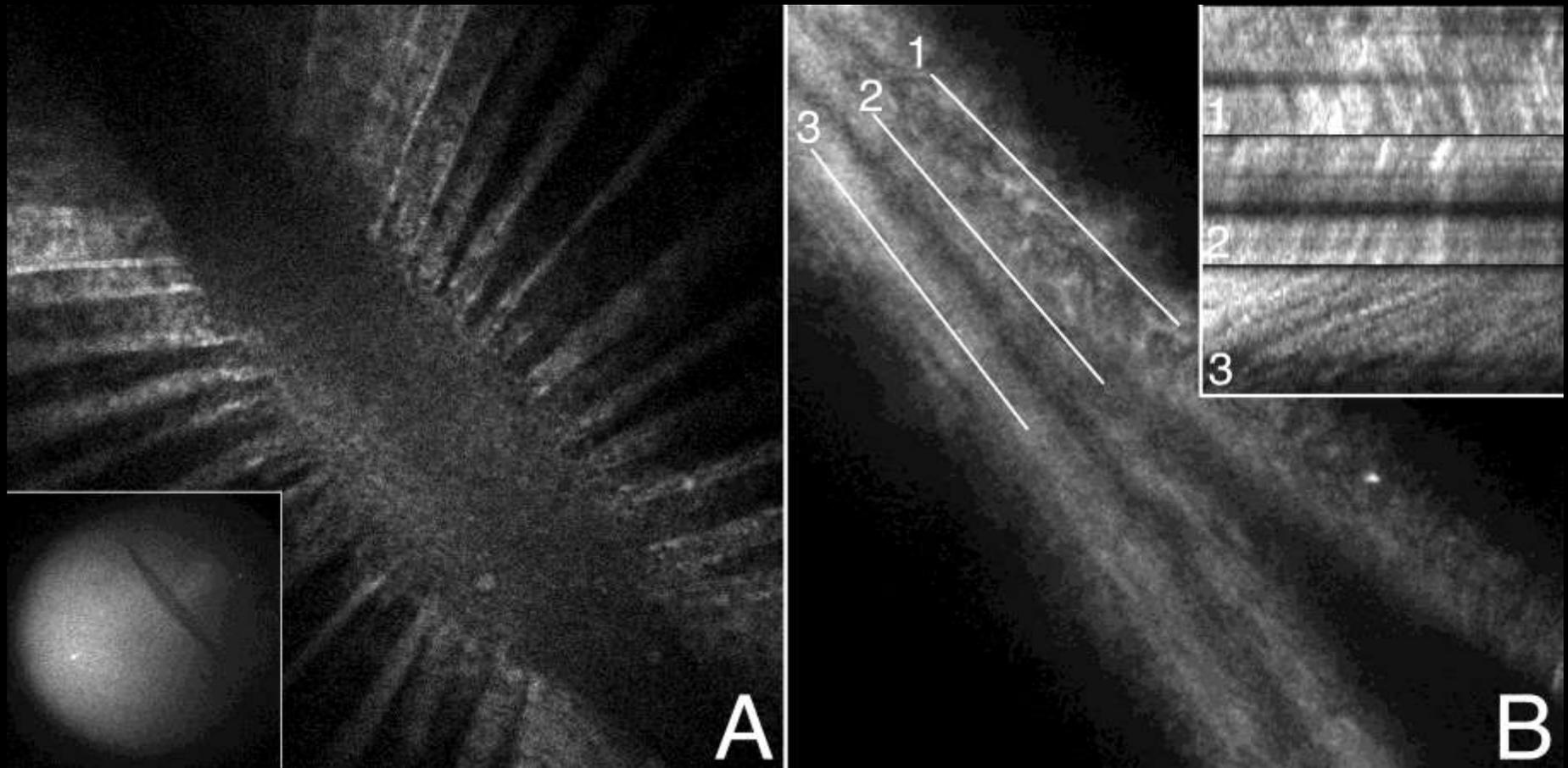
Noguchi&Mabuchi, 2000



Kamasuki&Mabuchi, 2007

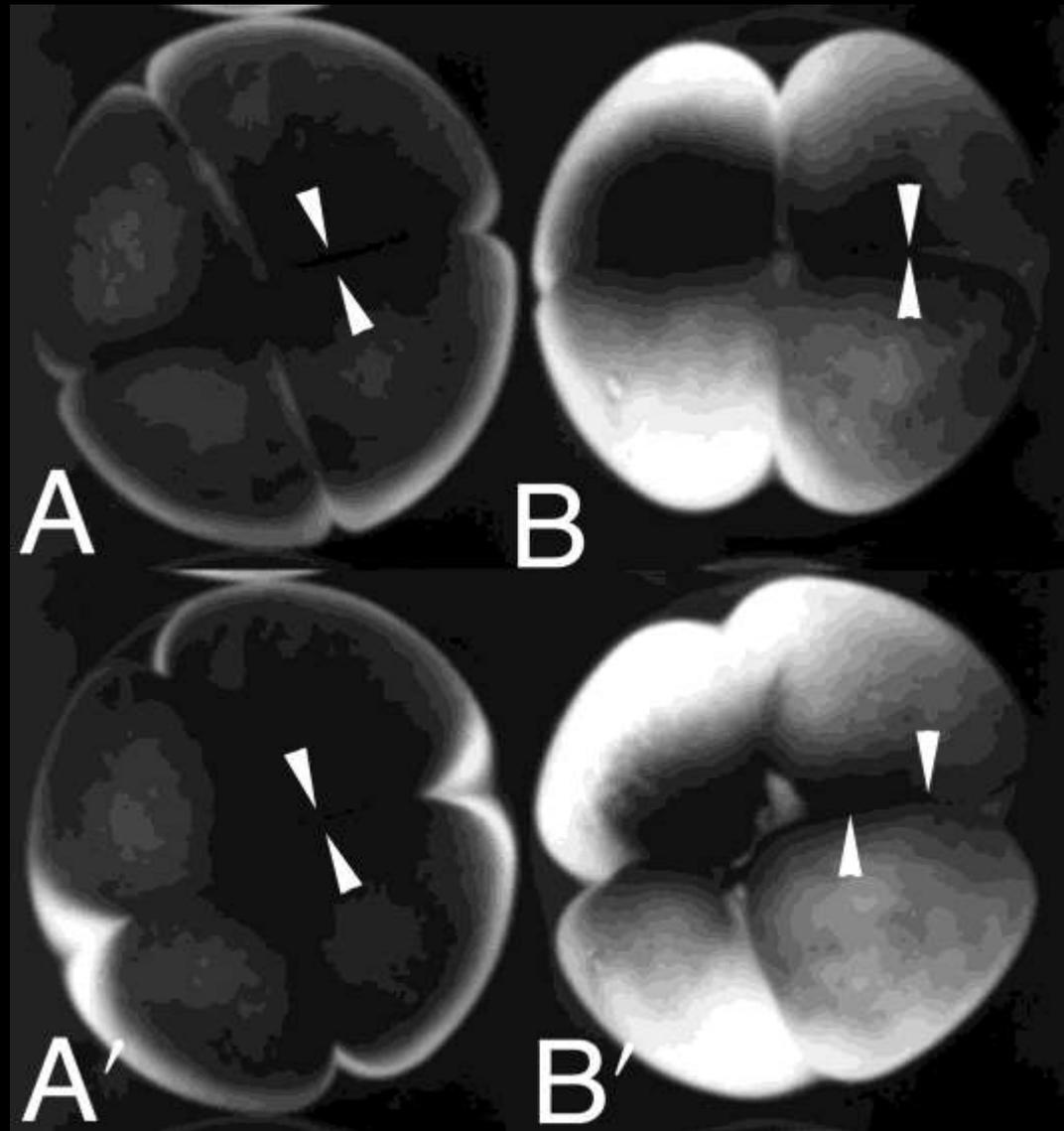


# Fluorescent actin participates in contractile ring assembly and reveals cortical actomyosin torsion

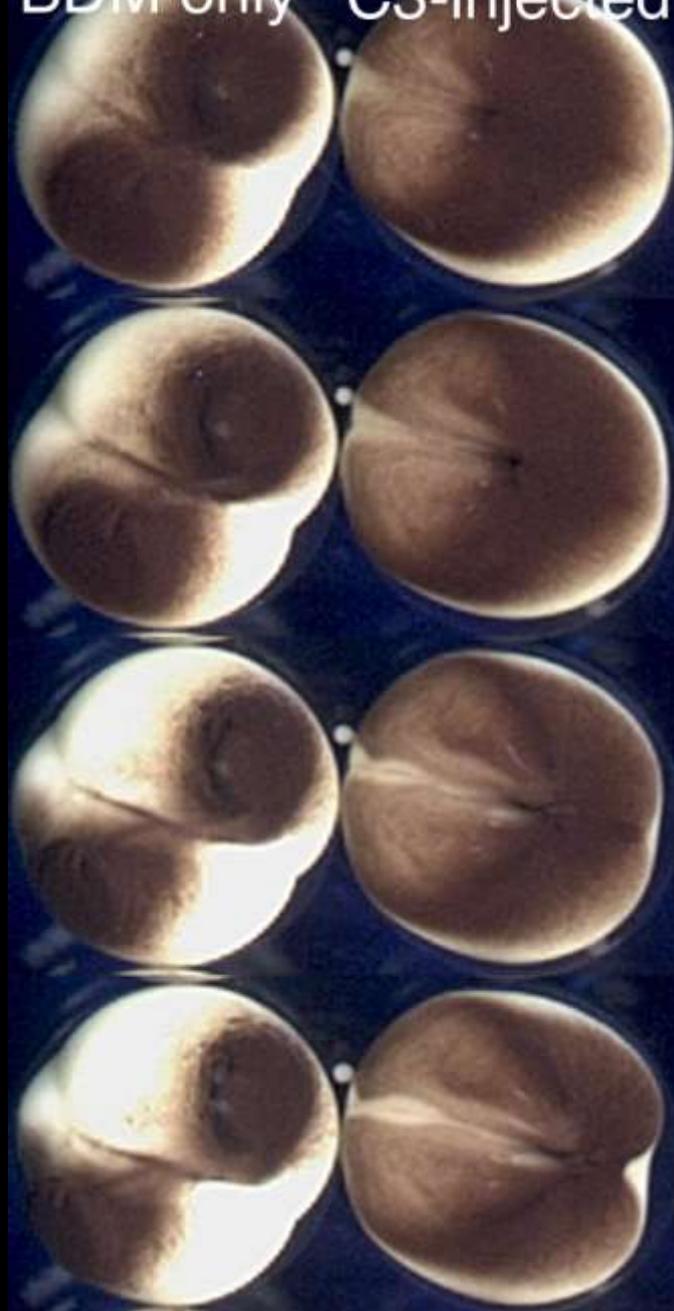


Play "movie6.mov"

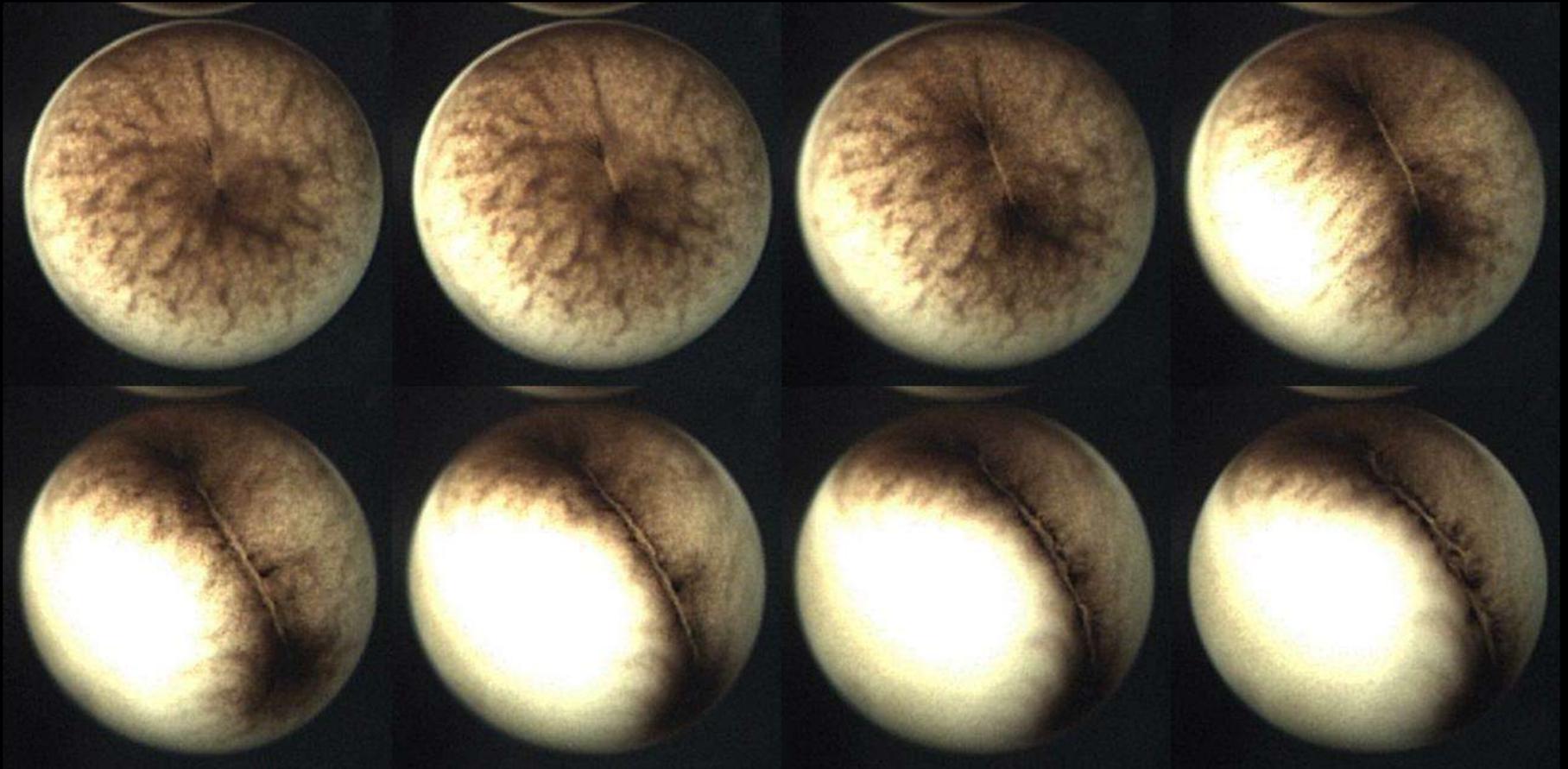
# Injected CA-Rho



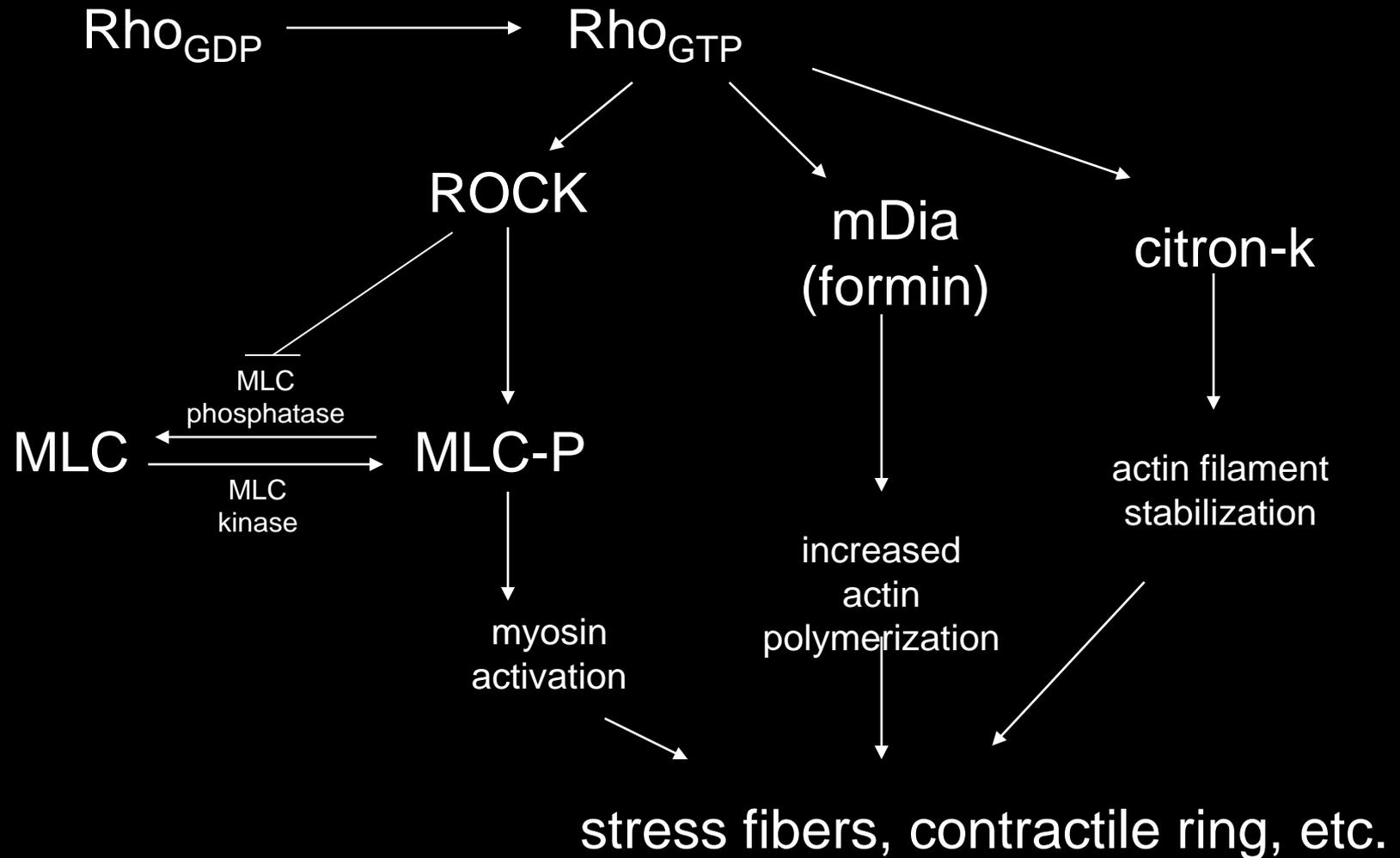
BDM only C3-injected



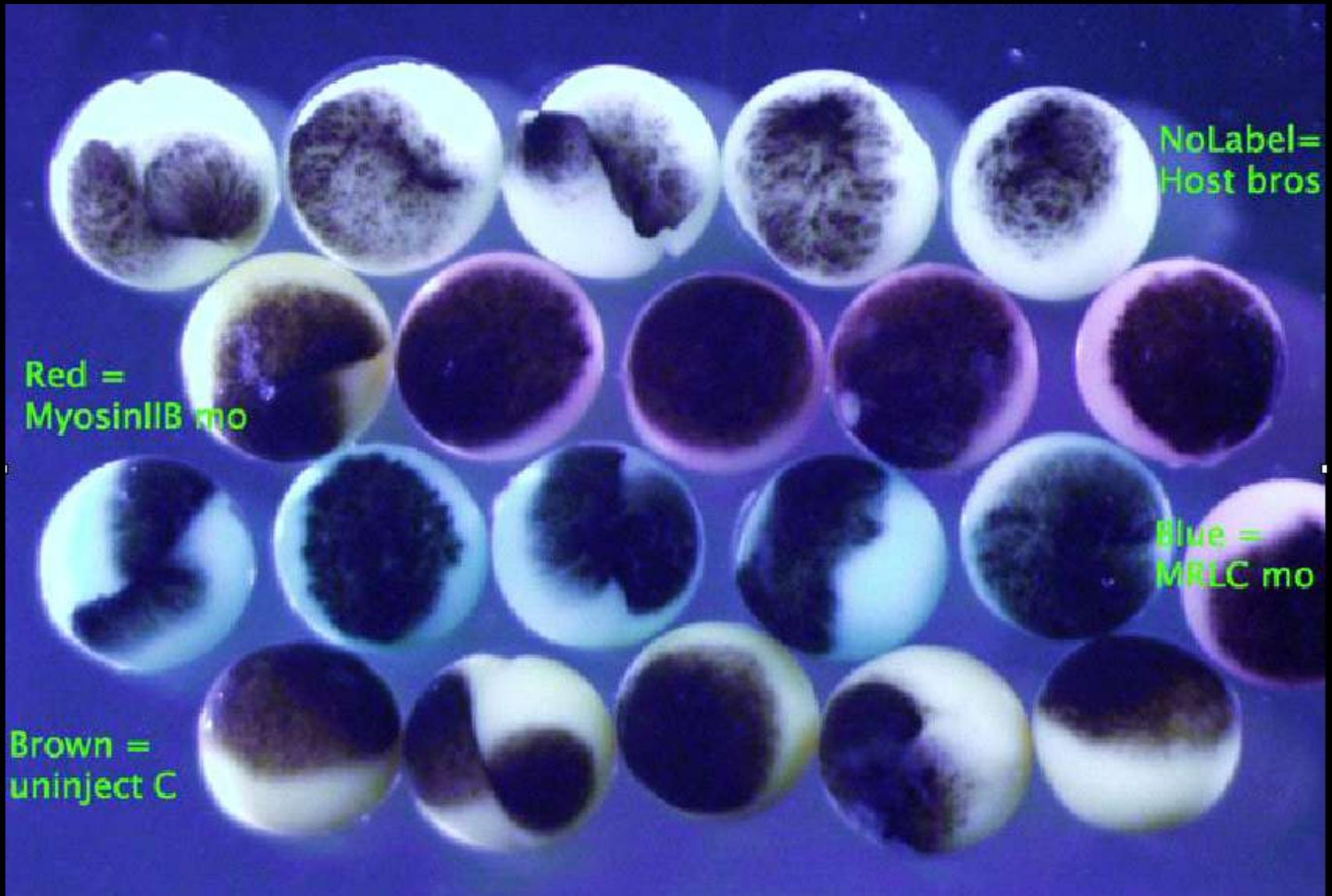
CA-Rho injected 70 min after activation induces  
CCW-shearing pseudofurrow

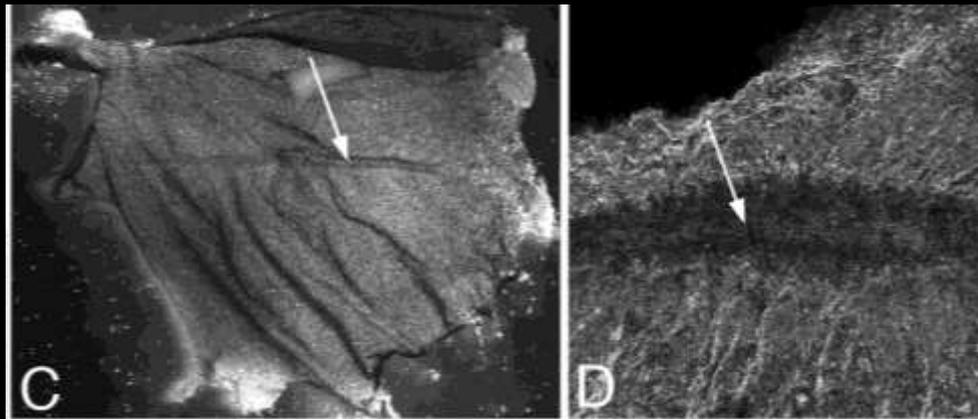


Play "movie9.mov"

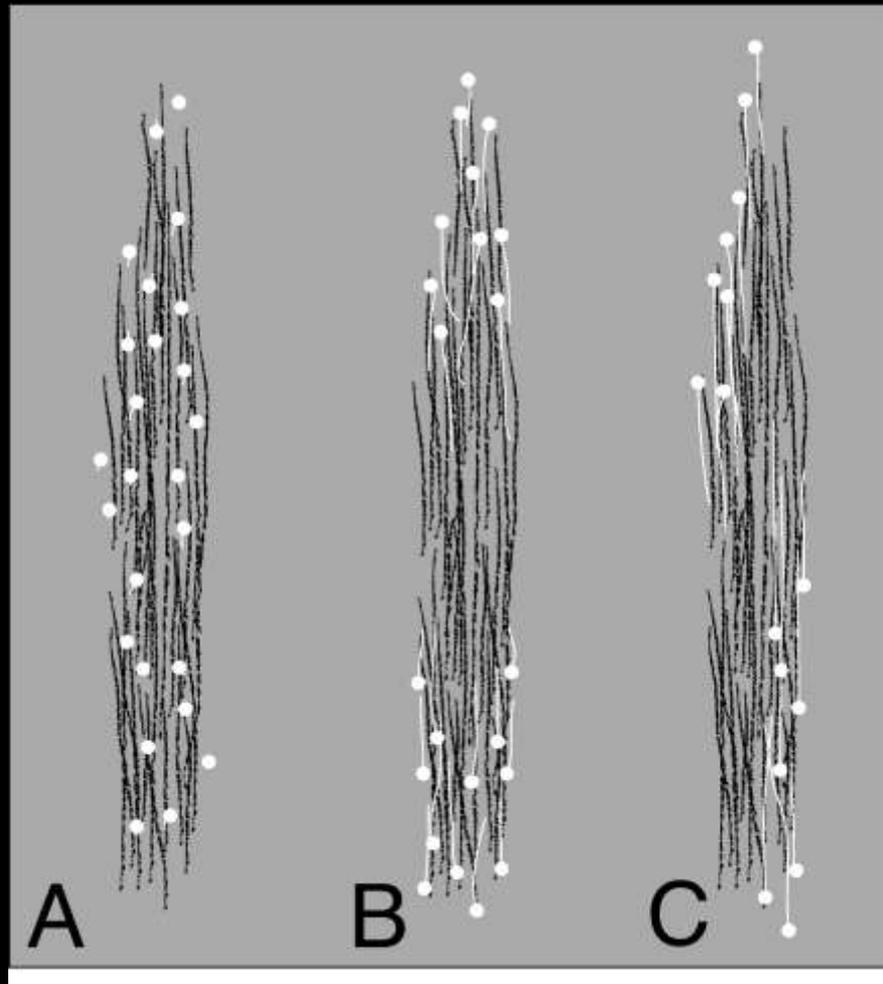


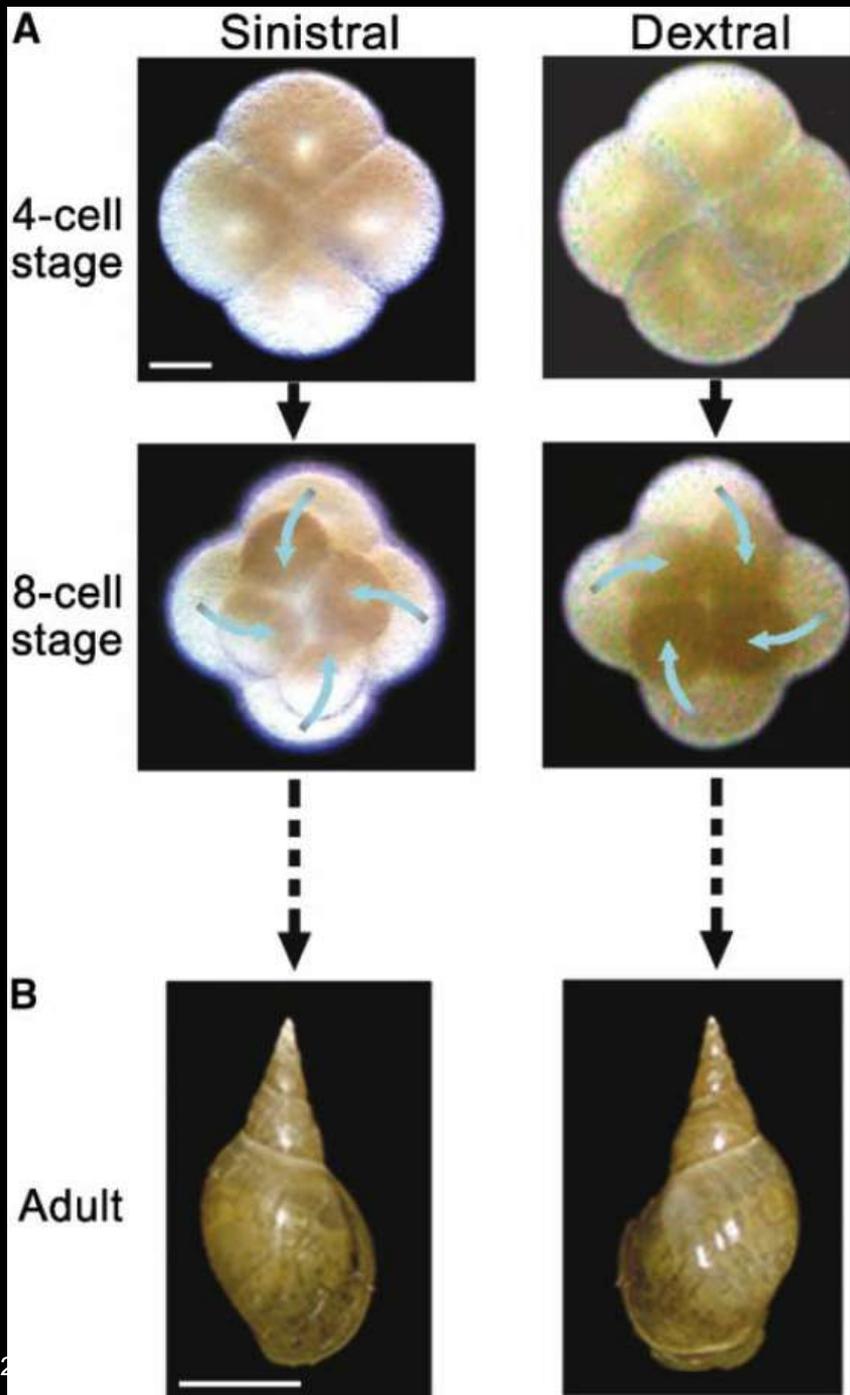
# MyoIIB morpholino KO interferes with chiral response to BDM





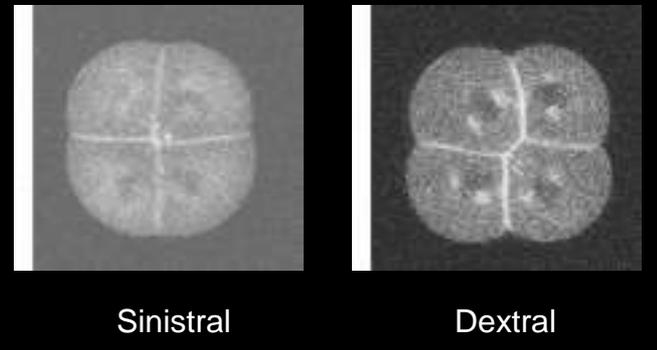
Phalloidin staining (for f-actin)





Shibazaki et al. (2004) Current Biology

## Spiral cleavage, *Lymnaea*



Wilhelm Roux's Archives 177, 193—203 (1975)  
© by Springer-Verlag 1975

### Asymmetrical Rotations of Blastomeres in Early Cleavage of Gastropoda

V. N. Meshcheryakov and L. V. Belousov

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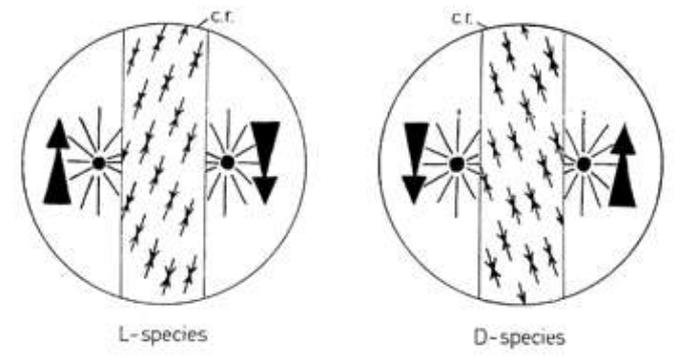
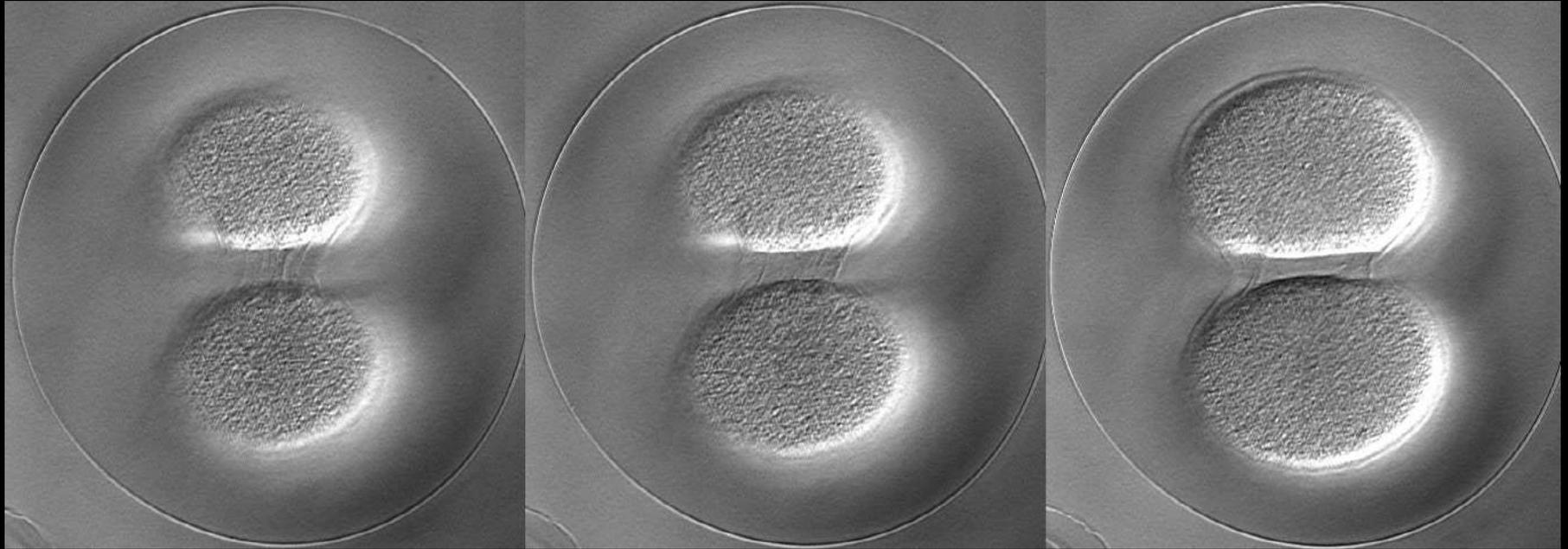
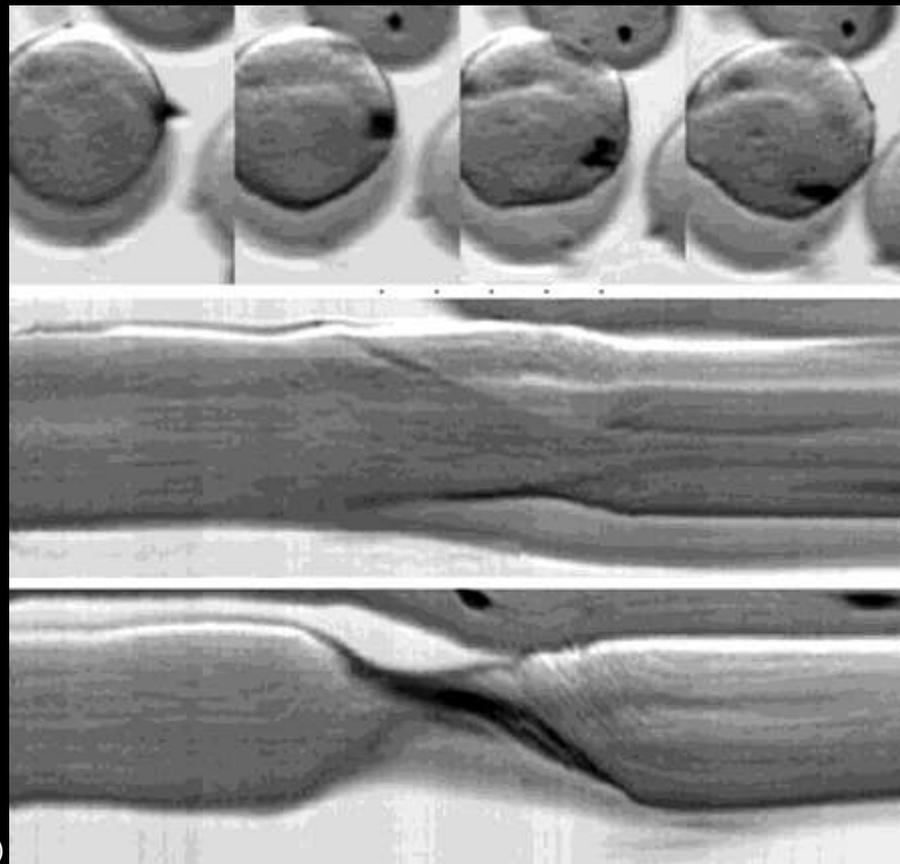
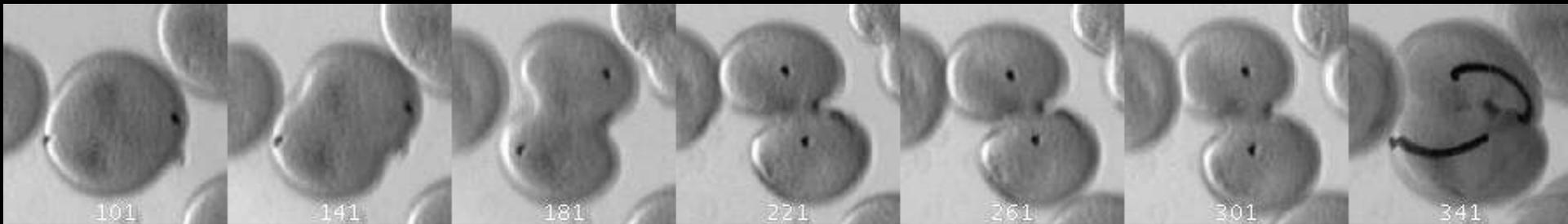


Fig. 8. A scheme, illustrating the hypothesis of the "spiral contractile ring". We postulate that a contractile ring (c.r.) of microfilaments would be characterized by a mechanical integrity and is bound with the plasma membrane. In order to shift the surfaces of sister blastomeres in a direction indicated by thick arrows, the forces of contractile deformation must be oriented within the ring as shown by thin arrows

*Dendraster excentricus*; no treatment



# BDM treatment induces CCW torsion in sand dollar embryo during contractile ring constriction



# Observations

- Normal cleavage in two deuterostomes shows subtle signs of consistent chirality, reminiscent of spiralian (protostome) cleavage (!)
- BDM-treatment provokes strongly chiral cleavage, probably by ectopically activating a step or steps in RhoA pathway
- Chirality is entirely a property of actomyosin in the cortex, not requiring instruction via MTs or centrioles
- BDM exposure during early cleavage period produces situs inversus & twinning, possibly by influencing/entraining MT vegetal-cortical organization

## Conclusions

- Cortical actomyosin reveals tendency to organize chirally during first cell cycle without input from microtubules
- Contractile ring actomyosin assembly also organizes and operates chirally
- A cleavage-stage step in left-right patterning exists

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