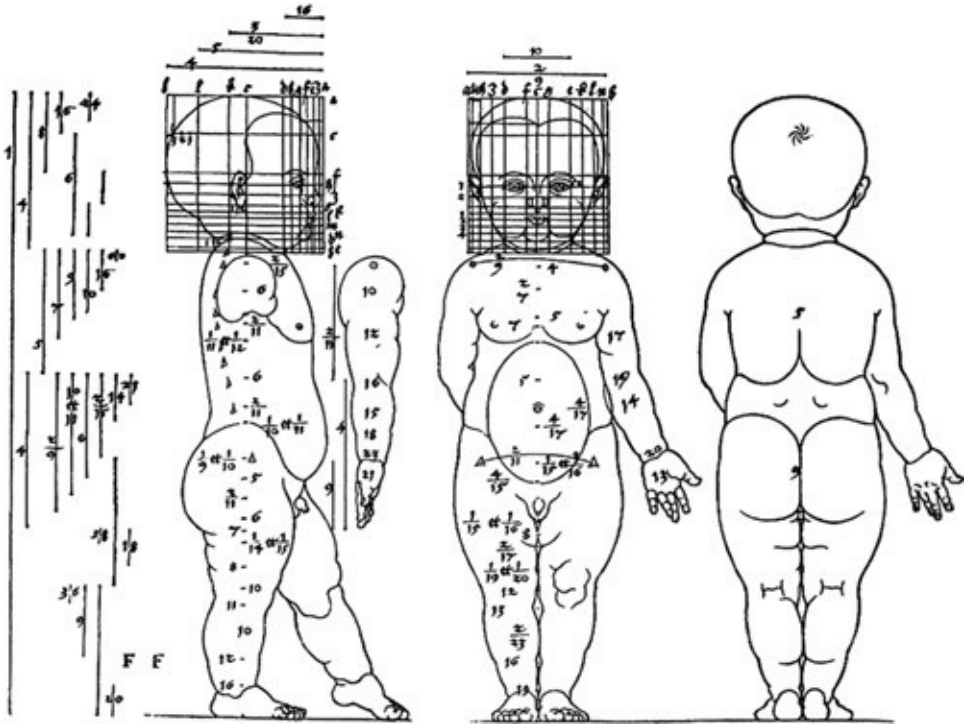
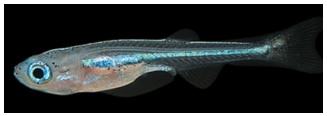
Breaking symmetry: embryonic establishment of body axes (I)

Sept. 11, 2024

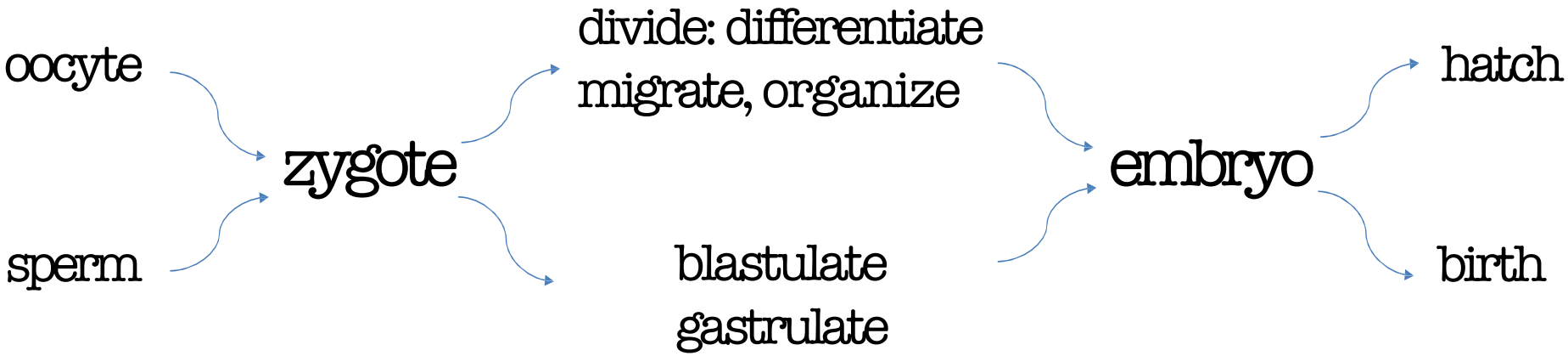
Three body axes define asymmetries



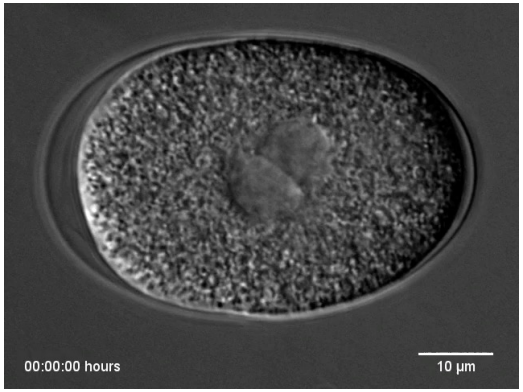
sketch: Albrecht Durer

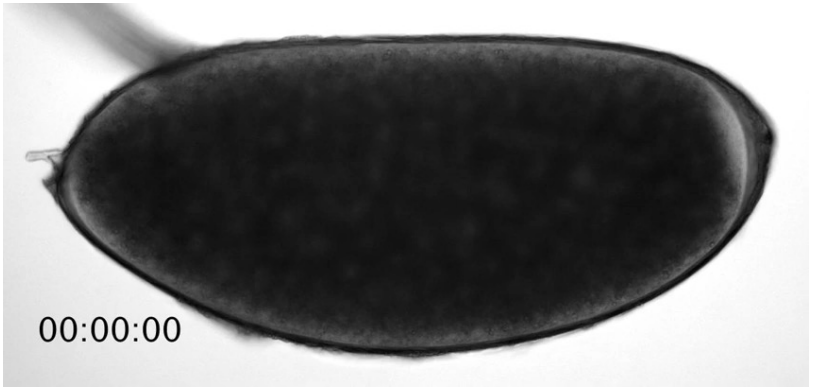


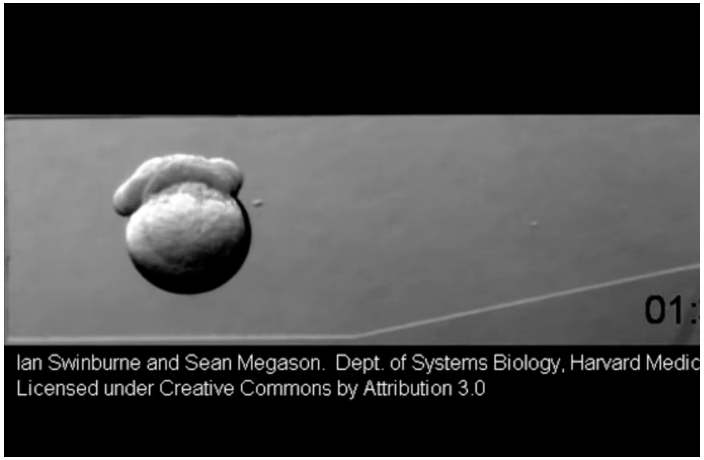
When do you start?

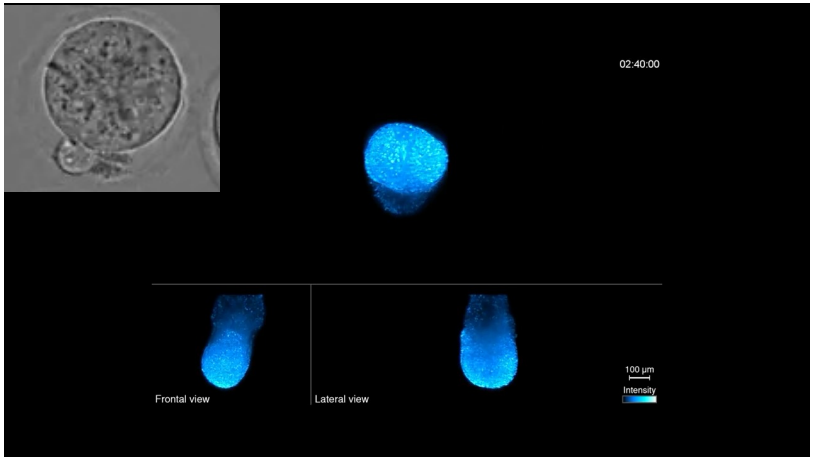


Zygotes: some break symmetry earlier than others









Does the early polarity relate to final body planes?

- How might we study this question?
- How is early polarity established?

What to ask, while we learn a bit about it? e.g.

Is there an order to three axial development?

How similar or different is it among animals?

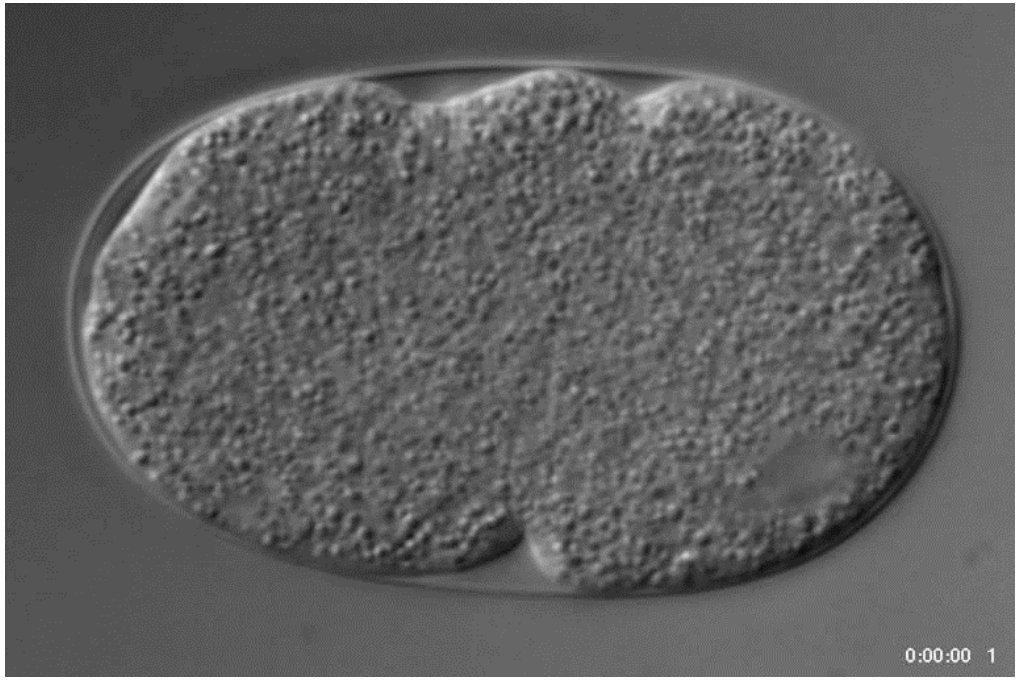
What drives the similarity and difference?

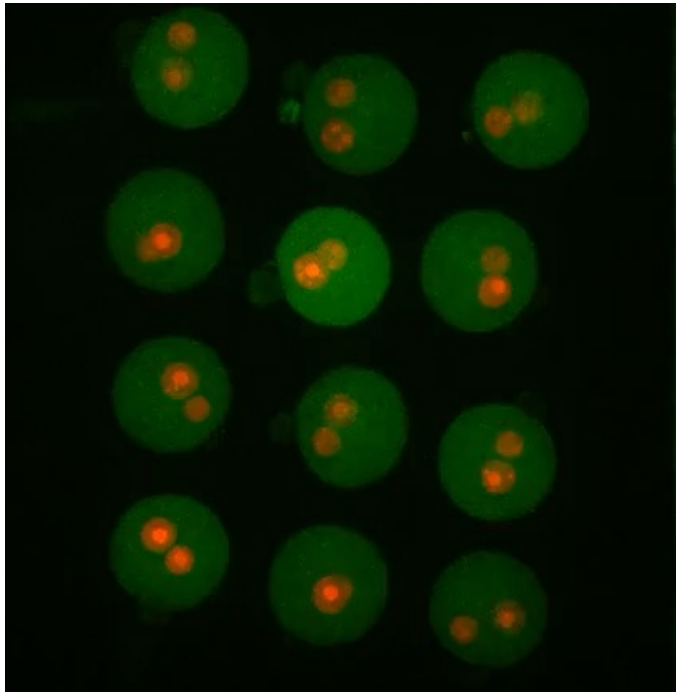
Why asymmetry at all?

How might we study this question?

- Watch and describe

live imaging

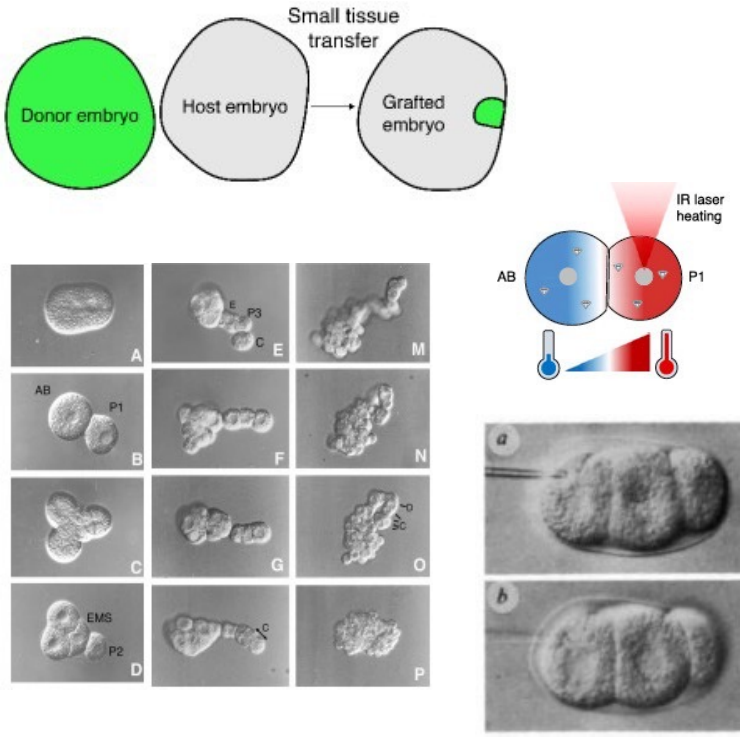




How might we study this question?

- Perturb and sort effects

cell-manipulation



gene-manipulation

- **Mutants**

forward genetic screens

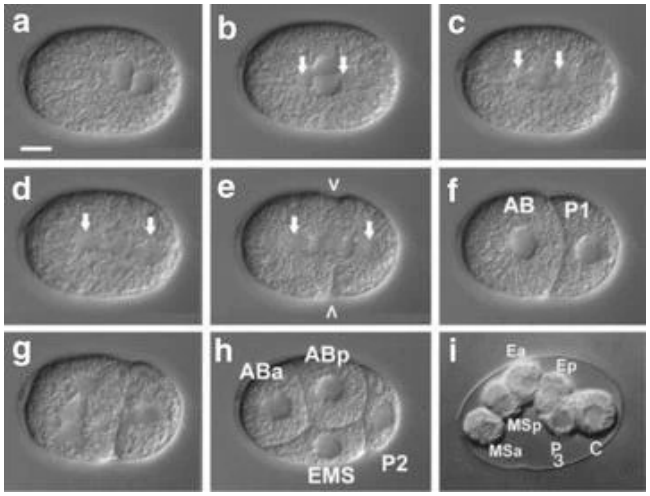
- **'Mutants'**

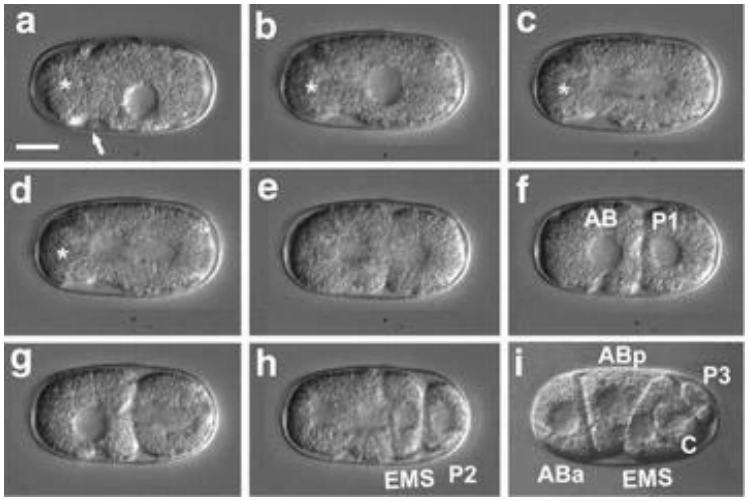
targettd or systematic (genome-wide) knockout, knock down, degradation

How might we study this question?

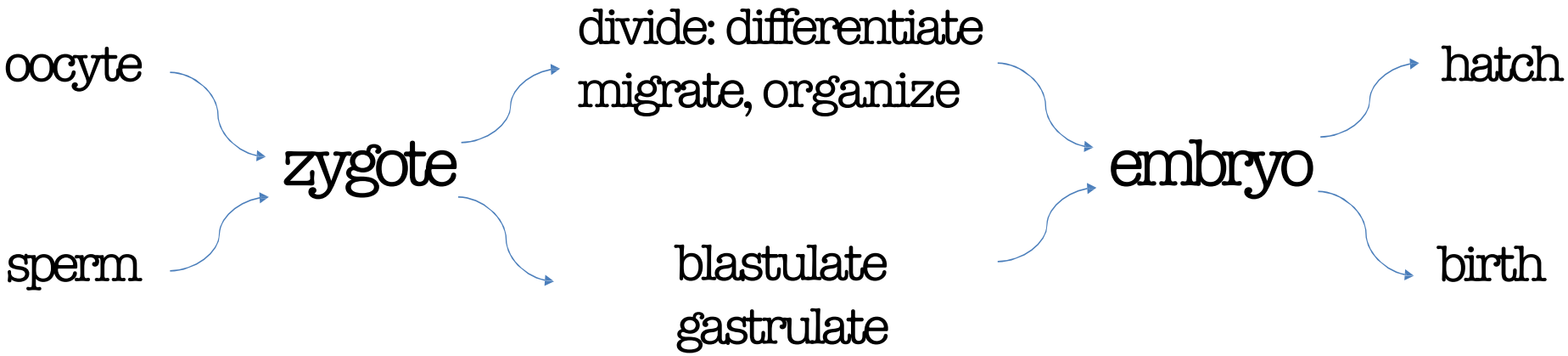
- Compare among sub-species

Correlate genomic-cellular variations





When do you start?



How early is ‘early’?

C. elegans is quite early:

sperm entry + first 3 rounds of divisions

5 asymmetric divisions at 3 planes:

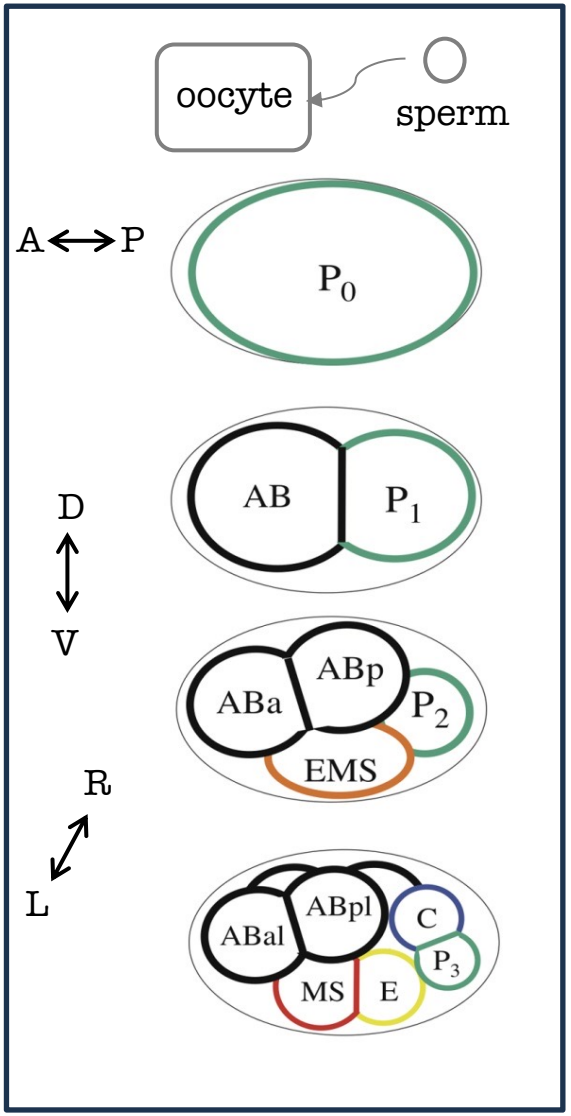
rough alignment with the body axes

6 founder cells (non-exchangeable fate):

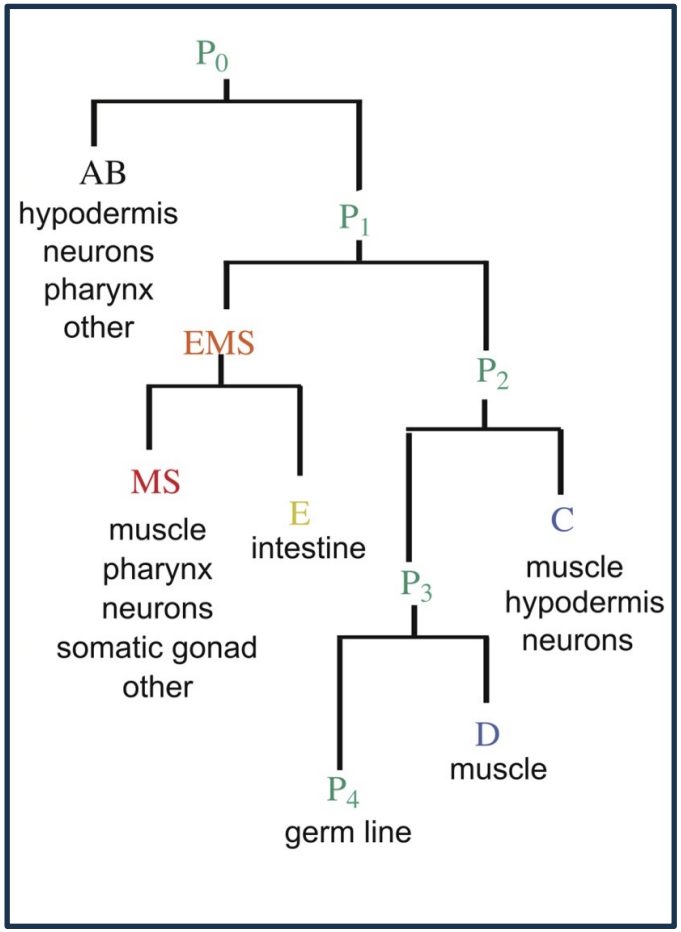
induction-determination

Gastrulation: the final body plane layout

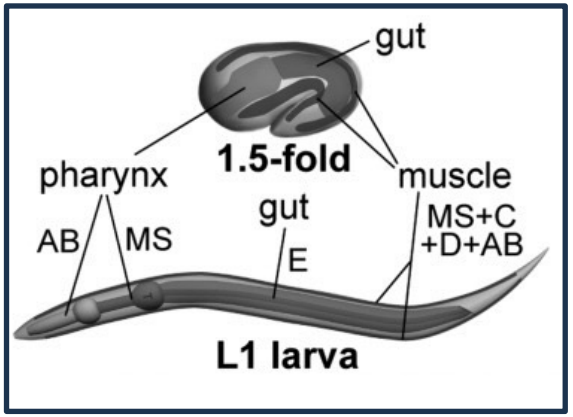
5 asymmetric divisions



6 founder cells



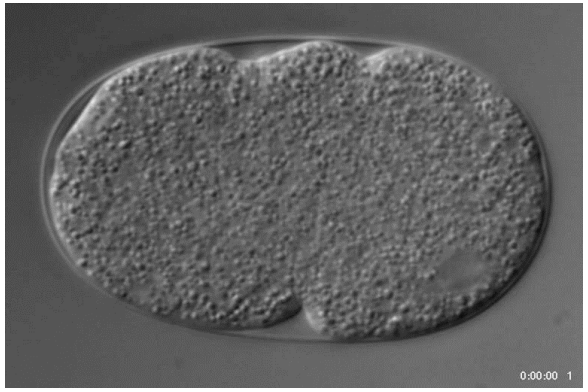
gastrulate & unfold

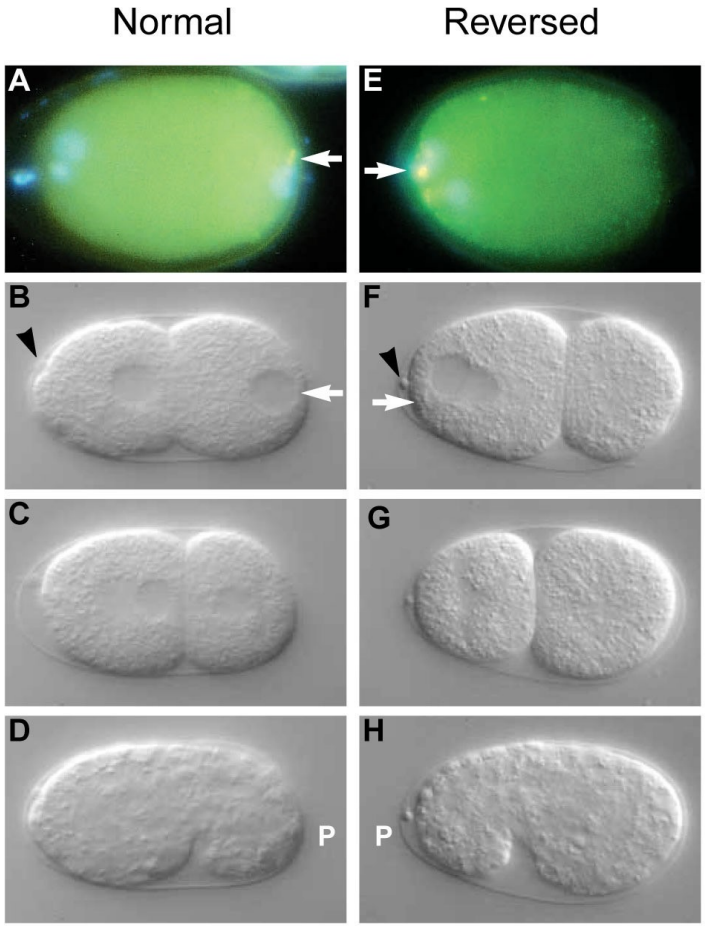


Let's review key evidences

1) A-P axis:

Sperm polarizes zygote, the and A-P asymmetry in the first division.





What do you see happening in a newly fertilized oocyte?

Oocyte meiosis: expulsion of polar bodies

Membrane ruffling: caused by contractions of cortical actomyosin network; sperm pronucleus moves close to posterior cortex.

Adjacent cortex stops ruffling: smooth membrane domain spreads toward anterior.

Cytoplasmic flows: as cortical cytoplasm flows toward anterior, deeper cytoplasm flows toward posterior.

Pronuclei migration: the sperm and oocyte pronuclei meet near centre of embryo

Mitotic spindle formation: pronuclei rotate, nuclear envelopes break down, spindle forms

Spindle oscillation/1st mitosis

Table I Maternal Loci in *C elegans*: Gene Names and Molecular Identities (See Text for References)

Gene	Name	Molecular identity
	Par Group Genes	
let-99	*Let*hal	?
par-1	*Par*titioning-defective	Ser–Thr kinase; binds a nonmuscle myosin
par-2	Same	Novel; ATP-binding site
par-3	Same	Novel; two PDZ domains
par-4	Same	Ser–Thr kinase
par-5	Same	?
par-6	Same	?
mes-1	*M*aternal-e*ff*fect *s*terile	?
	Blastomere Identify Group Genes	
P_1 subgroup		
pal-1	*P*osterior *al*ae defective	Homeodomain protein; putative transcription factor
pie-1	*P*harynx and *i*ntestine *e*xcess	TIS-ll-like Zn^{2+} finger ptn
skn-1	*Skn* excess	bZIP-like putative transcription factor; lacks a leucine zipper
pop-1	*P*osterior *p*harynx defective	HMG domain protein; putative transcription factor
mom-1	*M*o*m* e *m*esoderm	Porcupine homologue; ER protein required for Wnt secretion
mom-2	Same	Wingless/Wnt homologue; putative secreted glycoprotein ligand
mom-3	Same	?
mom-4	Same	?
mom-5	Same	Frizzled homologue; putative receptor for Wnt ligands
AB subgroup		
aph-2	*A*nterior *ph*arynx defective	Novel membrane-associated extracellular protein
apx-1	*A*nterior *p*harynx e*x*cess	Delta-like transmembrane protein; putative GLP-1 ligand
glp-1	*G*erm*l*ine *p*roliferation defective	Notchlike transmembrane protein; putative receptor
	Intermediate Group Genes	
mex-1	*M*uscle *ex*cess	TIS-11-like Zn^{2+} finger ptn
mex-3	Same	Two KH domains; putative RNA-binding protein
pos-1	*Pos*terior localized mRNA	TIS-11-like Zn^{2+} finger ptn

What might be the sperm's polarity cue?

Its pronucleus or DNA? No!

embryos show normal polarity when oocytes are fertilized by anucleate sperm (Sadler and Shakes, 2000. Development 127: 355-366.)

Its centrosomes? Yes!

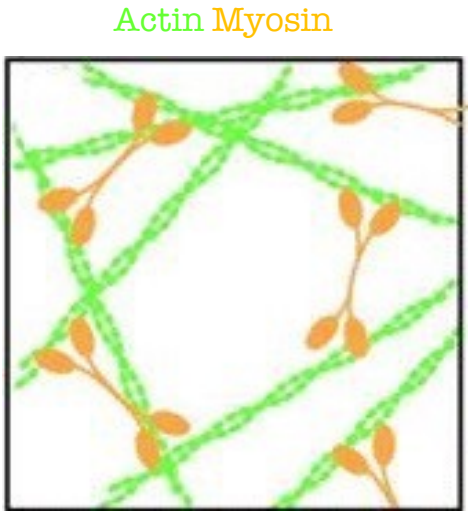
embryo fails to polarize when its centrosome was destroyed by a laser (Cowan and Hyman, 2004. Nature 431: 92-96.)

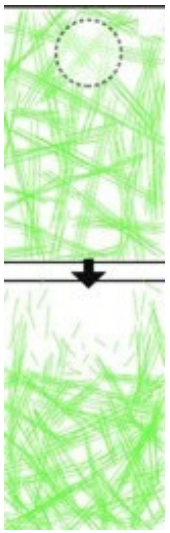
Requirement for initiating embryo polarity, from the centrosome:

its microtubule extension to cortex
its close association with cortex
its component: e.g. Aurora kinase AIR-1

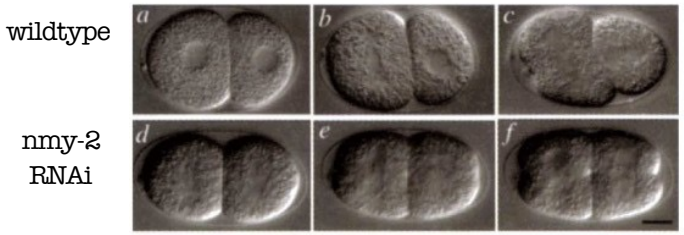
How might the centrosome polarize the zygote?

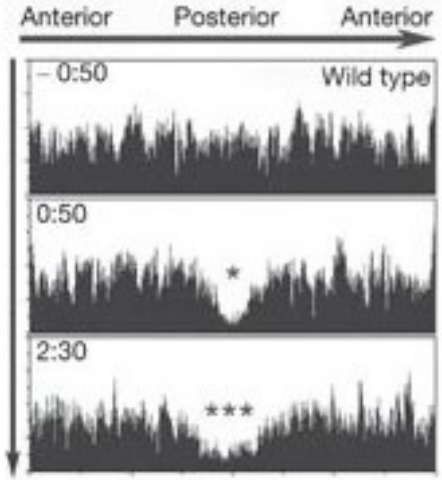
asymmetric cortical actomyosin contraction





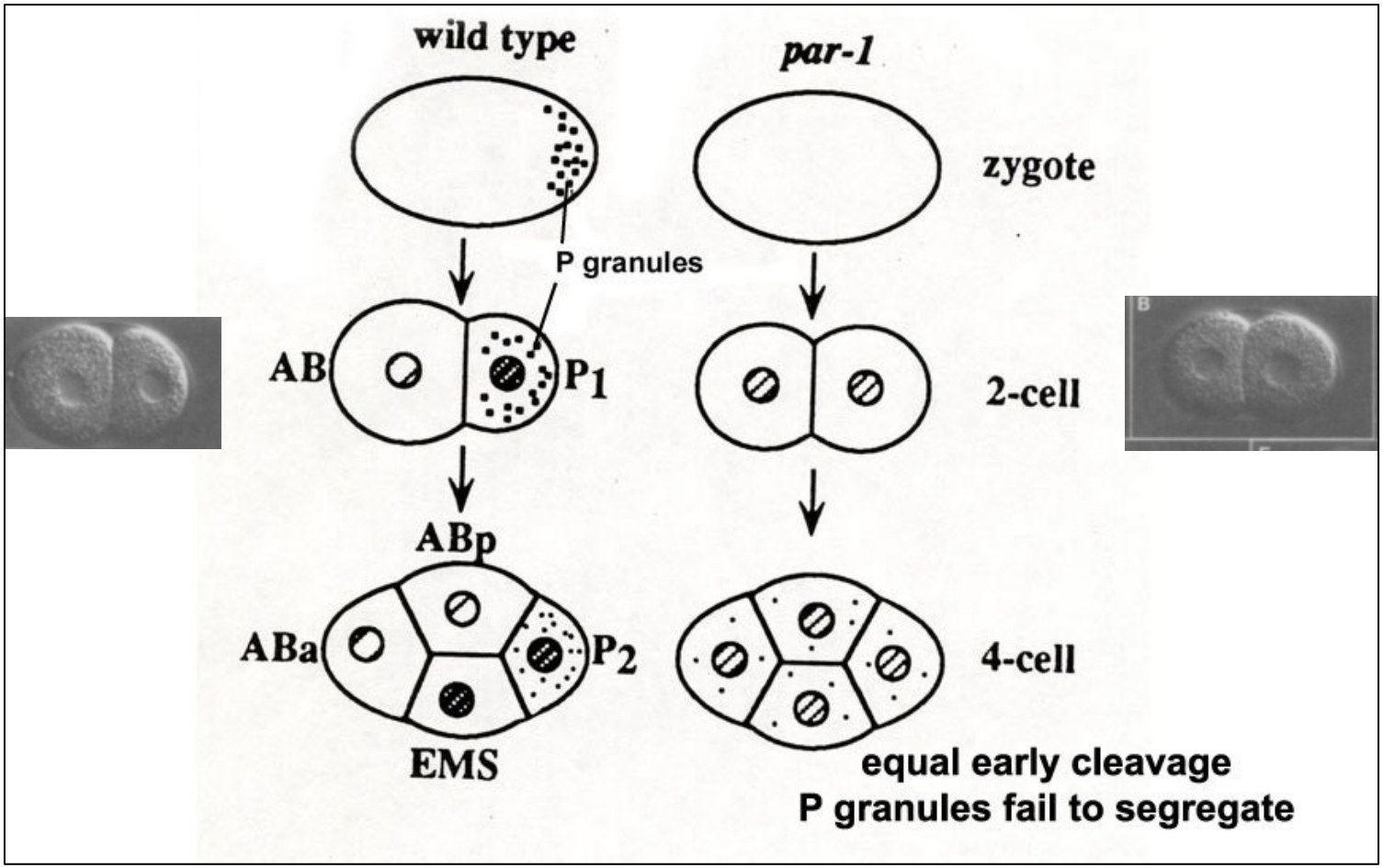
- Cytochalasin D blocks all division asymmetry
- Removing non-muscle myosin blocks polarity
- Posterior cortex RhoGEF cortex is excluded, which requires centrosome proteins





How might cortical contraction polarize the zygote?

polarized cortical par location (I)



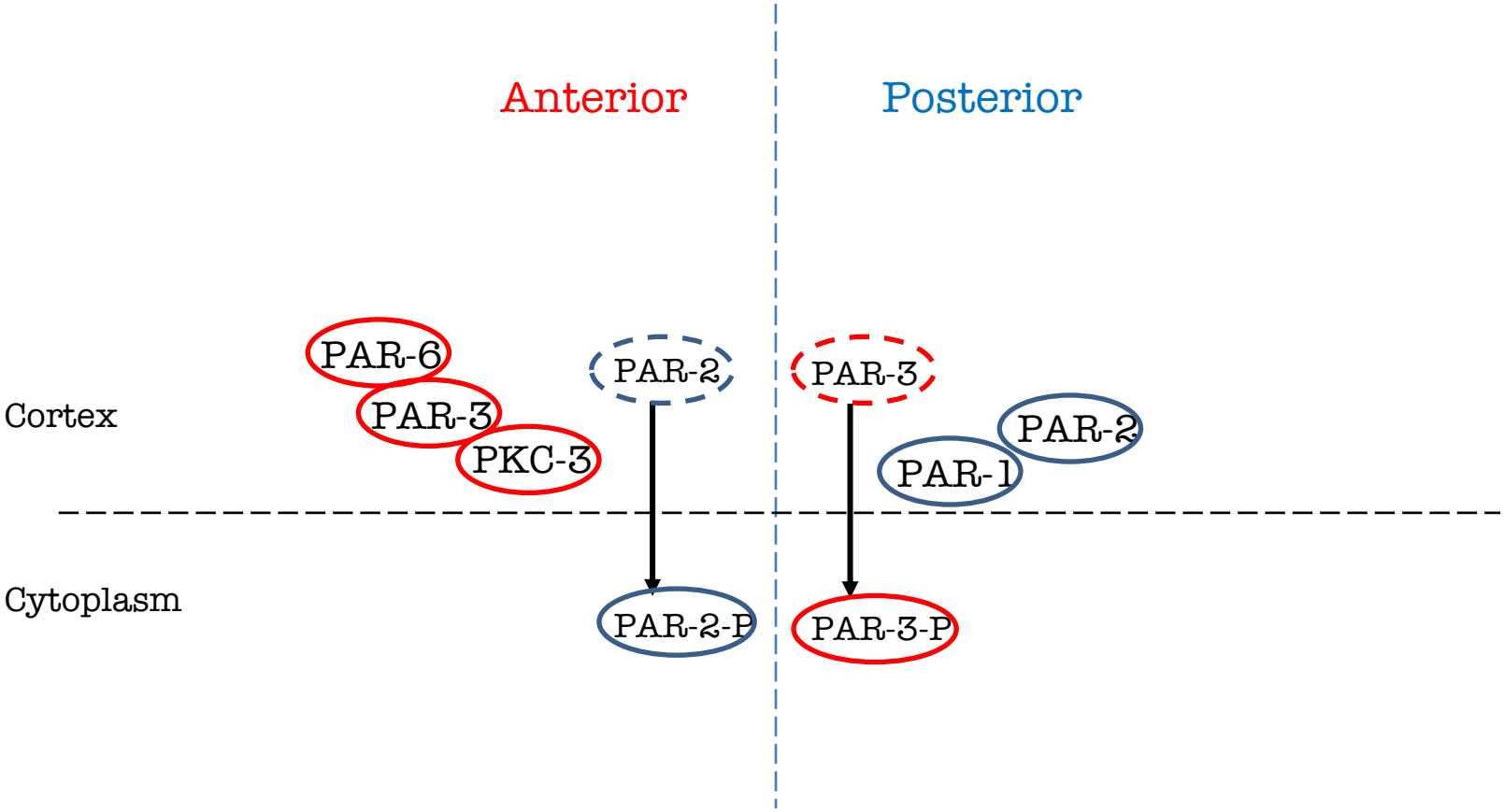
How might cortical contraction polarize the zygote?

polarized cortical par location (II)

PAR-6

PAR-2

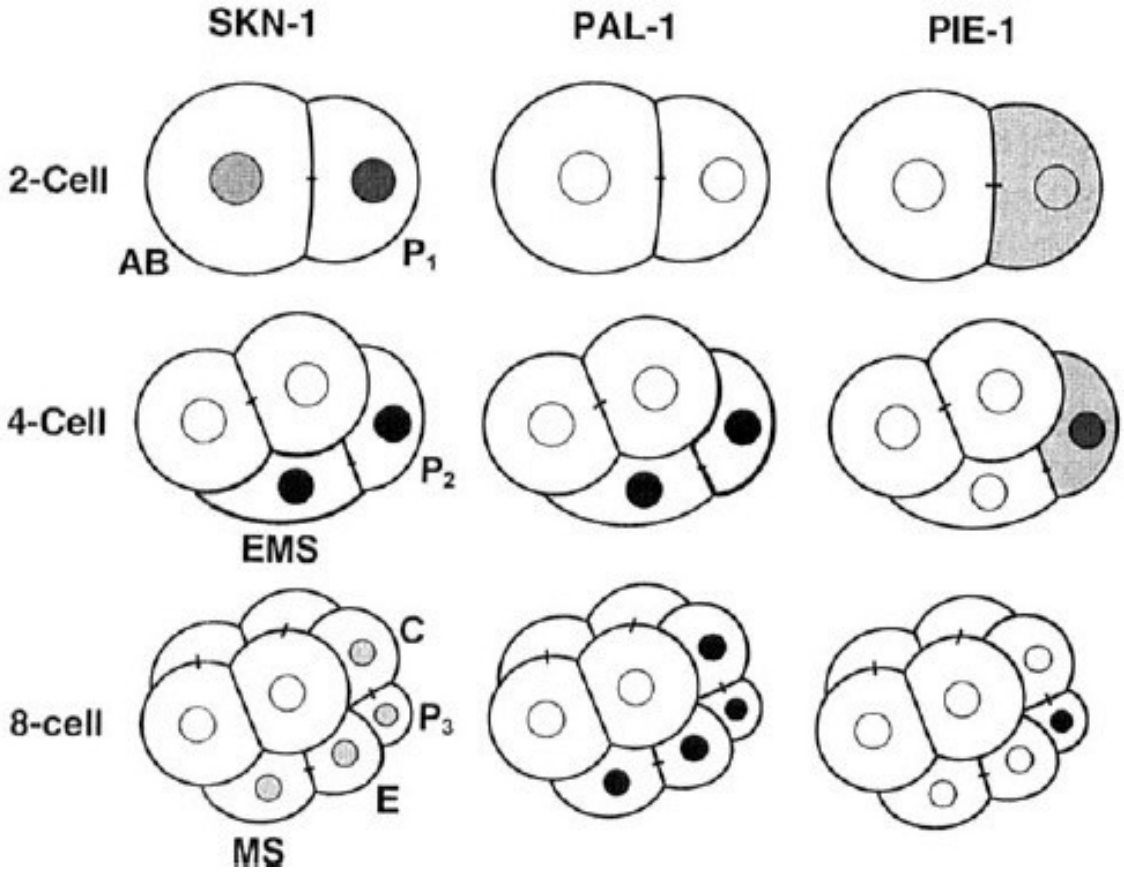
Maintenance: mutual inhibition between PAR Proteins



PKC-3 phosphorylates PAR-2, prevents its cortical localization.
PAR-1 phosphorylates PAR-3, excludes anterior PARs from cortex

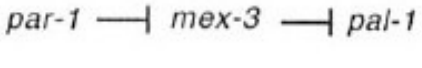
How might the blastomere cell fate be specified?

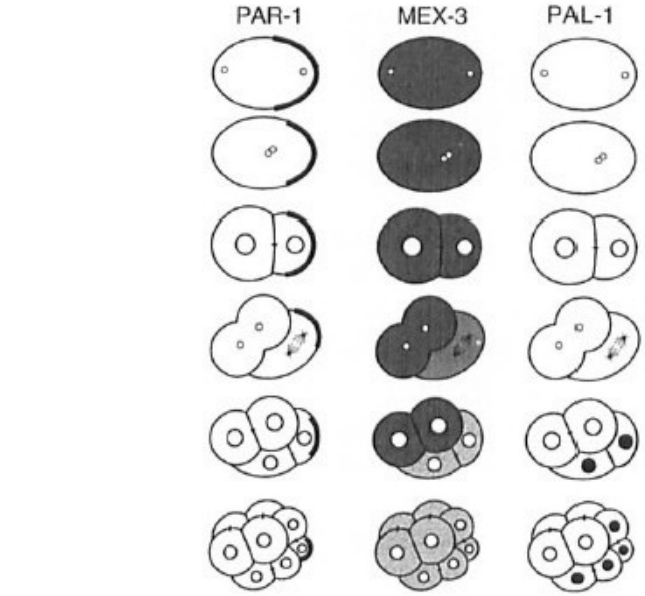
founder cell transcription factors

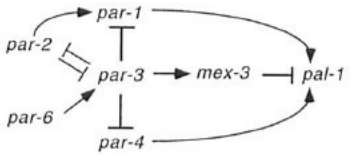


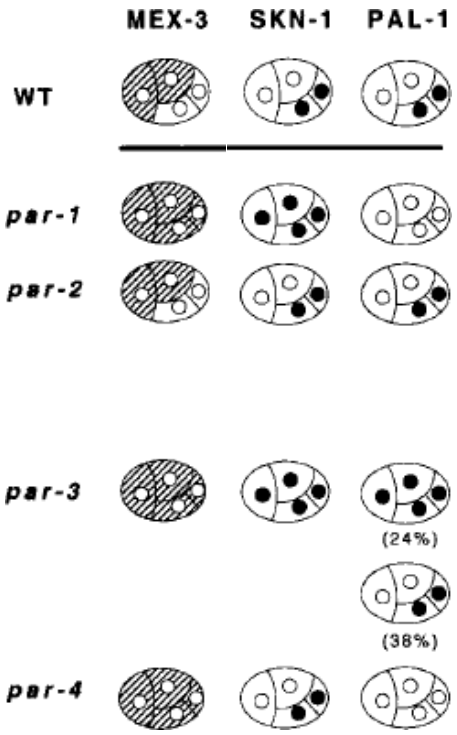
How might the blastomere cell fate be specified?

founder cell transcription factors

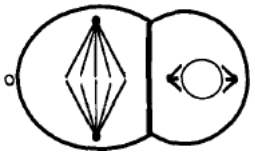


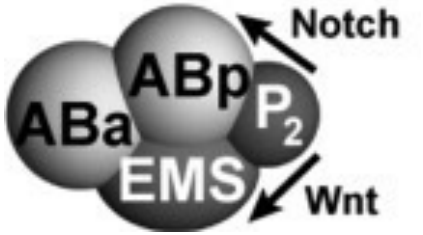


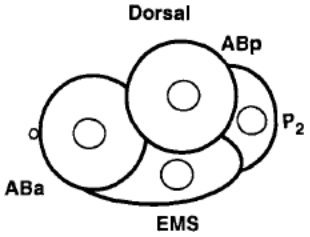


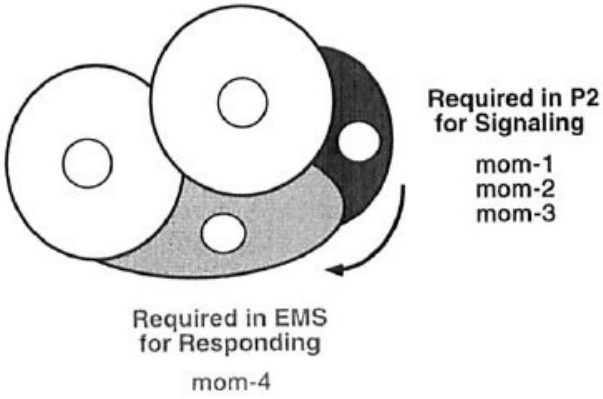


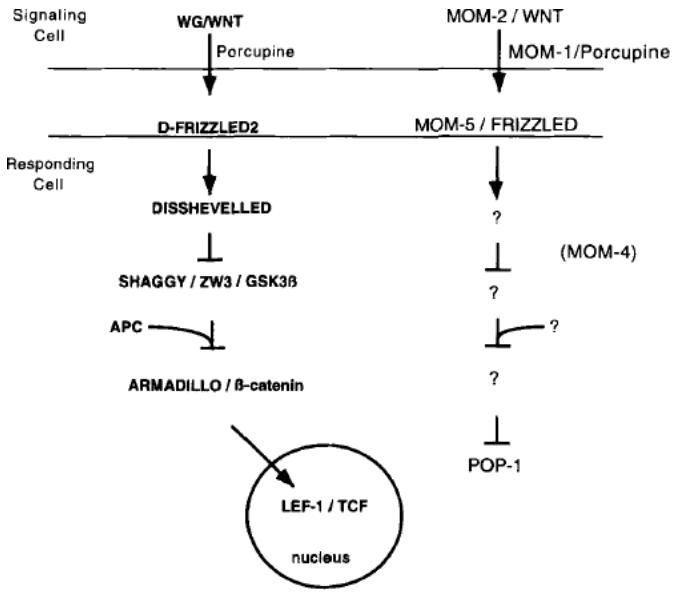
The second round of divisions: D-V axis and fate induction



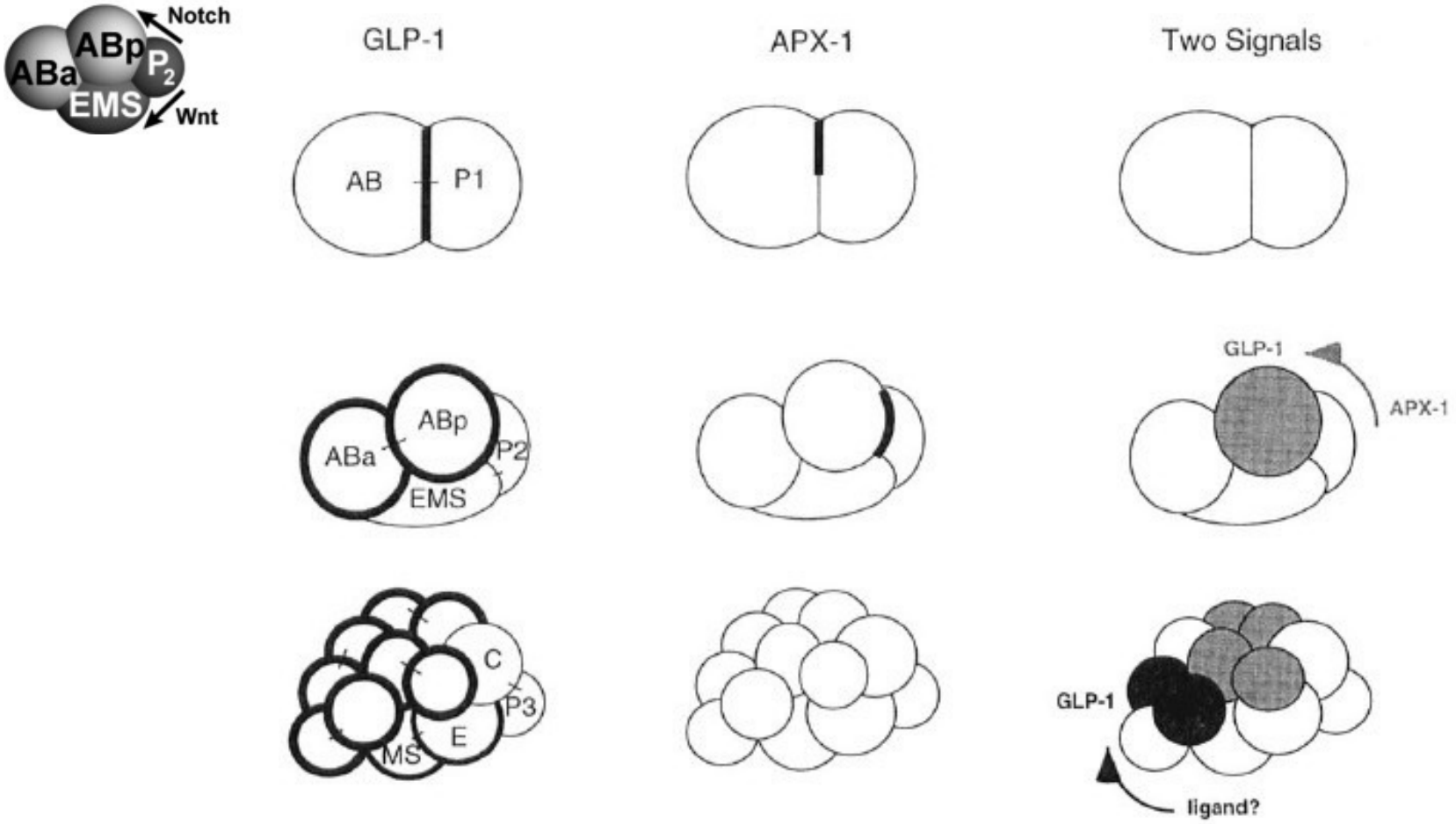




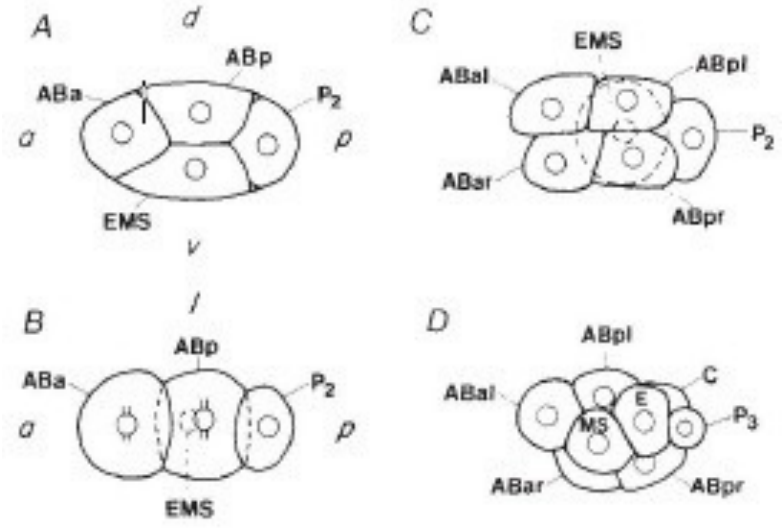


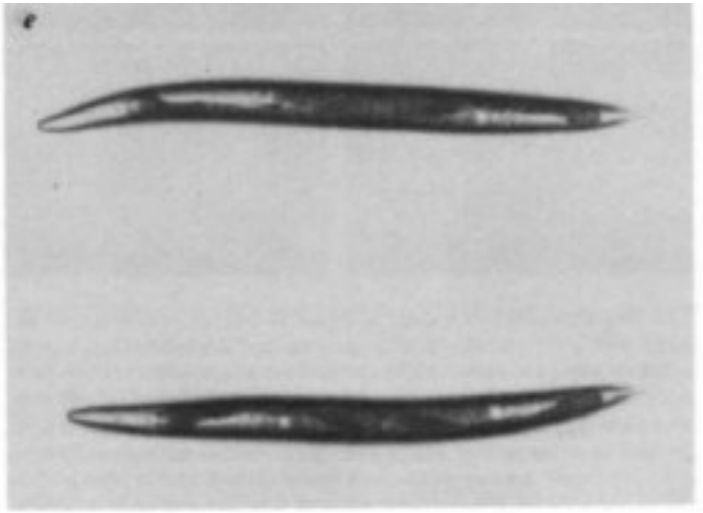


The second round of divisions: DV axis and fate induction



The third-round division: L-R axis





A brief recap:

C. elegans axis patterning starts early: sperm entry

The first 3 rounds of zygote divisions generate 6 founder cells with asymmetry in the division plane, size or morphology, and unique fate.

The establishment of A-P axis is followed by D-V, and by (or in parallel) L-R

A brief recap:

Steps and purposes of blastomere patterning:

- Initiate polarized actomyosin contraction
- Partition anterior-posterior PAR complex
- Establish intrinsic or induced founder cell's transcription factors

Cell fate maps: roughly aligned with future body planes

Final body planes laid out in gastrulation

Is this early?