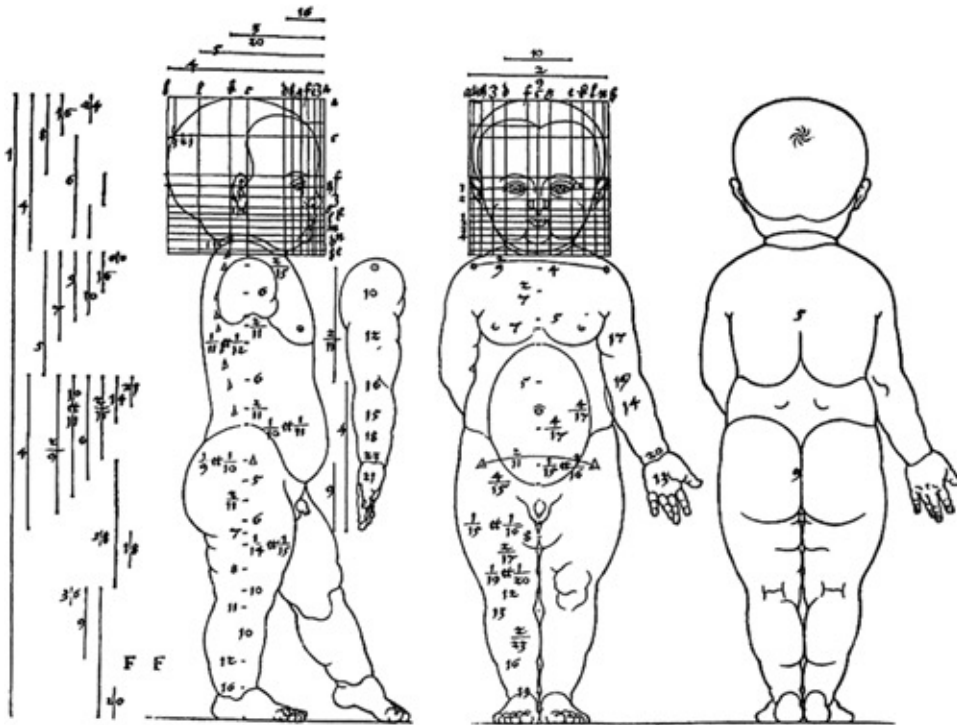


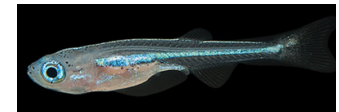
Breaking symmetry: embryonic establishment of body axes (I)

Sept 3, 2024

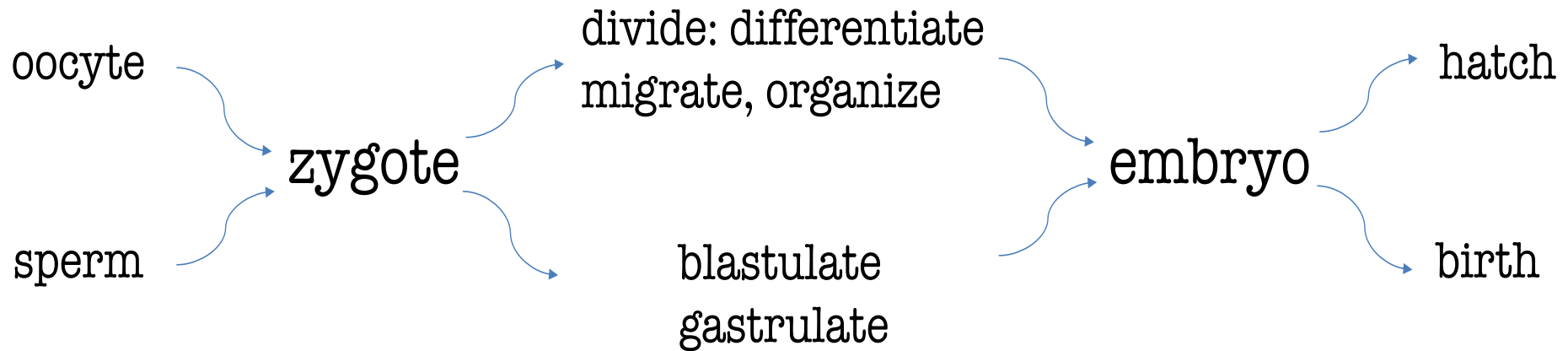
Three body axes define asymmetries



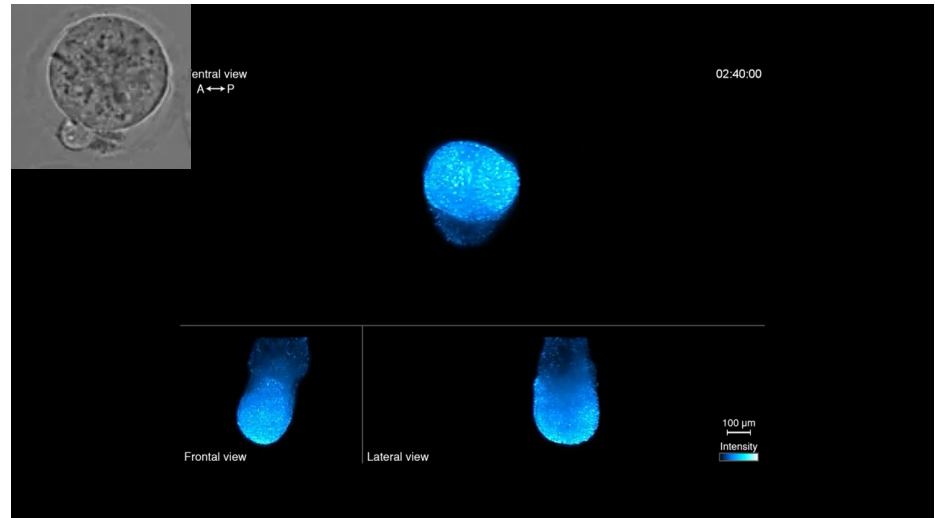
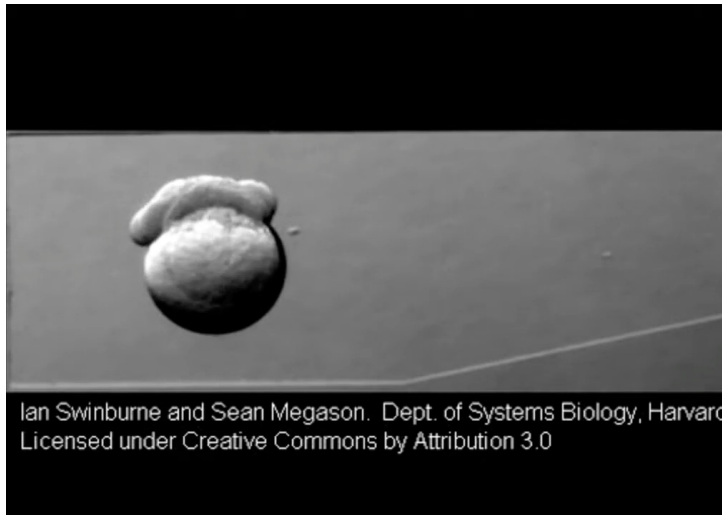
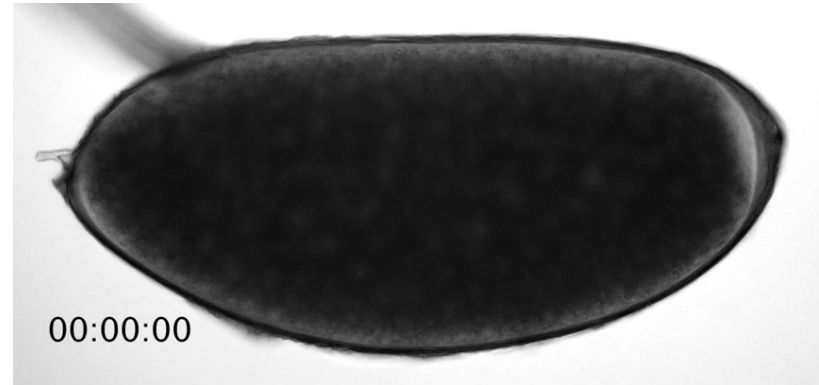
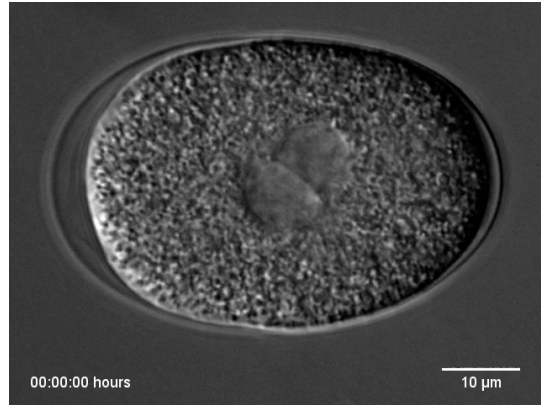
sketch: Albrecht Durer



When do you start?



Some zygotes 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?

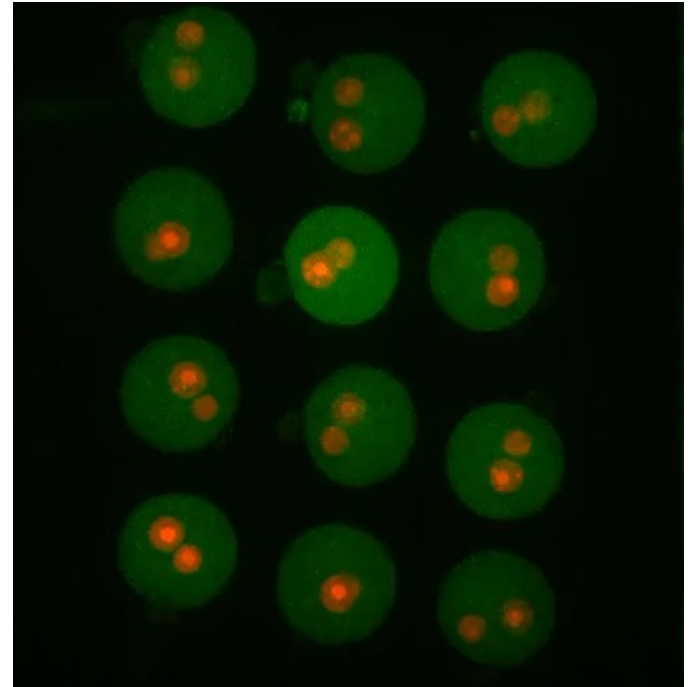
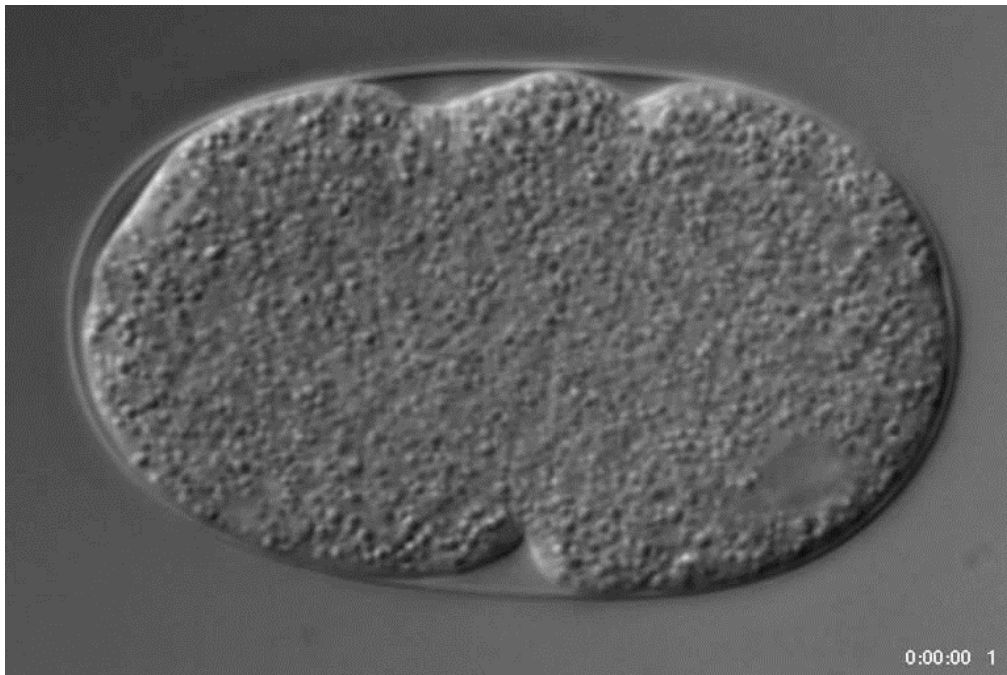
What drives the similarity and difference?

Why asymmetry at all?

How might we study this question?

- Watch and describe processes

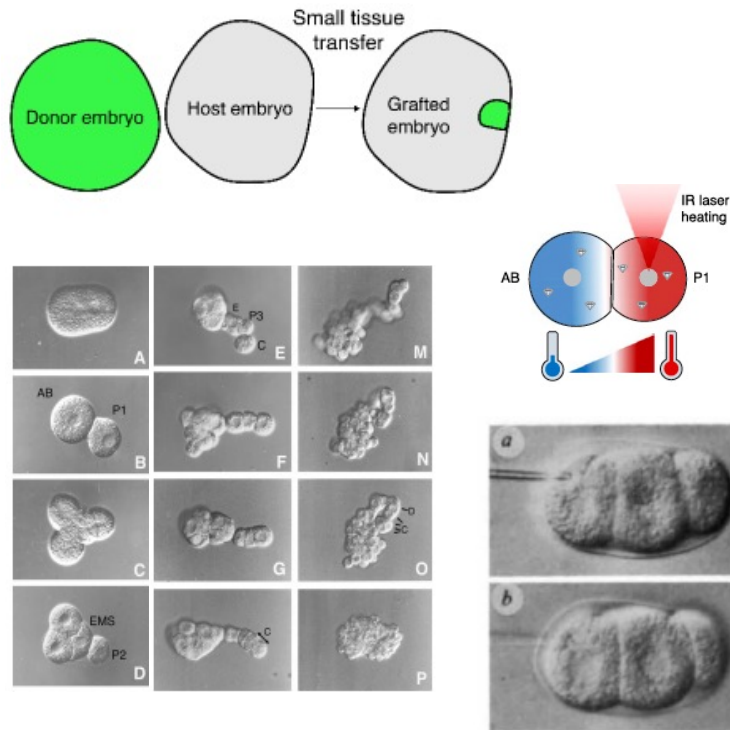
live imaging



How might we study this question?

- Perturb and sort effects

cell-manipulation



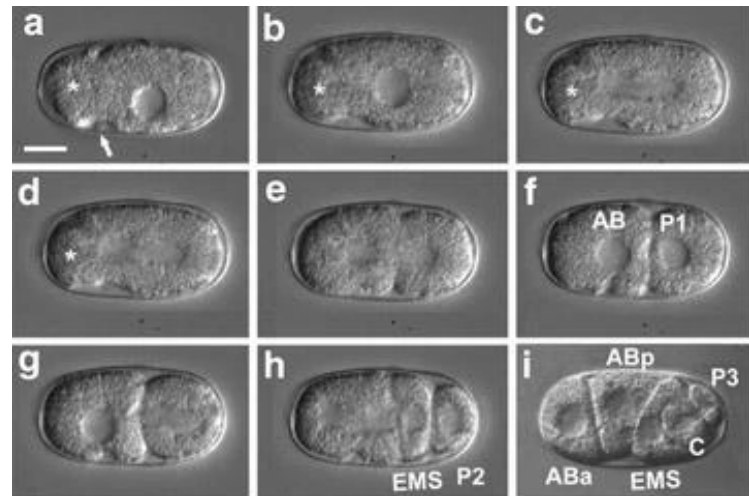
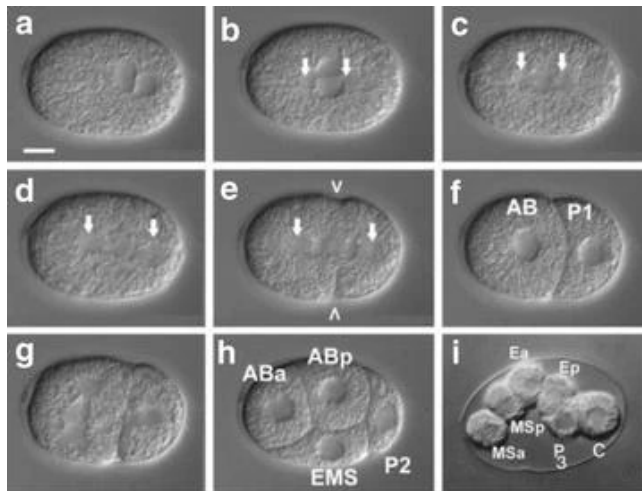
gene-manipulation

- Mutagenesis
(forward genetic screens)
- Mutagenesis
(reverse genetic or
'genome-wide' screens)

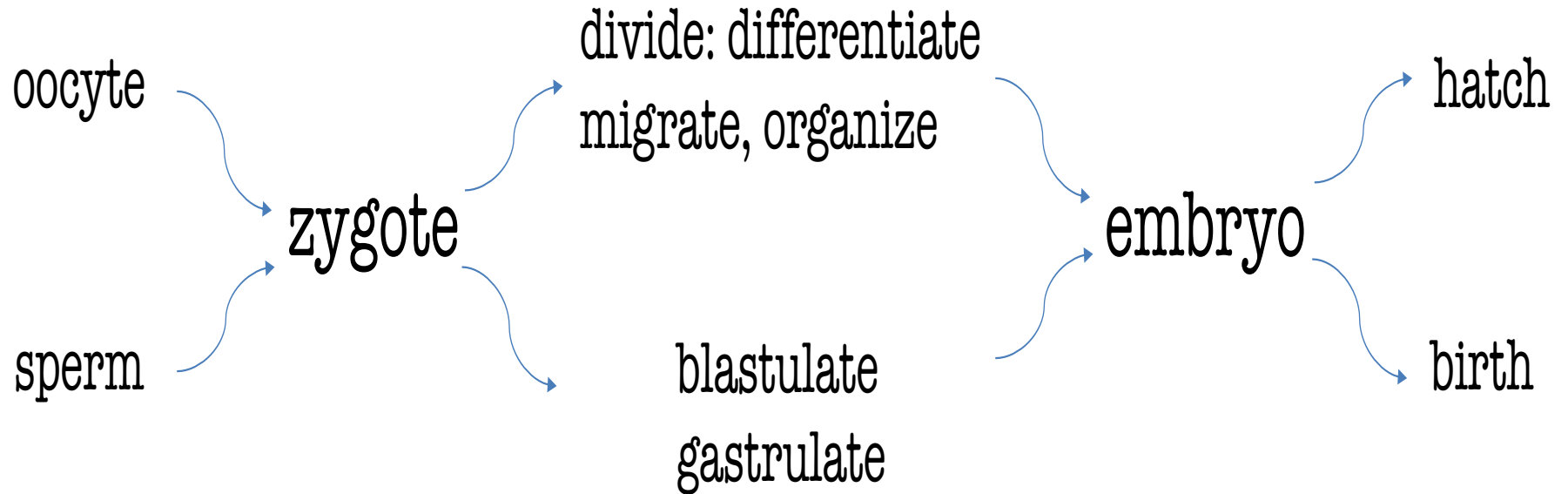
How might we study this question?

- 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:

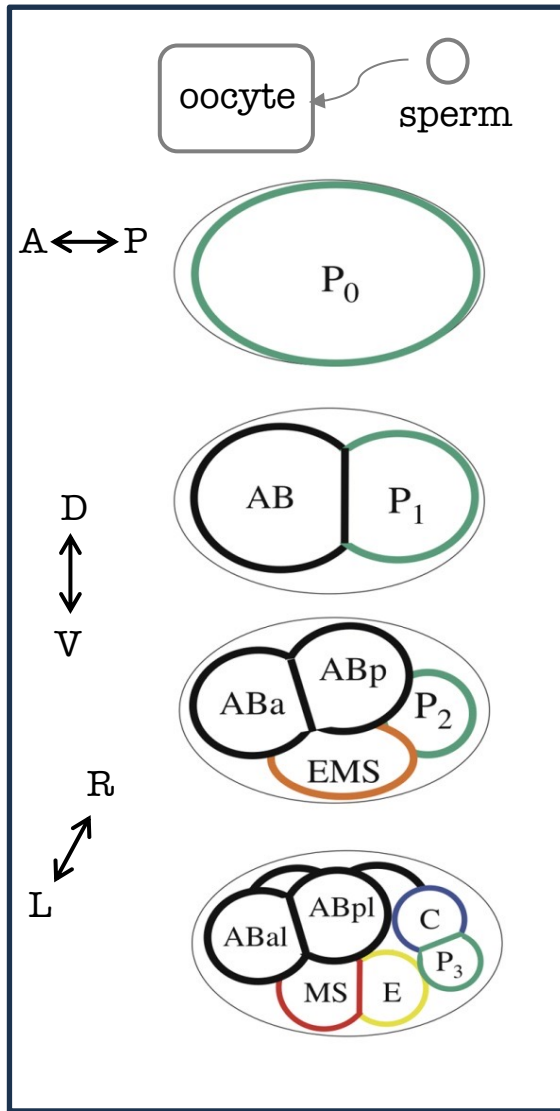
rough alignment with body axes

6 founder cells (non-exchangeable fate):

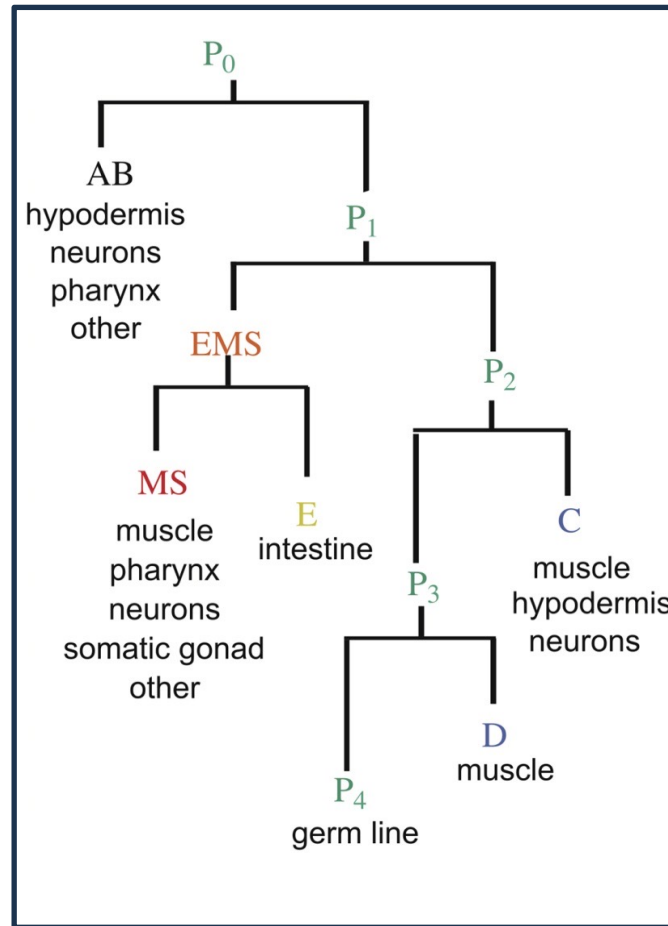
induction-determination

Gastrulation: the final body plane layout

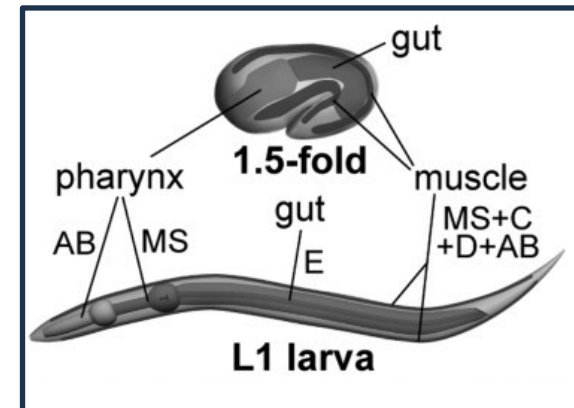
5 asymmetric divisions



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.

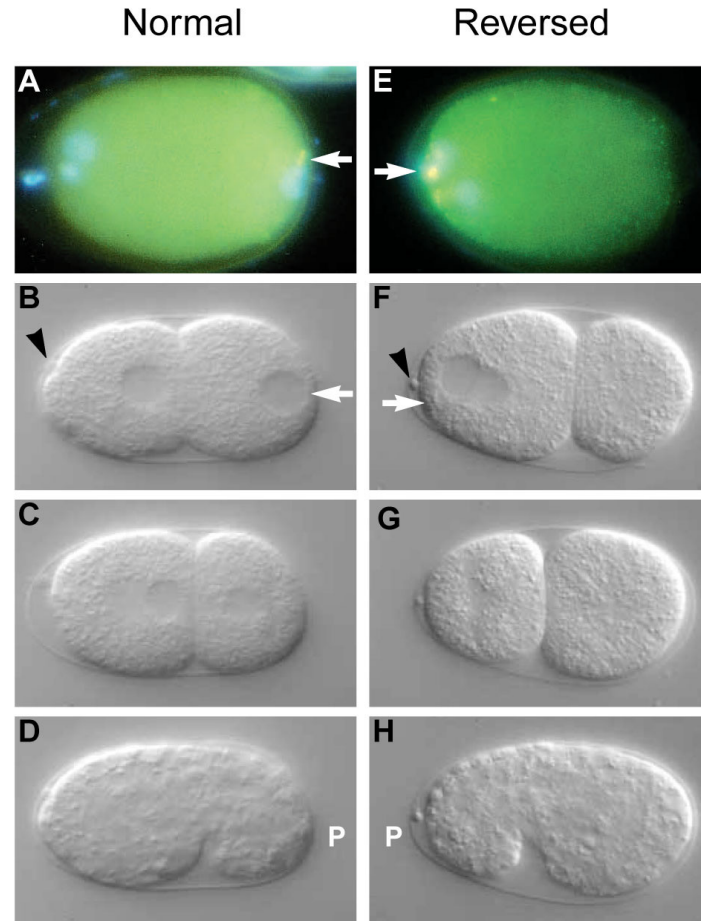
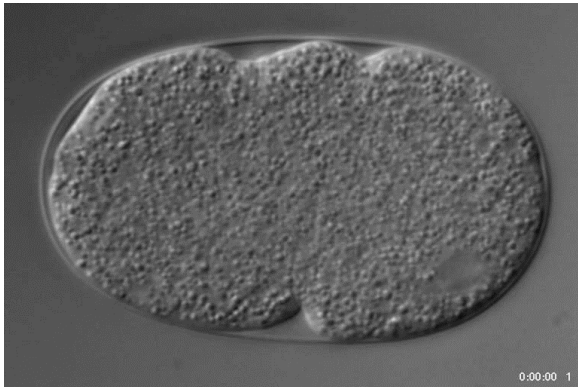


Table 1 Maternal Loci in *C. elegans*: Gene Names and Molecular Identities (See Text for References)

Gene	Name	Molecular identity
Par Group Genes		
<i>let-99</i>	<i>Lethal</i>	?
<i>par-1</i>	<i>Partitioning-defective</i>	Ser-Thr kinase; binds a nonmuscle myosin
<i>par-2</i>	Same	Novel; ATP-binding site
<i>par-3</i>	Same	Novel; two PDZ domains
<i>par-4</i>	Same	Ser-Thr kinase
<i>par-5</i>	Same	?
<i>par-6</i>	Same	?
<i>mes-1</i>	<i>Maternal-effect sterile</i>	?
Blastomere Identify Group Genes		
P ₁ subgroup		
<i>pal-1</i>	<i>Posterior alae defective</i>	Homeodomain protein; putative transcription factor
<i>pie-1</i>	<i>Pharynx and intestine excess</i>	TIS-11-like Zn ²⁺ finger ptn
<i>skn-1</i>	<i>Skin excess</i>	bZIP-like putative transcription factor; lacks a leucine zipper
<i>pop-1</i>	<i>Posterior pharynx defective</i>	HMG domain protein; putative transcription factor
<i>mom-1</i>	<i>More mesoderm</i>	Porcupine homologue; ER protein required for Wnt secretion
<i>mom-2</i>	Same	Wingless/Wnt homologue; putative secreted glycoprotein ligand
<i>mom-3</i>	Same	?
<i>mom-4</i>	Same	?
<i>mom-5</i>	Same	Frizzled homologue; putative receptor for Wnt ligands
AB subgroup		
<i>aph-2</i>	<i>Anterior pharynx defective</i>	Novel membrane-associated extracellular protein
<i>apx-1</i>	<i>Anterior pharynx excess</i>	Delta-like transmembrane protein; putative GLP-1 ligand
<i>glp-1</i>	<i>Germline proliferation defective</i>	Notchlike transmembrane protein; putative receptor
Intermediate Group Genes		
<i>mex-1</i>	<i>Muscle excess</i>	TIS-11-like Zn ²⁺ finger ptn
<i>mex-3</i>	Same	Two KH domains; putative RNA-binding protein
<i>pos-1</i>	<i>Posterior localized mRNA</i>	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:

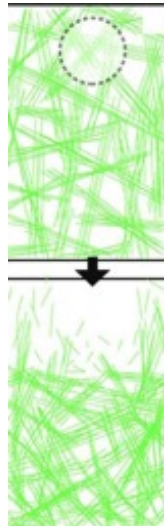
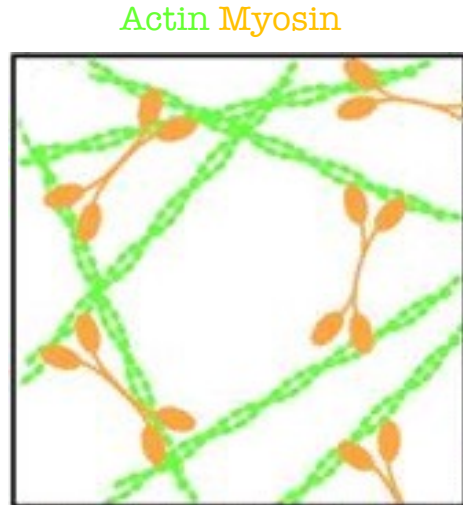
its microtubule extension to cortex

its close association with cortex

its component: e.g. Aurora kinase AIR-1

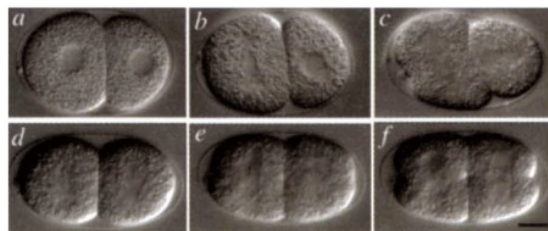
How might the centrosome polarize the zygote?

asymmetric cortical actomyosin contraction

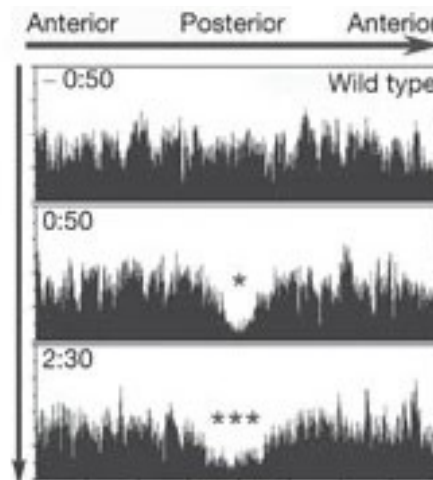


- Cytochalasin D blocks all division asymmetry
- Removing non-muscle myosin blocks polarity
- Posterior cortex RhoGEF cortex is excluded, which requires centrosome proteins

wildtype

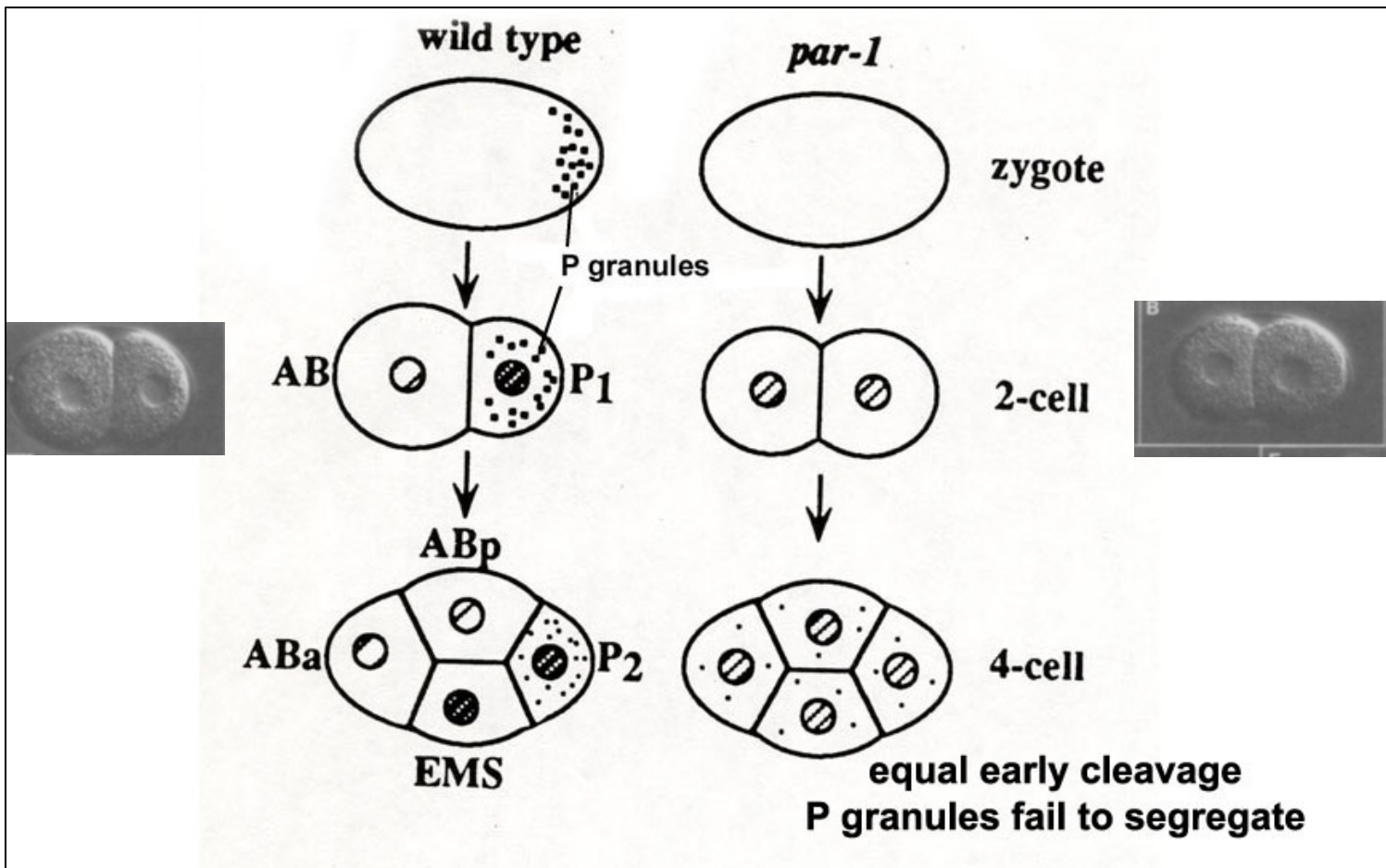


nmy-2
RNAi

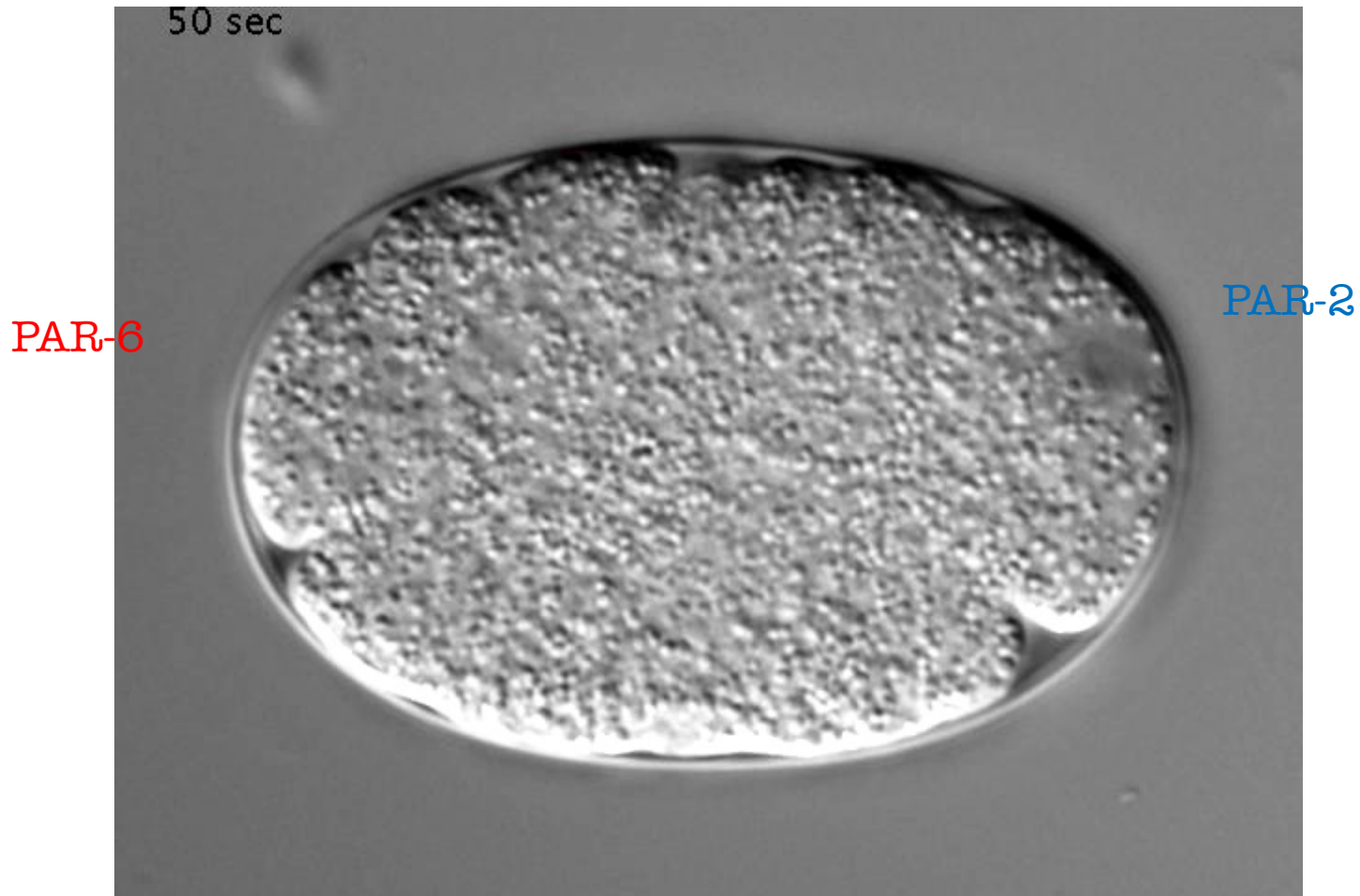


How might cortical contraction polarize the zygote?

polarized cortical par location (I)

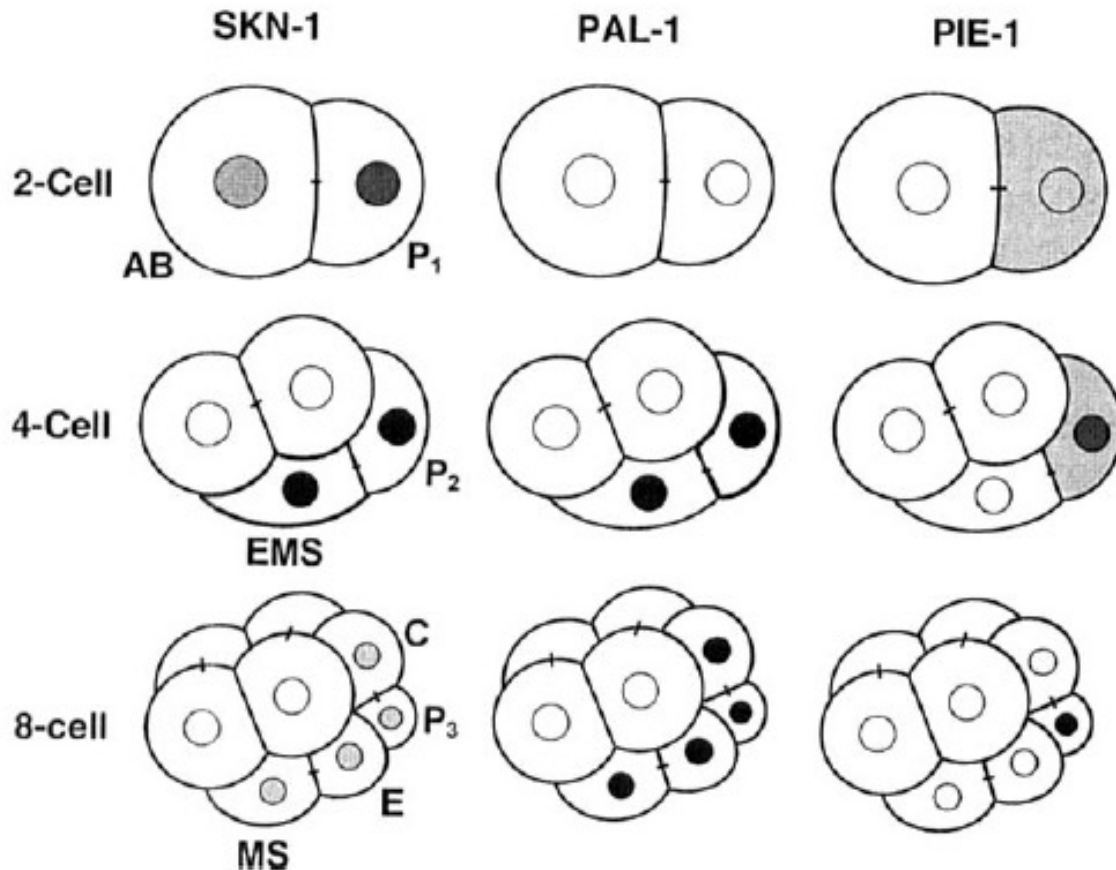


polarized cortical par location (II)



How might the blastomere cell fate be specified?

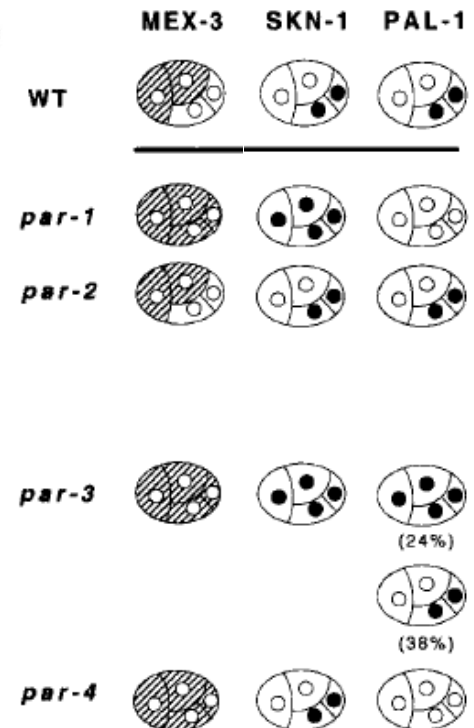
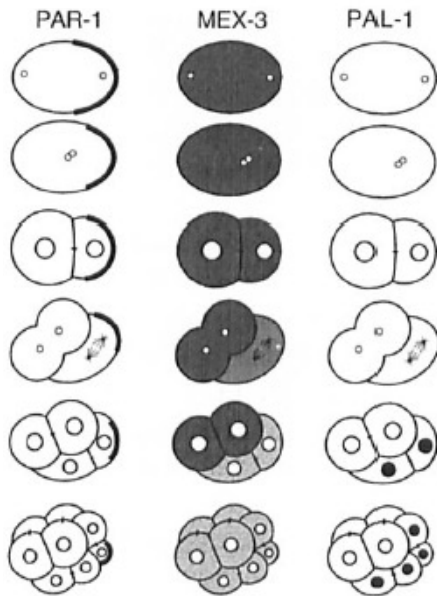
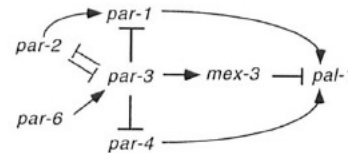
founder cell transcription factors



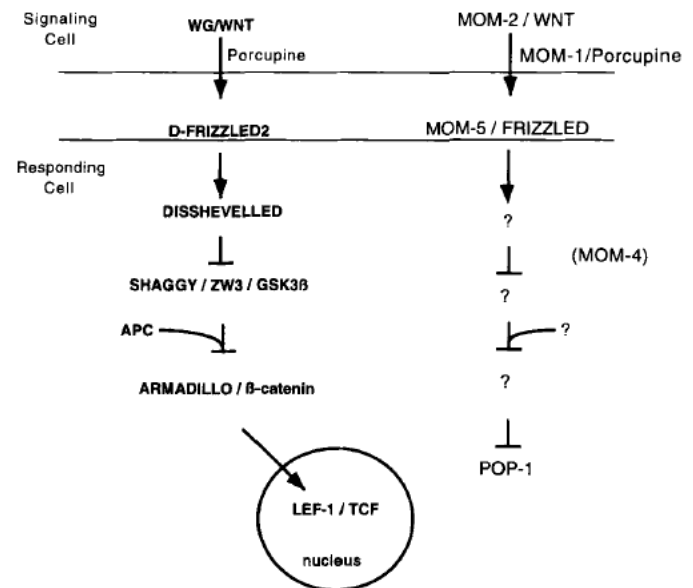
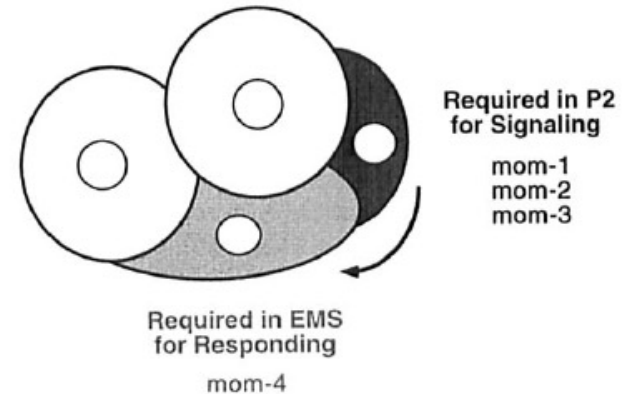
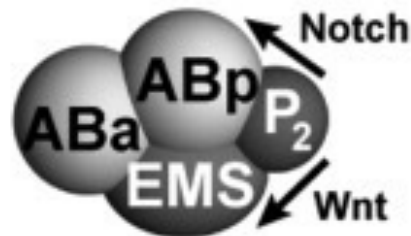
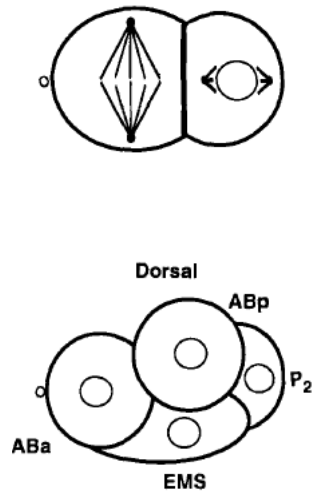
How might the blastomere cell fate be specified?

founder cell transcription factors

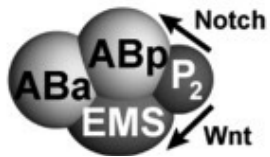
$par-1 \rightarrow mex-3 \rightarrow pal-1$



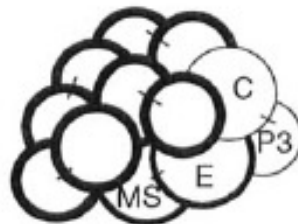
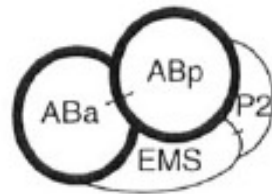
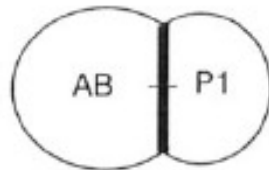
The second round of divisions: D-V axis and fate induction



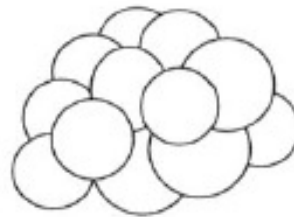
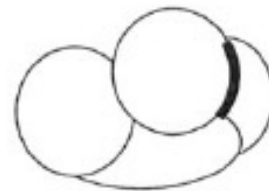
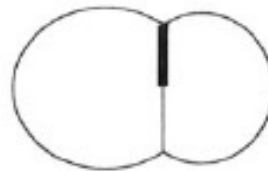
The second round of divisions: DV axis and fate induction



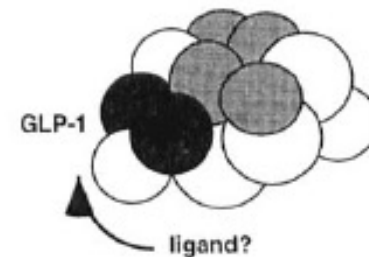
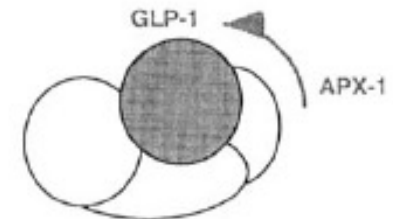
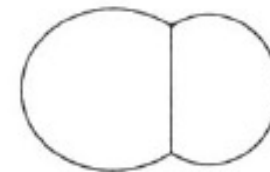
GLP-1



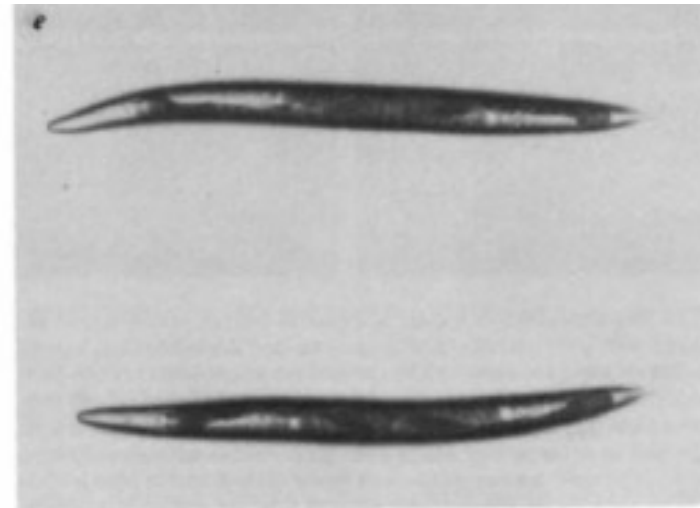
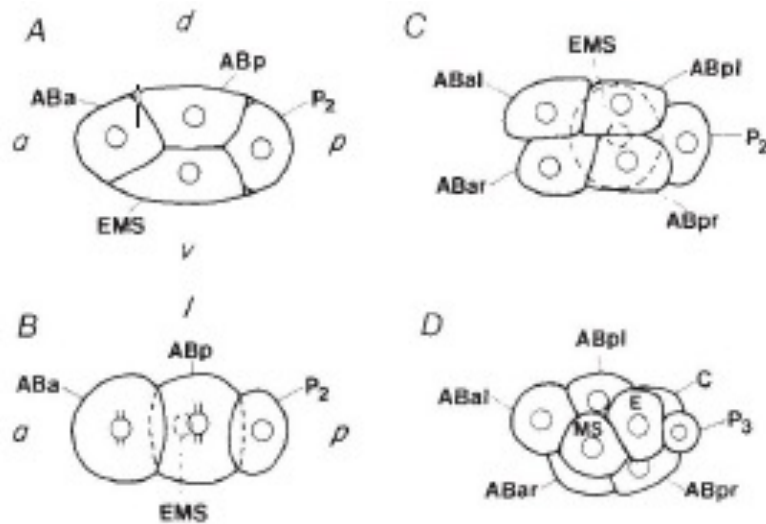
APX-1



Two Signals



The third-round division: L-R axis



A brief recap:

C. elegans axis patterning starts early: sperm entry

The first 3 rounds of zygotic divisions generate 6 founder cells with asymmetry in 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:

Mechanism and purpose of early patterning:

Division asymmetry:

Initiate polarized actomyosin contraction

Partition anterior-posterior PAR complex distribution

Allow intrinsic or induced founder cell transcription factors that establish the cell fate map.

Final body plane laid out in gastrulation

Is this early?