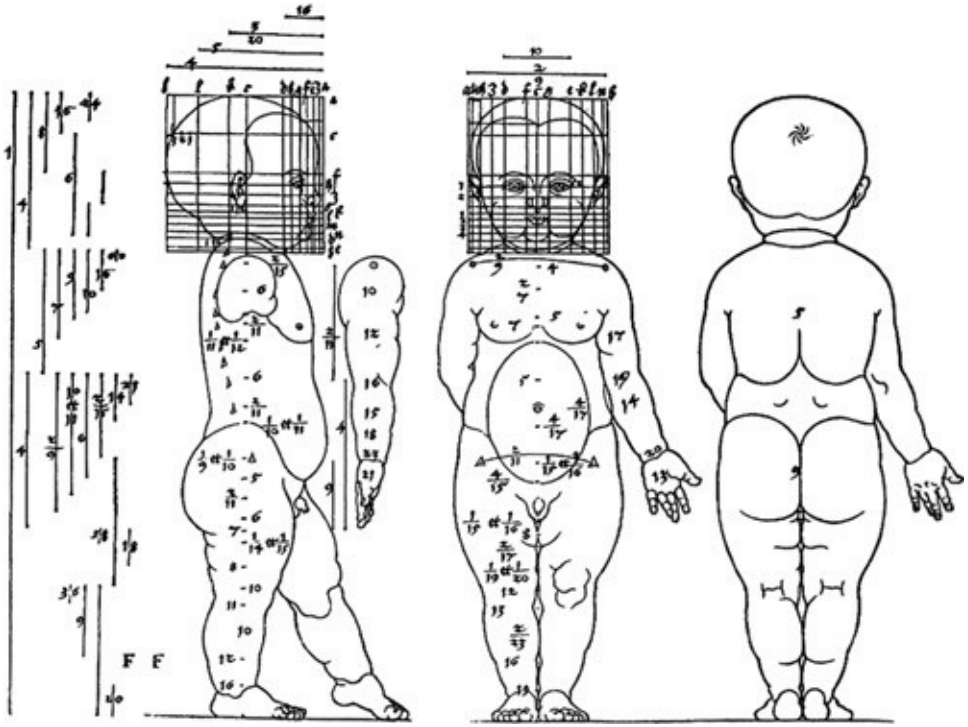
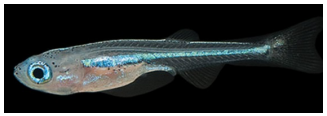
Breaking symmetry: embryonic establishment of body axes (I)

Sept. 11, 2024

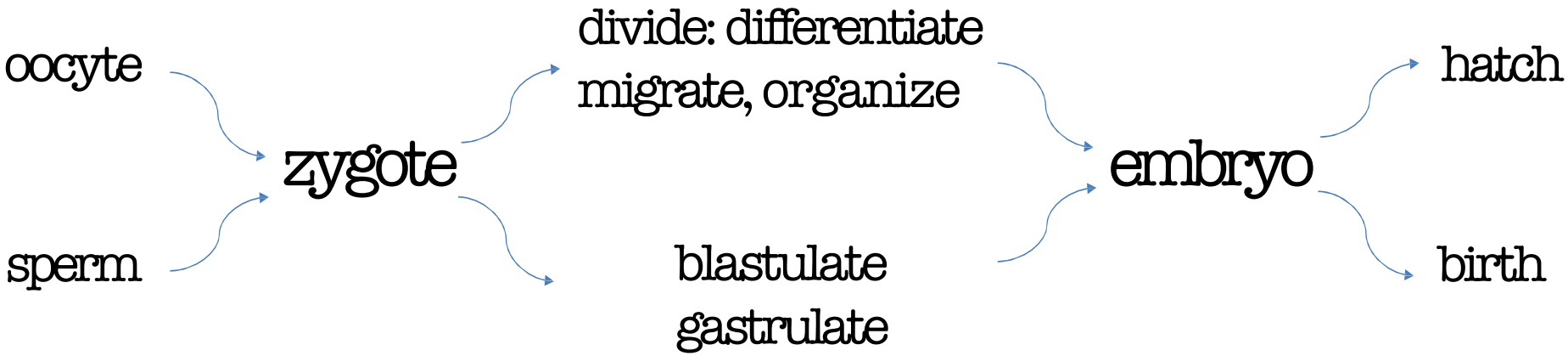
Three body axes define asymmetries



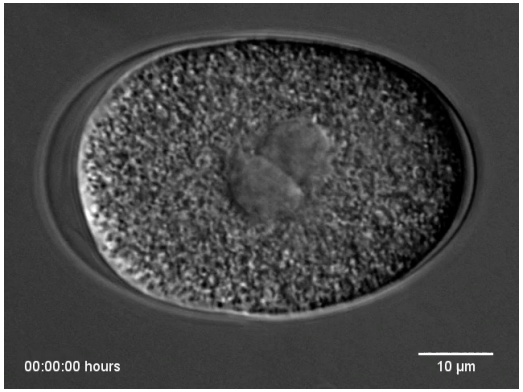
sketch: Albrecht Durer

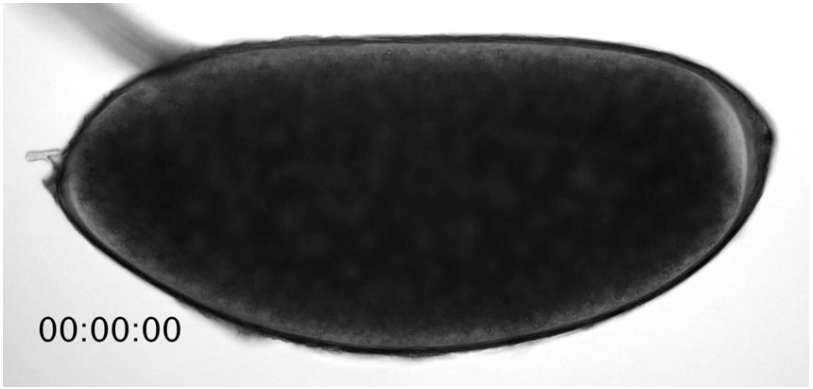


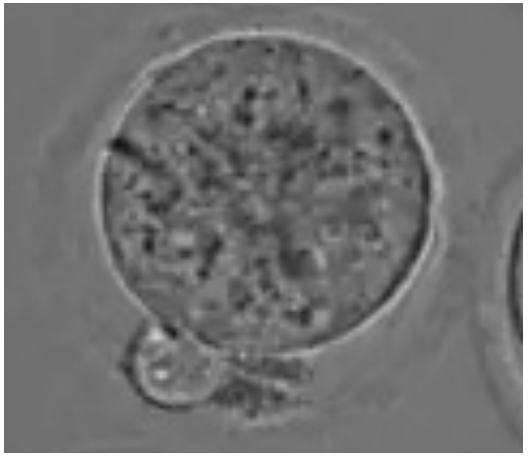
When do you start?



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?

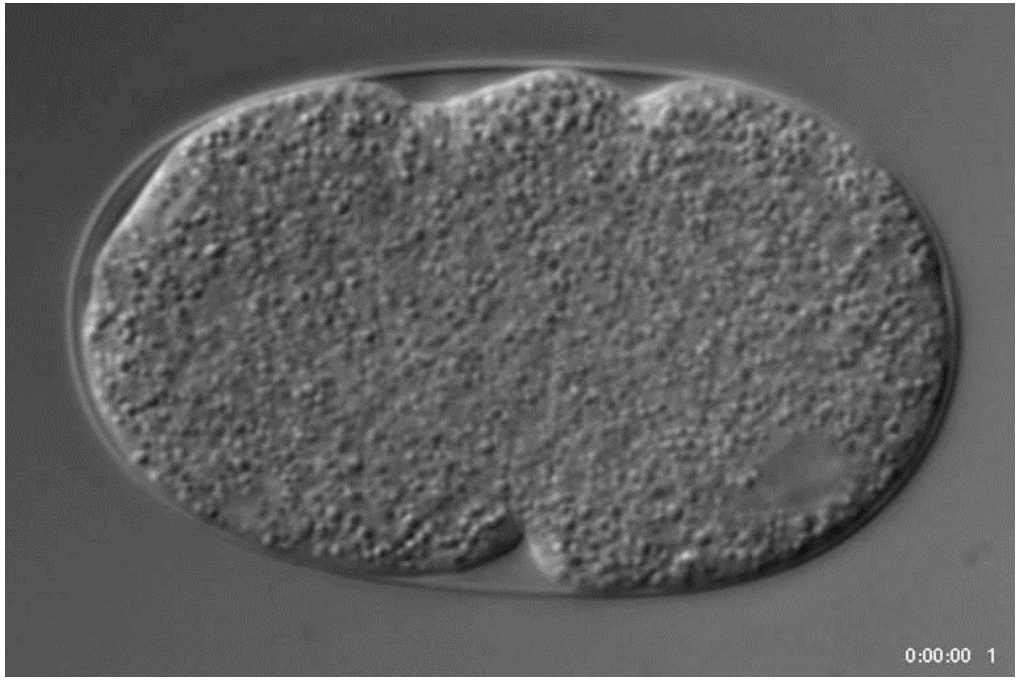
What drives the similarity and difference?

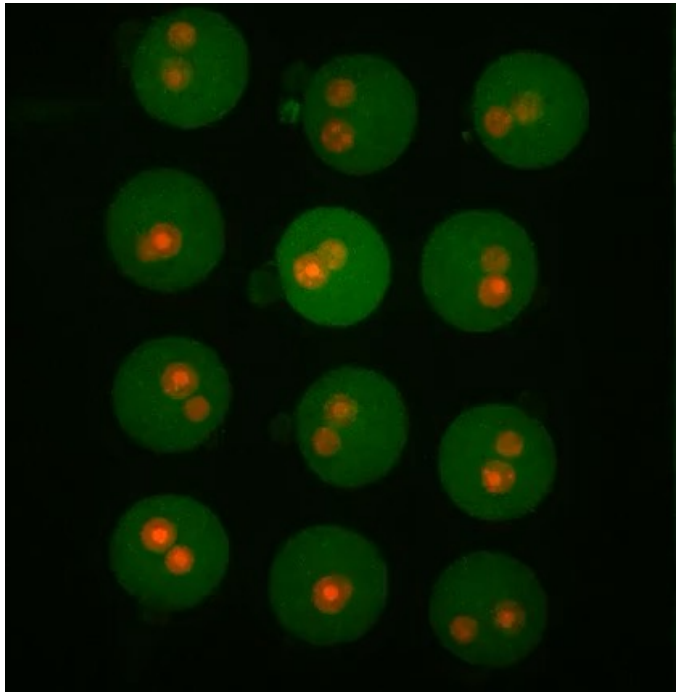
Why asymmetry at all?

How might we study this question?

- Watch and describe

live imaging

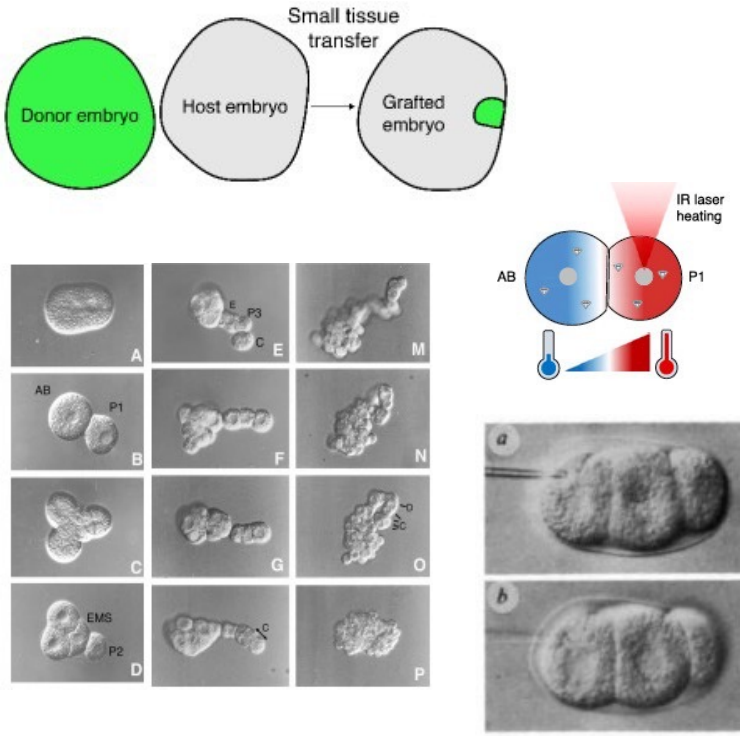




How might we study this question?

- Perturb and sort effects

cell-manipulation



gene-manipulation

- **Mutants**

forward genetic screens

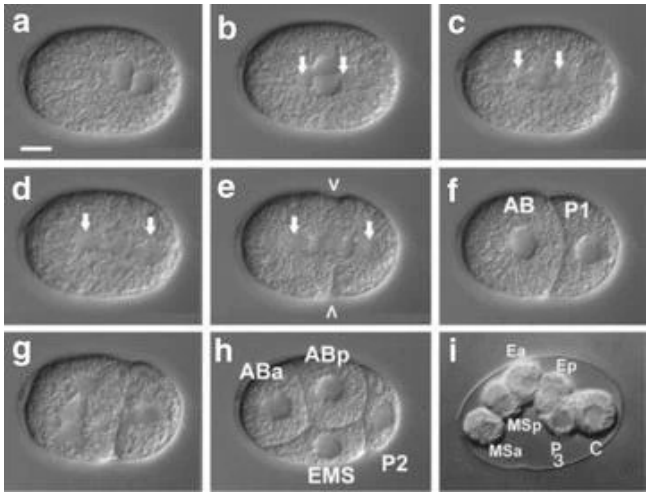
- **'Mutants'**

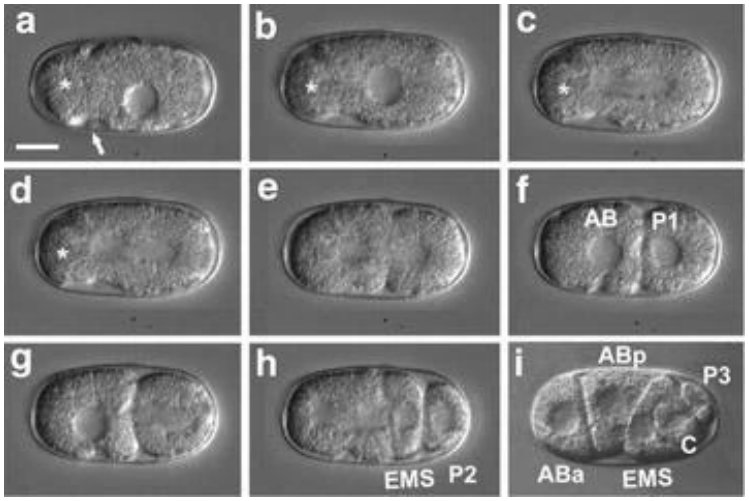
targetted or systematic (genome-wide) knockout, knock down, degradation

How might we study this question?

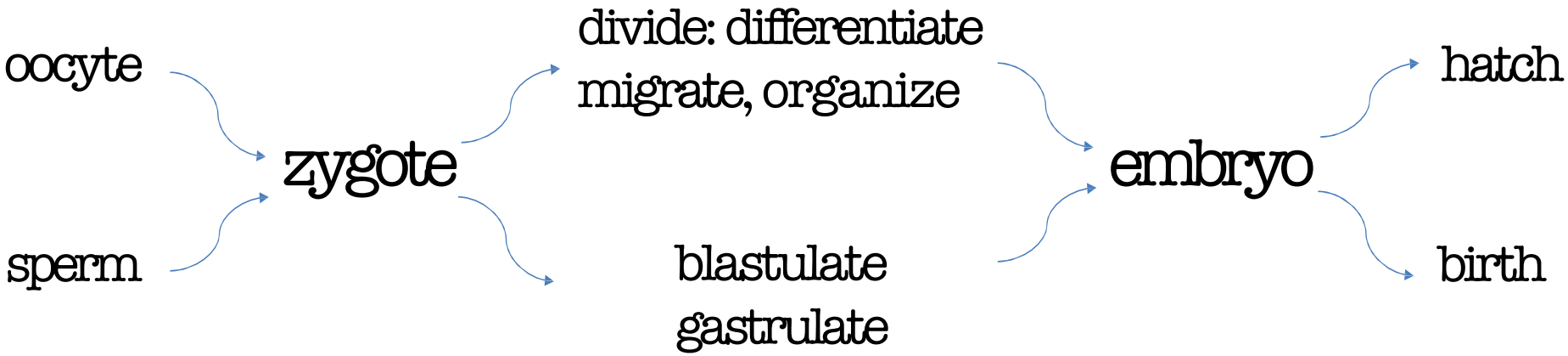
- Compare among sub-species

Correlate genomic-cellular variations





When do you start?



How early is ‘early’?

C. elegans is early:

sperm entry + first 3 rounds of divisions

5 asymmetric divisions:

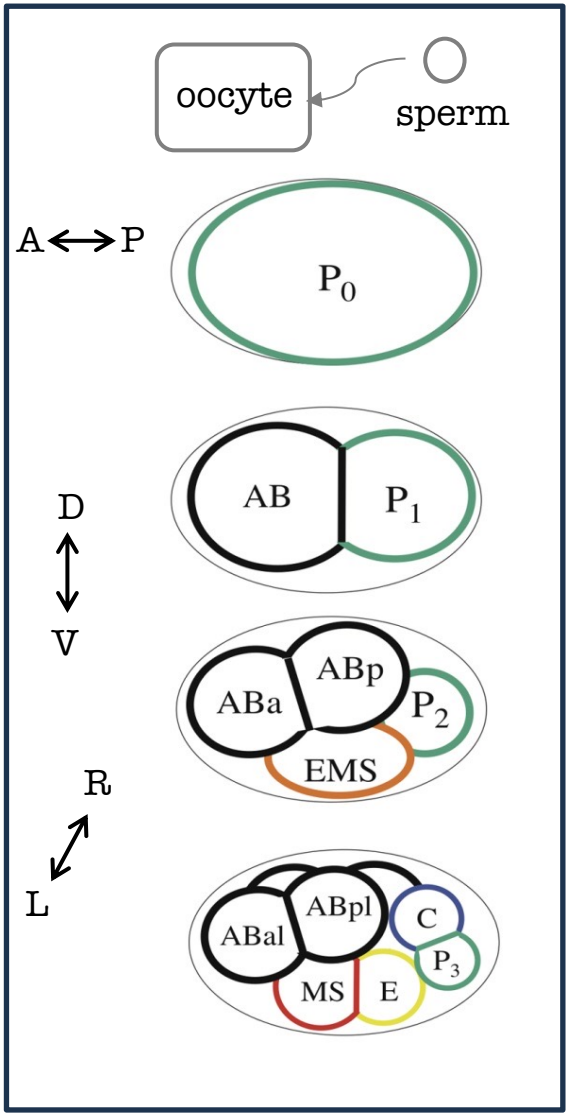
polarization for future body axes

6 blastomere (founder) cells:

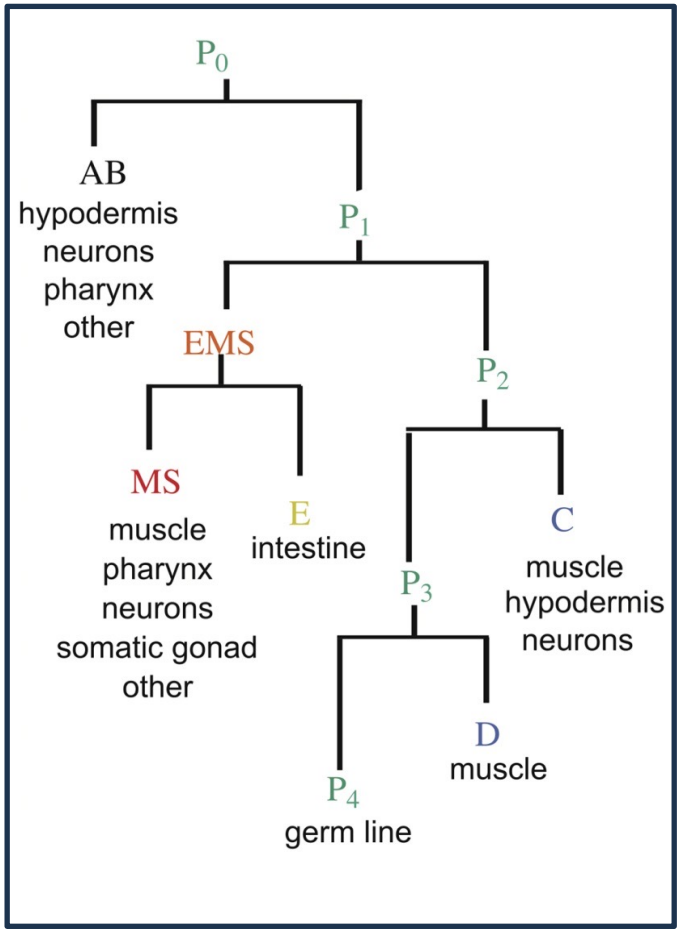
non-exchangeable fates

Gastrulation: the final body plane layout

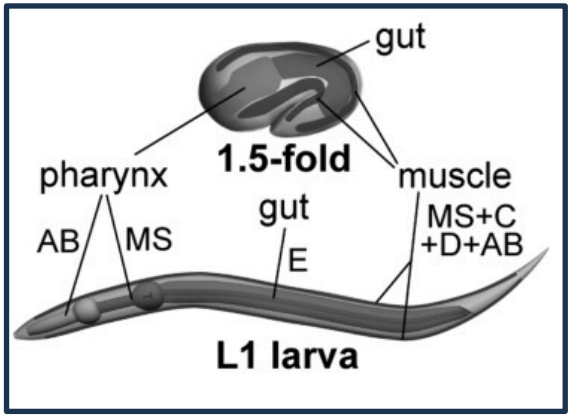
5 asymmetric divisions



6 blastomeres (founder cells)



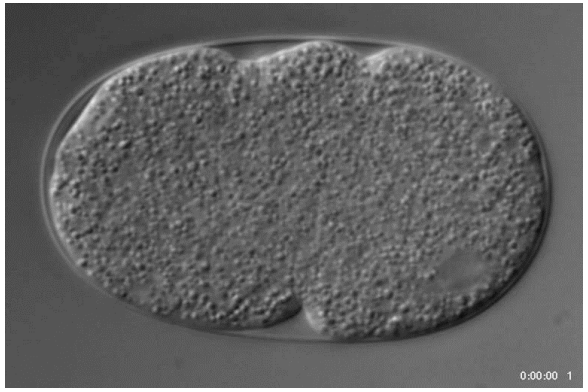
gastrulate & unfold



Let's review key evidences

1) A-P axis:

Sperm initiates polarization of zygote, establishing A-P asymmetry in the first division.



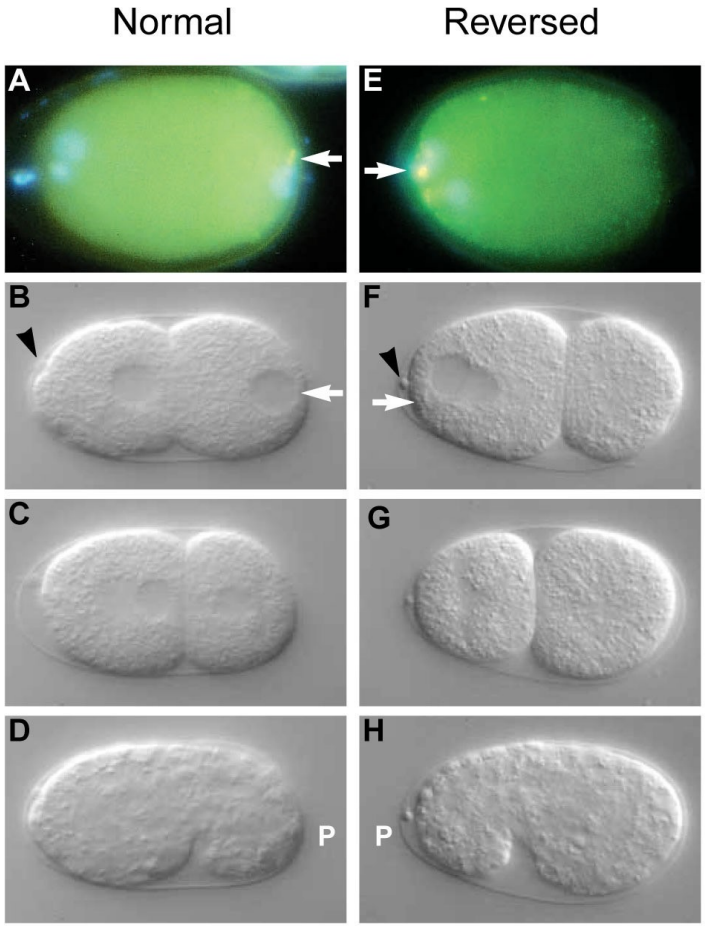


Table I Maternal Loci in *C elegans*: Gene Names and Molecular Identities (See Text for References)

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.

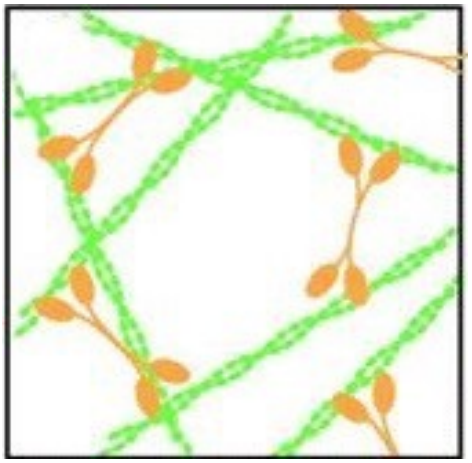
Requirement for initiating embryo polarity, from the centrosome:

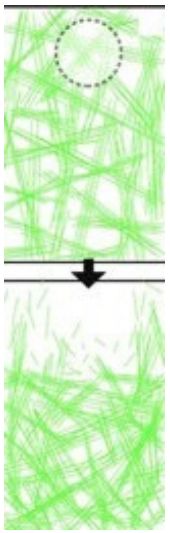
its microtubule extension to cortex
its close association with cortex
its component: e.g. Aurora kinase AIR-1

How might the sperm centrosome polarize the zygote?

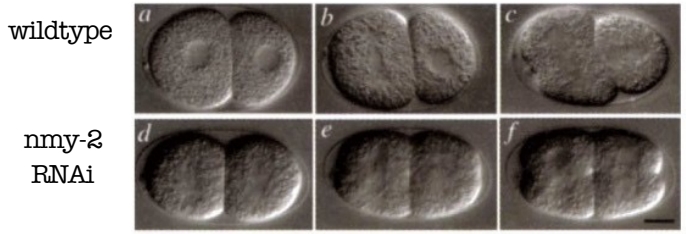
asymmetric cortical actomyosin contraction: cytoplasmic flow

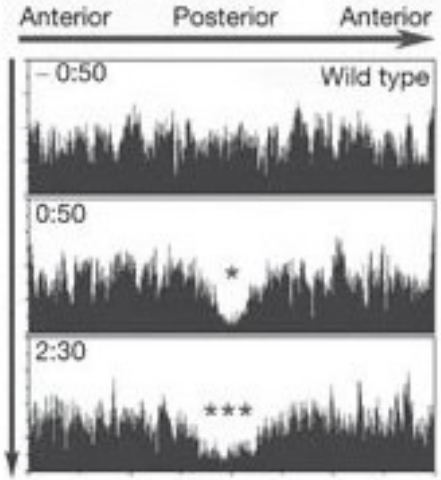
Actin Myosin





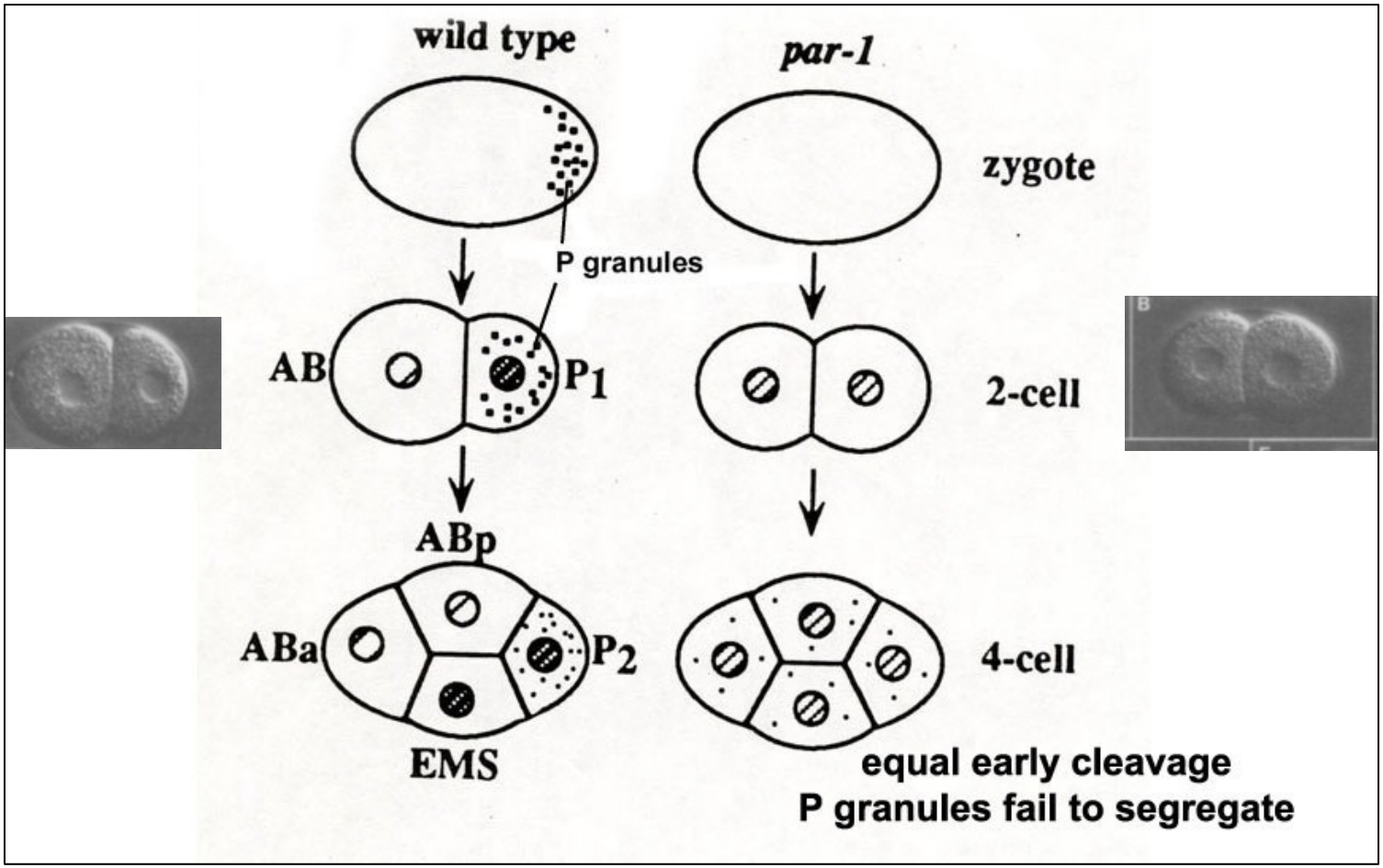
- Cytochalasin D blocks all division asymmetry
- Removing non-muscle myosin blocks polarity
- Posterior cortex excludes RhoGEF, which requires centrosome proteins





How might asymmetric cortical contraction polarize the zygote?

polarized cortical par localization (I)



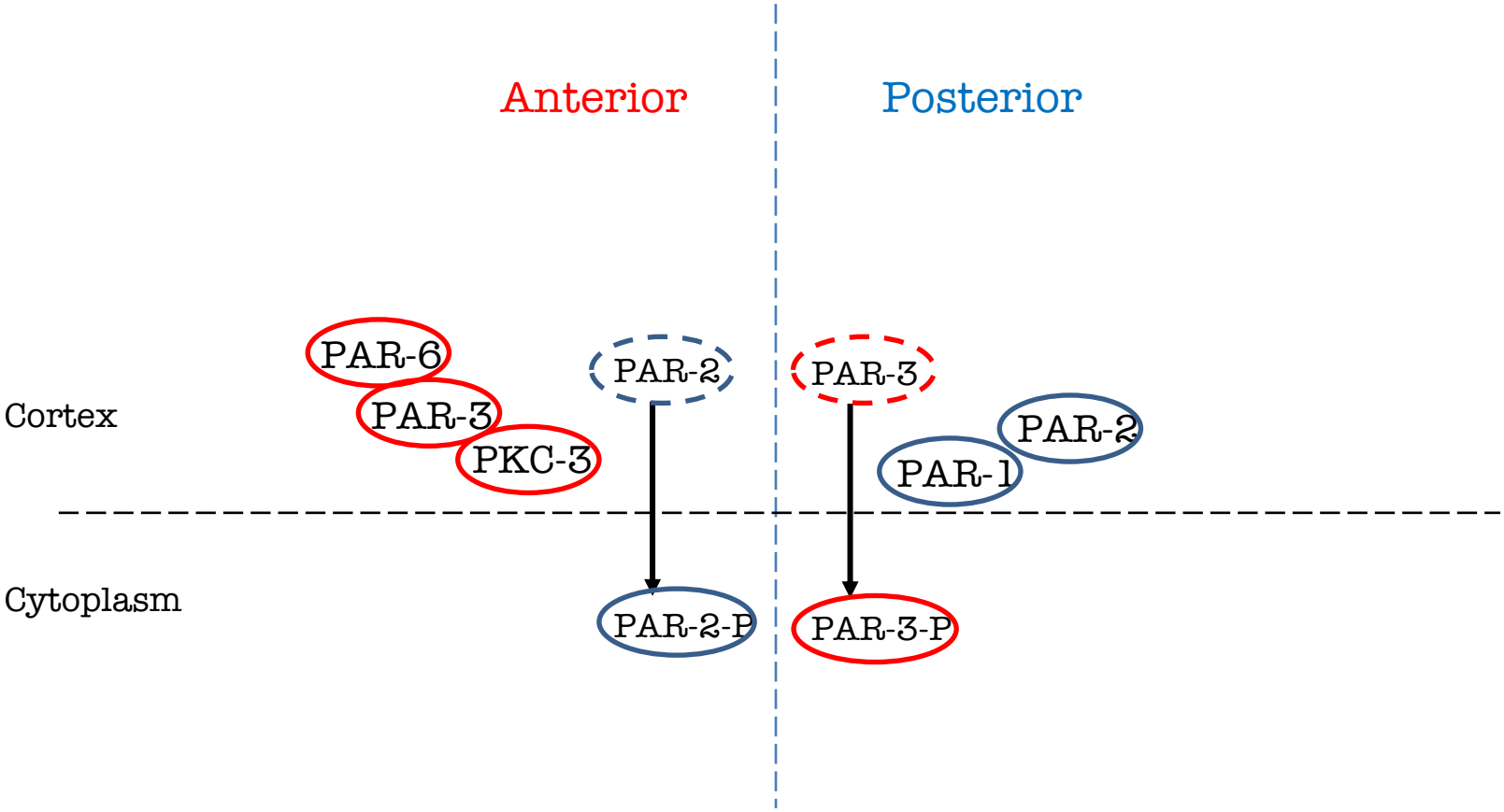
How might cortical contraction polarize the zygote?

polarized cortical par location (II)

PAR-6

PAR-2

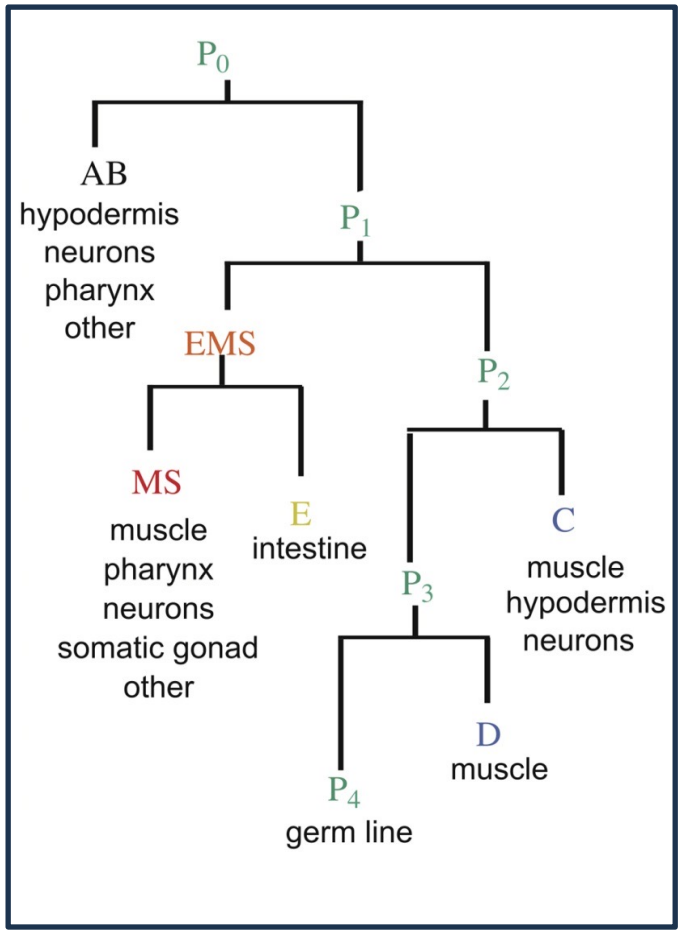
Mutual inhibition between PAR Proteins



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

How might blastomere cell fates be specified?

6 blastomeres



3 groups of fate-determinants

Anterior (AB descendants)

- MEX-3
- GLP-1

Posterior (P1 descendants)

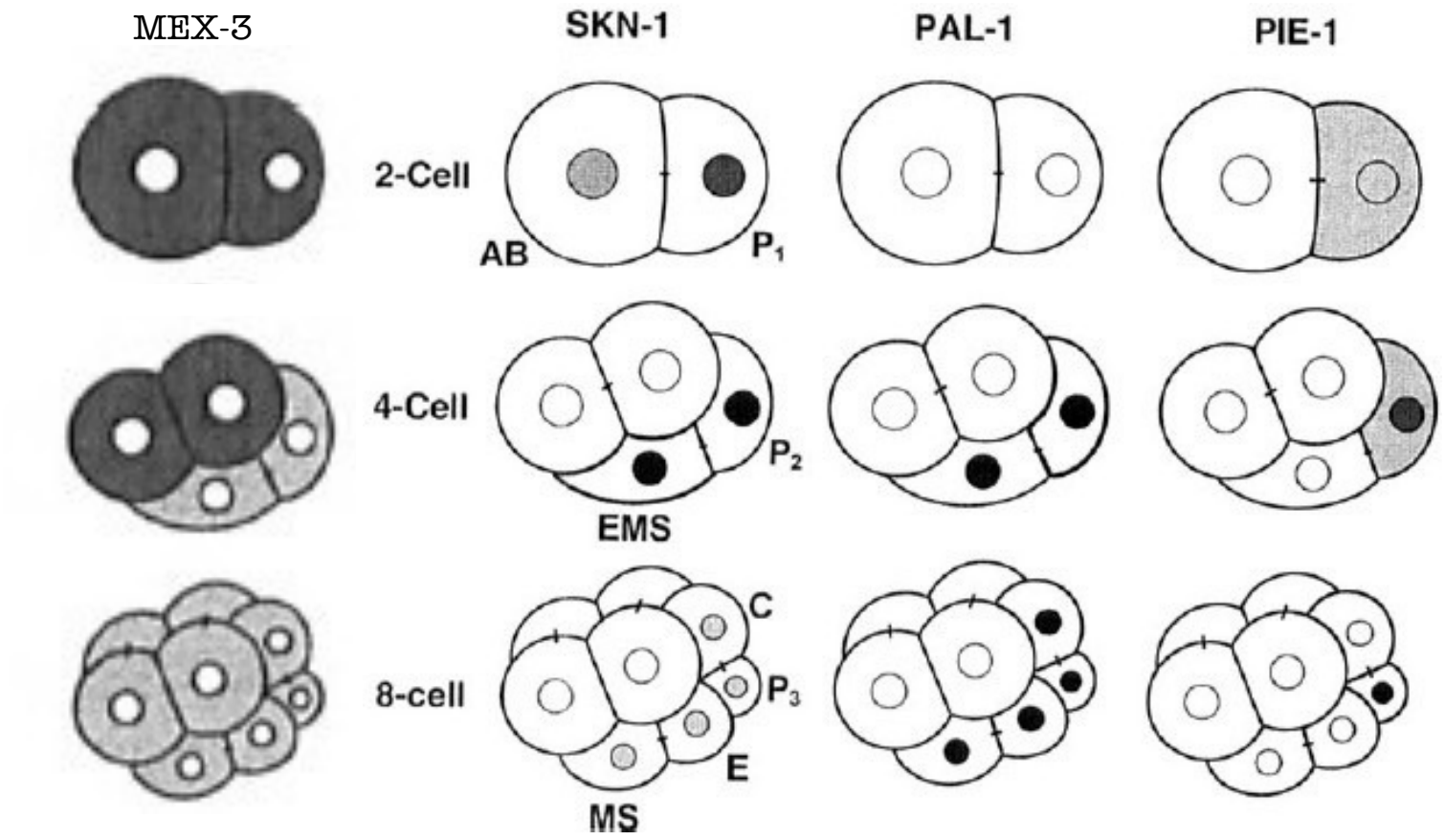
- SKN-1
- PAL-1

Germline (P1 descendants)

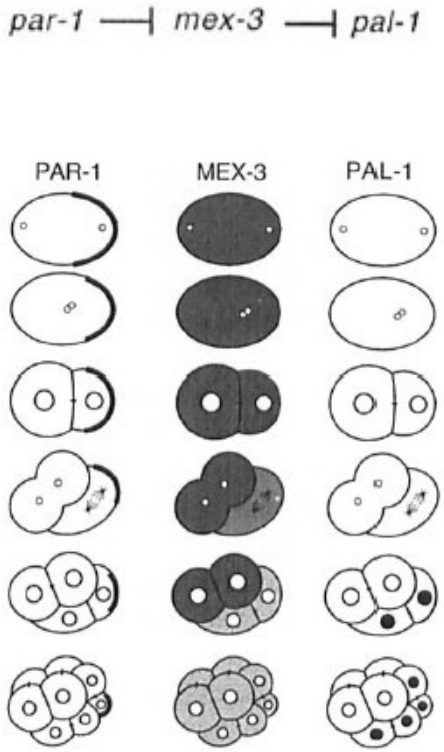
- PIE-1
- MEX-1
- POS-1
- P granules

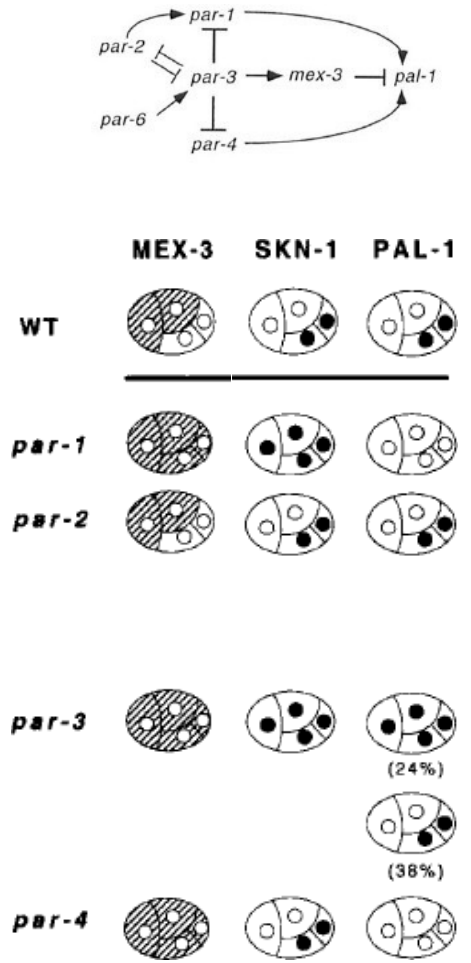
How might blastomere cell fates be specified?

transcription factors

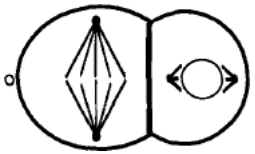


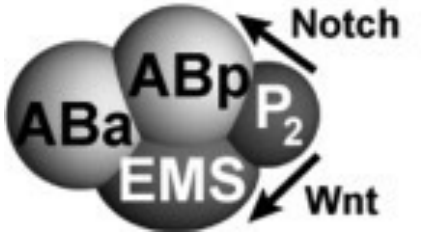
How might blastomere cell fates be specified?

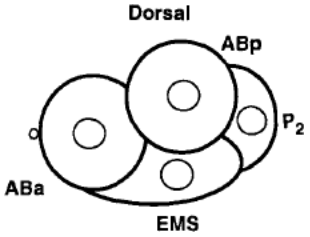


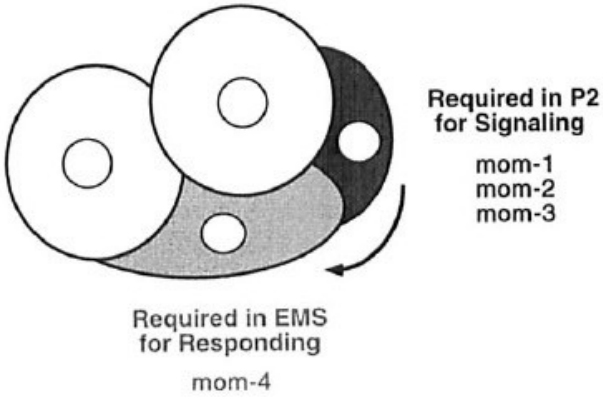


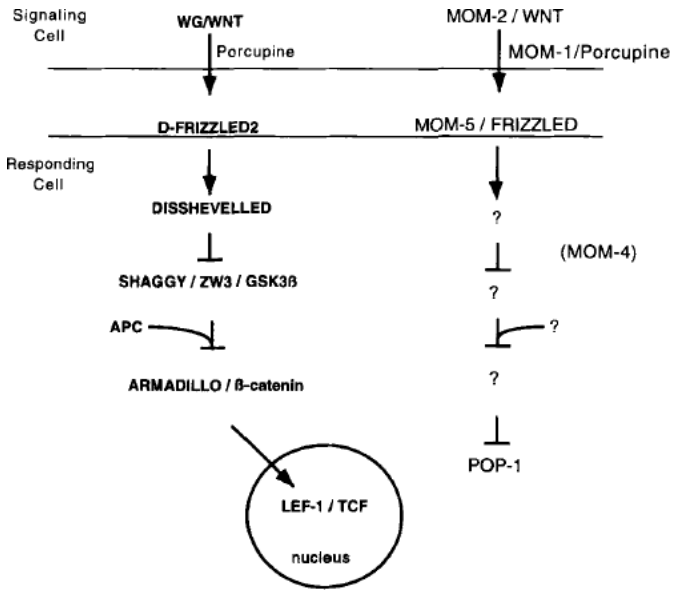
The second round of divisions: D-V axis and fate induction



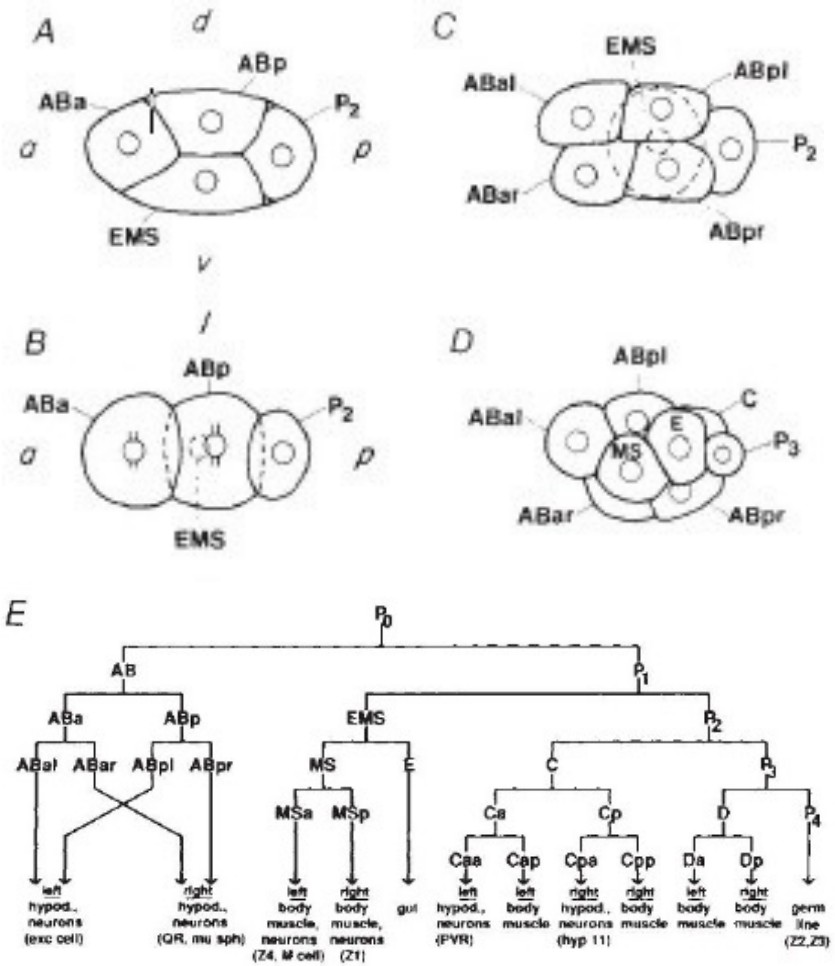


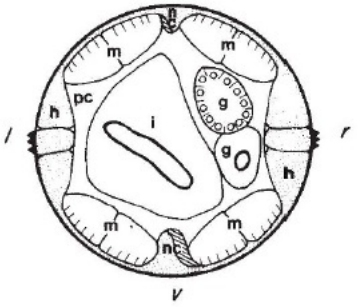


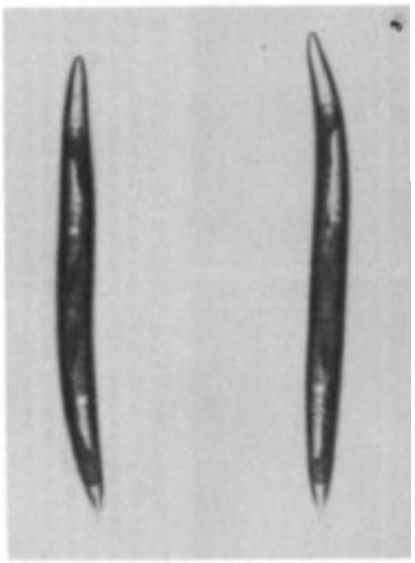


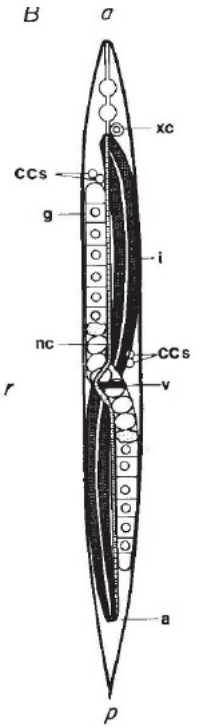


The third-round division: L-R axis









A brief recap:

Initiated by sperm entry, the fertilized zygote starts off with 5 asymmetric divisions that establish the A-P, D-V, and L-R axes, and generate 6 blastomeres with unique fates.

A brief recap:

Key cellular events of blastomere patterning:

- Sperm centrosome marking the posterior
- Polarized actomyosin contraction and cytoplasmic flow
- Partition of anterior-posterior PAR complexes
- Established fate determinants (TF & induction)

Cell fate maps: roughly aligned with body planes

Final body planes: laid out during gastrulation

Is this early?

Recommended reading:

Overview (Review)

Bowerman. Maternal control of pattern formation in early *Caenorhabditis elegans* embryos. Curr Top Dev Biol 39:73-117, 1998

Initiation – cortical contraction

Cowan and Hyman. Centrosomes direct cell polarity independently of microtubule assembly in C. elegans embryos, Nature. 431(7004):92-6, 2004

PAR and fate determinants (Review)

Kemphues. PARsing embryonic polarity, Cell, 101, 345–348, 2000

Induction

Thorpe, Schlesinger, Carter and Bowerman. Wnt signaling polarizes an early C. elegans blastomere to distinguish endoderm from mesoderm, Cell 22;90(4):695-705, 1997

Chirality

Wood. Evidence from reversal of handedness in C. elegans embryos for early cell interactions deter- mining cell fates. Nature, 349:536–538, 1991