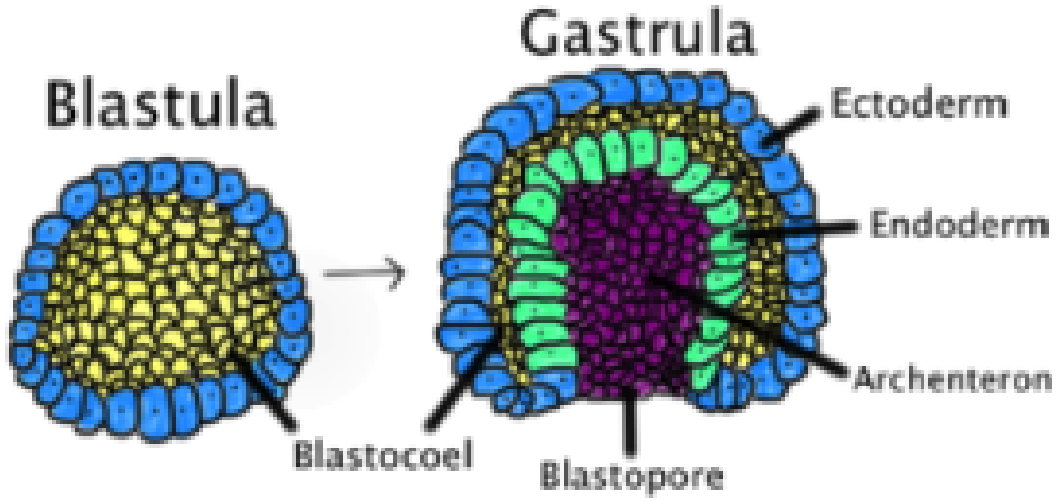
Pattern Formation and Morphogenesis

Mammals:

- zygote (fertilized egg)
- morula (solid ball of cells)
- blastula (hollow sphere)
- gastrula (invagination, germ layers: ecto/meso/endoderm)

http://iupr1.cs.uni-kl.de/ tmb/simso-videos/embryo.mp4

Blastula and Gastrula



Just weird biology?

Computational problem:

- each cell is a little finite state automaton
- cells send signals to each other

3D structure is determined by:

- cell differentiation and resulting mechanical properties
- cables and volumes
- adhesion between cells

http://iupr1.cs.uni-kl.de/ tmb/simso-videos/modular-robot.mp4

Related problems in computer science:

- self-organizing, robust networks
- robust modular robotics, robot self-assembly
- 4D printing

Basic processes in morphogenesis:

- signaling (communication)
- replication
- migration
- differentiation
- controlled adhesion

Drosophila Embryogenesis

Understanding of embryogenesis in mammals is complicated due to the complex interaction of 3D geometry, cell volumes, and signals.

Drosophila is a much simpler models system.

Segmentation:

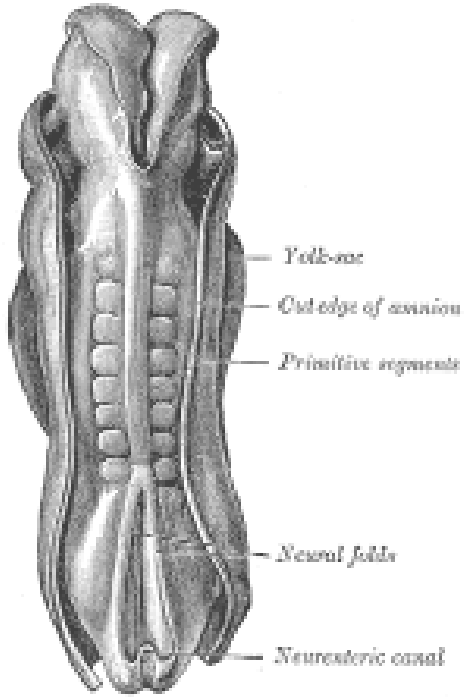
- higher biological organisms have complex body plans
- body plans are generally created as a sequence of *segments*

General developmental sequence:

- start of with an undifferentiated tube
- divide the tube into segments
- differentiate each segment (attach legs, eyes, etc.)

Drosophila with segments

segmentation in human embryos



human segmentation - each somite generates a muscle

Drosophila embryogenesis:

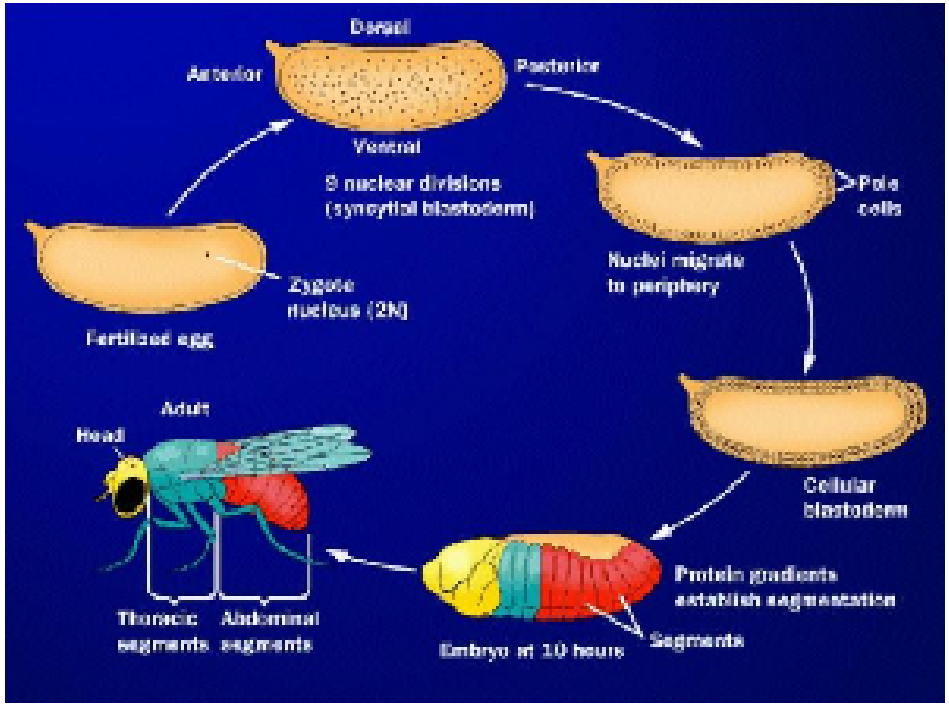
Mammals:

- cells divide, then migrate and differentiate
- each cell has a single nucleus
- communication / signaling between cells is complicated by cell membranes

Drosophila:

- the egg starts out with a single nucleus
- the nucleus divides 8 times, yielding 256 nuclei
- the 256 nuclei distribute themselves around the wall of the egg
- nuclei can send and receive signaling molecules that move via diffusion

Drosophila embryogenesis



Starting point:

- elongated container with 256 nuclei around the wall
- nuclei are *not* differentiated
- we want to create a sequence of segments

How do we do that? What kind of signaling can create such patterns?

Videos for Fly Embryogenesis:

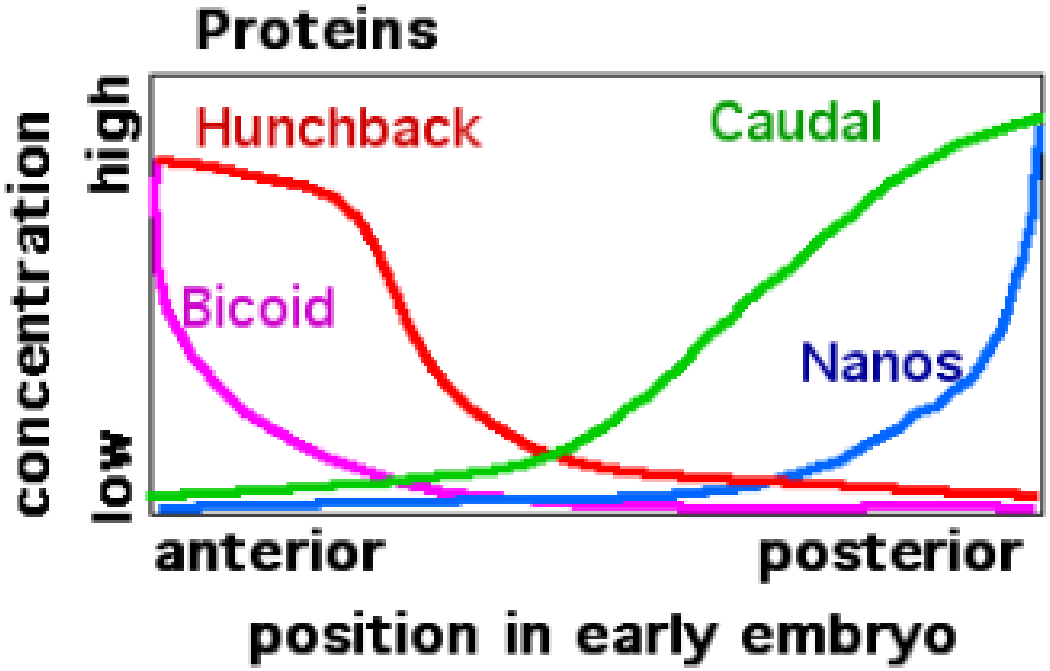
http://iupr1.cs.uni-kl.de/ tmb/simso-videos/fly-embryo-real-time.mp4

http://iupr1.cs.uni-kl.de/ tmb/simso-videos/embryogenesis.mp4

Mom helps:

- during egg formation, mother deposits molecules at one end and the other
- these molecules give rise to concentration gradients

initial concentration gradients



What happens next?

- naive approach: concentration sensing
- take the concentration of Caudal, or the ratio of Caudal to Hunchback
- divide the range into a bunch of disjoing regions
- "if ratio in $[1.7, 2.4]$, then develop into segment 7"

That approach doesn't work; the signal is far too noisy.

How does it actually work?

- a series of *reaction-diffusion* networks of morphogens
- morphogens enhance or repress both their own production and the production of other morphogens
- the whole network is similar to a complex network of predators, prey, and migration

morphogens

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1 subplot(121); fig("http://upload.wikimedia.org/wikipedia/commons
      /7/73/Gap_ene_expression.png")
2 subplot(122); fig("http://upload.wikimedia.org/wikipedia/commons/b/
      b9/Pair_rule.jpg")file:/home/tmb/simso-videos/brusselator.mp4
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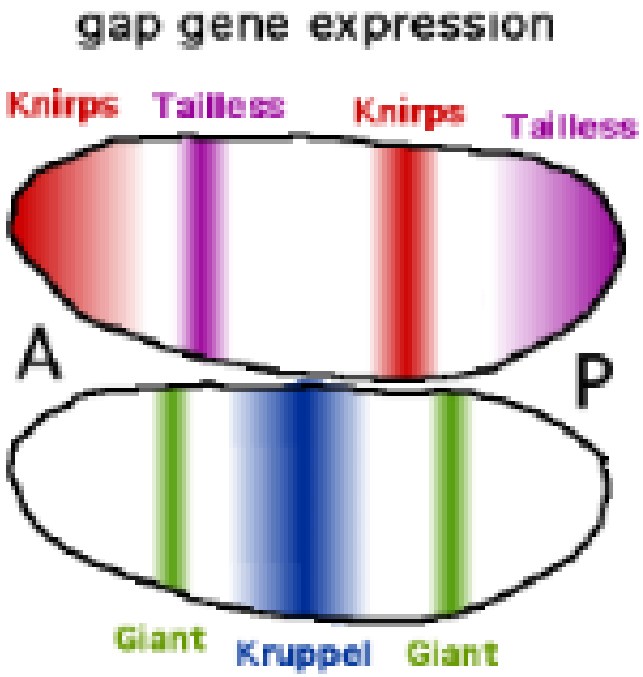
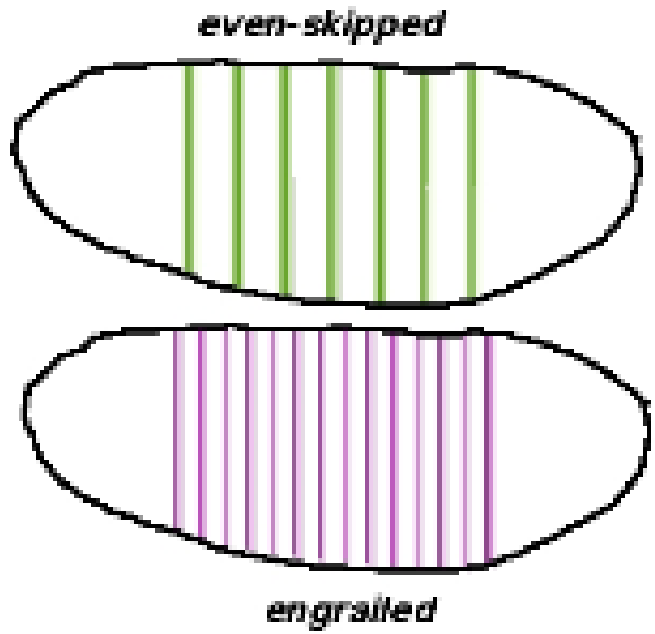
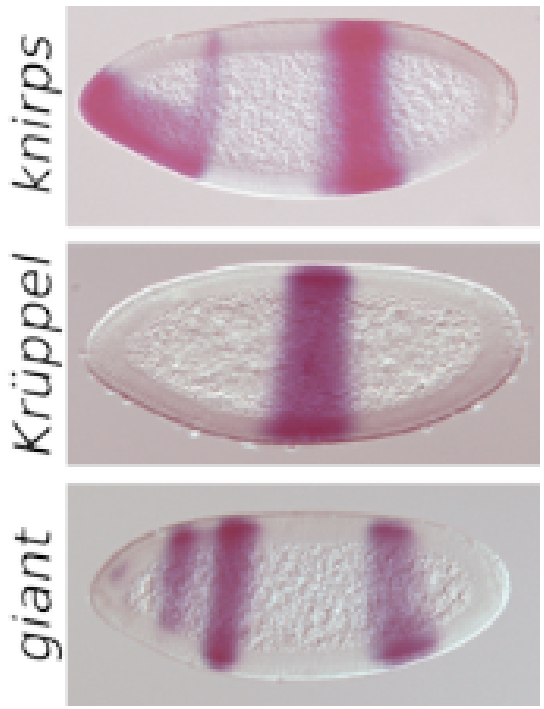




gap genes in the actual egg



How did people find this?

- irradiate Drosophila
- look for interesting mutants
- problem: most interesting mutants end up dead, so how do you breed for them?
- problem: this is very tedious and boring work

1995 Nobel Prize: Nsslein-Volhard, Lewis, Wischaus

Regulatory networks during morphogenesis:

Principles:

- interaction between morphogens establish disjoint regions (segments) within the organism
- each segment has an identifier based on the combination of morphogens expressed in them

High level view:

- analog signalling and non-linear interactions are used to establish a digital/binary code for morphogenesies
- regions are contiguous and have the correct topology (neighborhood relationships) with very high probability