Lecture 20: Drosophila embryogenesis

Mitotic recombination/clonal analyses
Embrygenesis
Four classes of genes:
- Maternal genes
- Gap genes
- Pair-rule genes
- Segment polarity genes

Homeotic genes

Read 140-141; 826-837 Fig. 5.25; 5.26; D18-D27; 19.2; 19.16

"Molecular Biology of the Cell" ed. By Bruce Albert et al. (free online through ncbi books)

Genetic mosaic

Genetic Mosaic:

Composed of cells of more than one genotype

How to generate:

Generated by mitotic recombination (X-ray induced mutations cause crossing-over in homologues in somatic cells)

Purpose of mosaic:

1) to determine whether a gene acts Autonomously or nonautonomously

2) To determine developmental potential of precursor cells

Fig. 5.25

Mitotic recombination induced mosaics

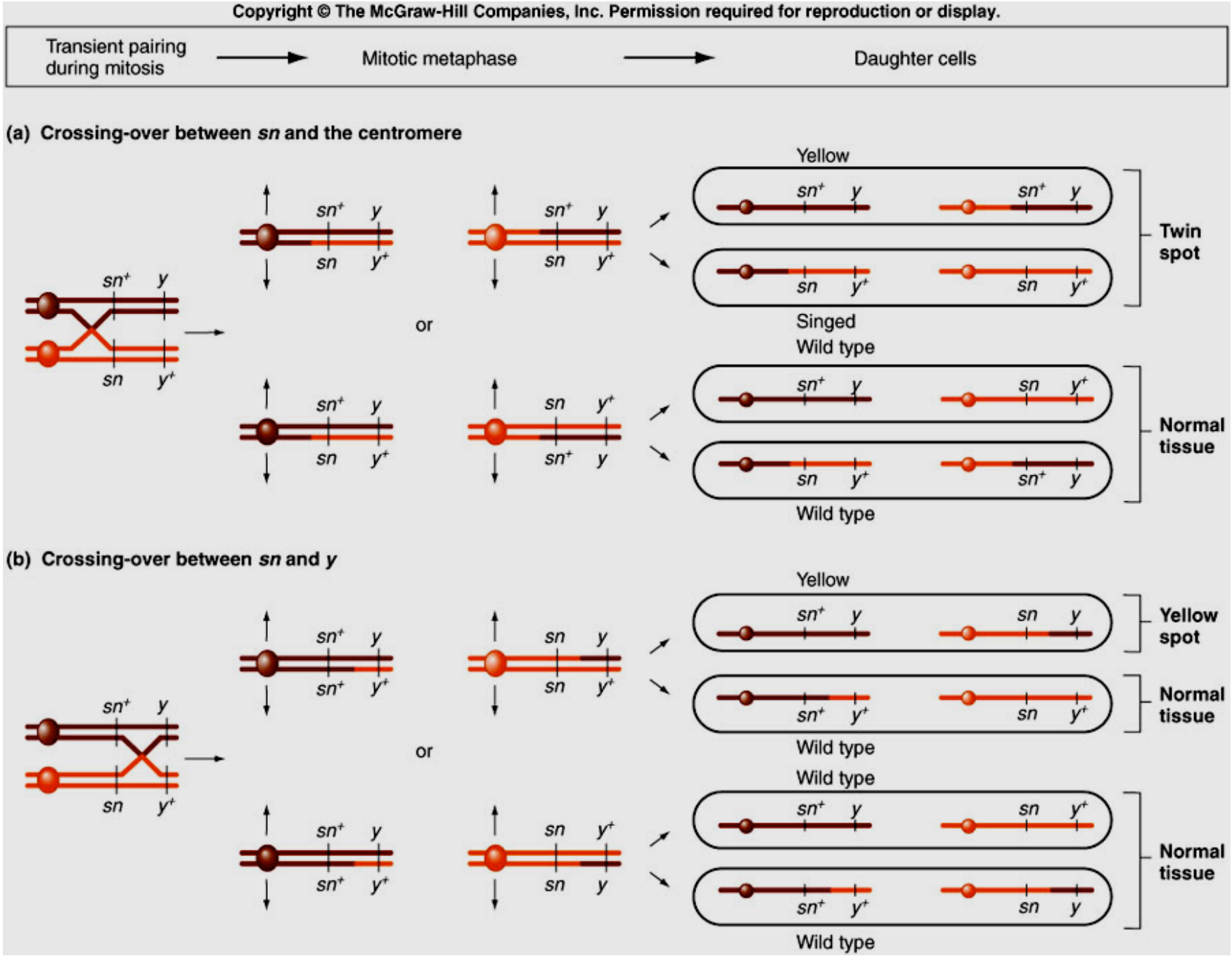


Fig. 5.26

Drosophila oocyte

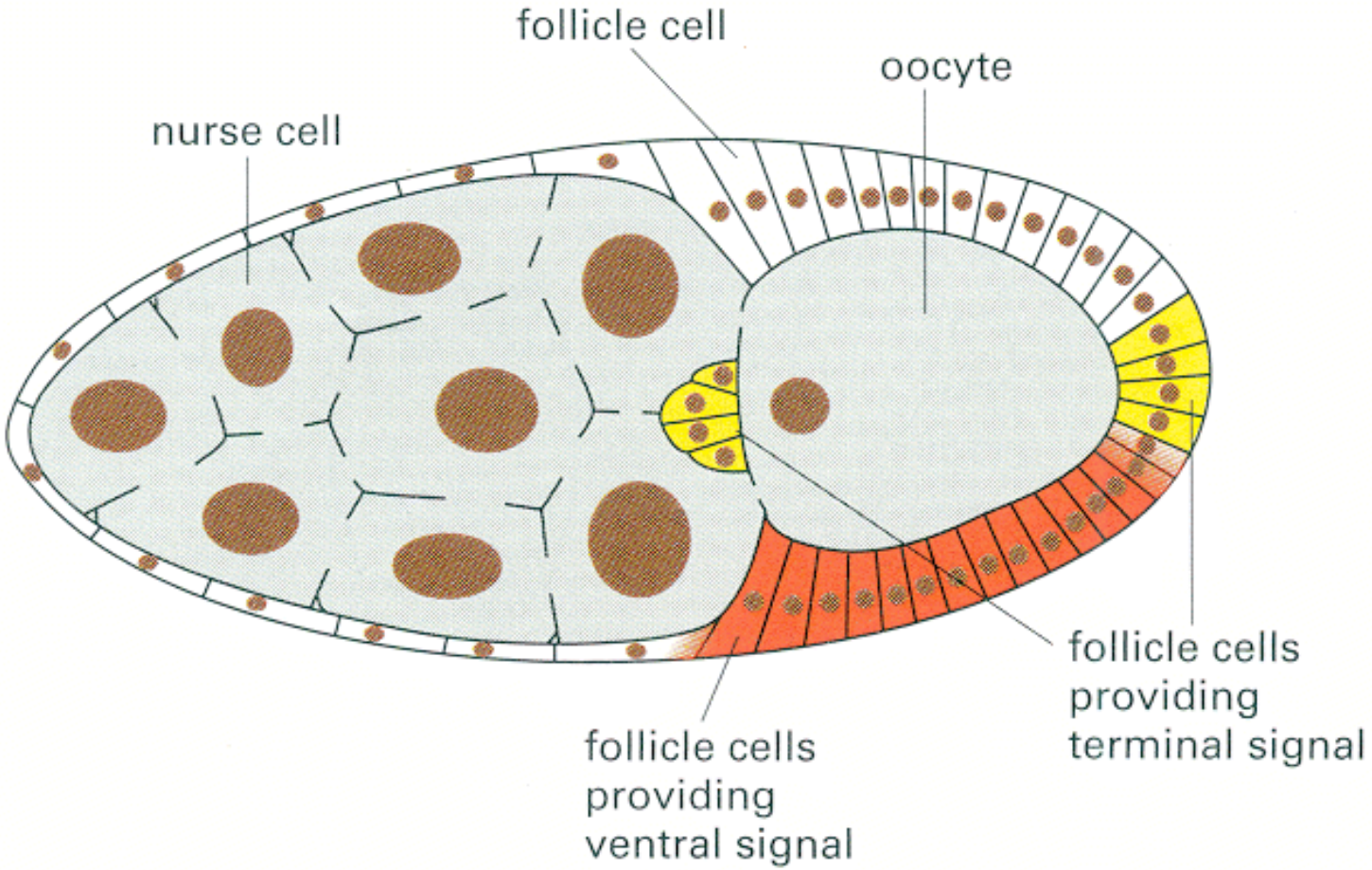
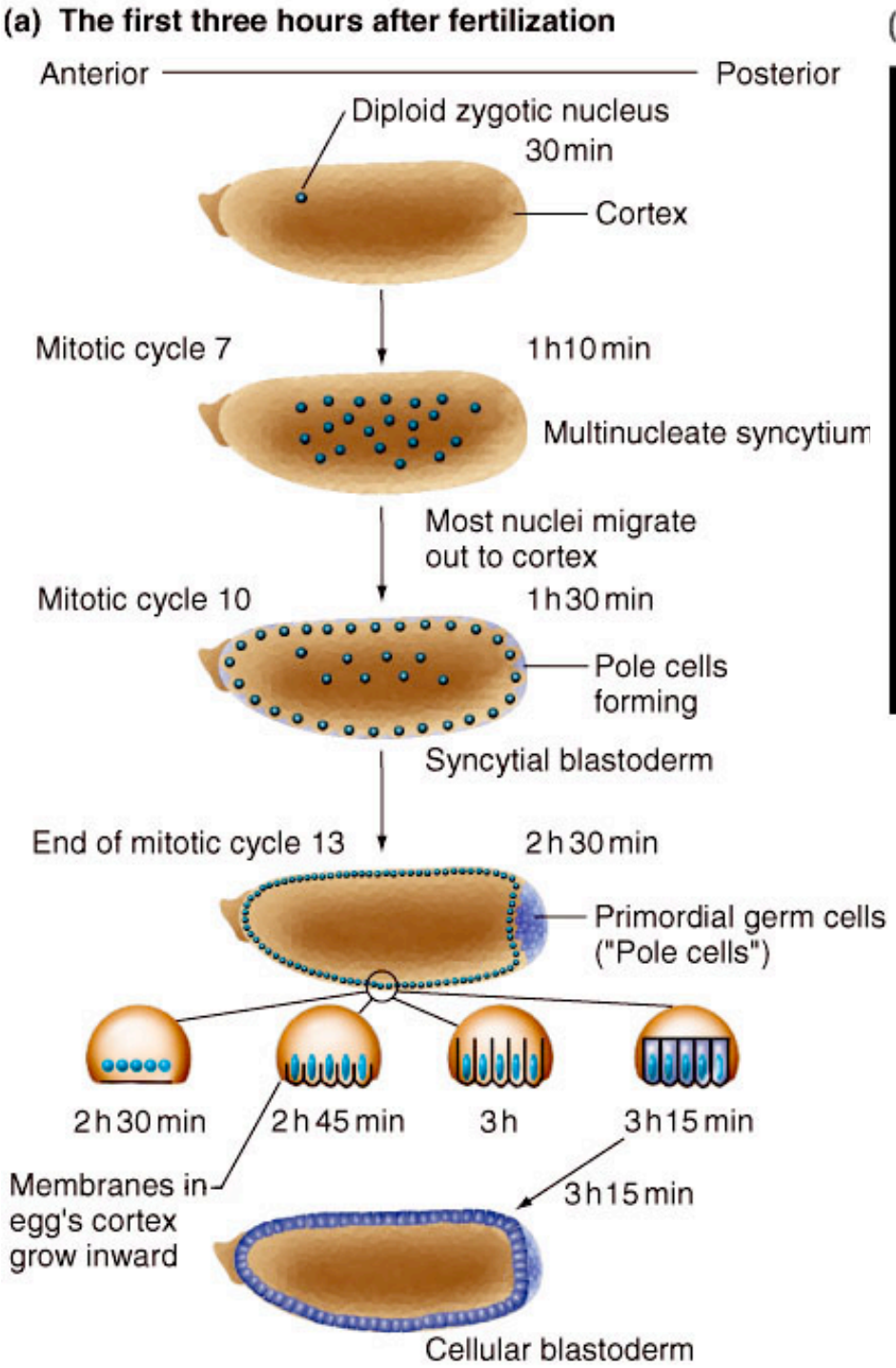
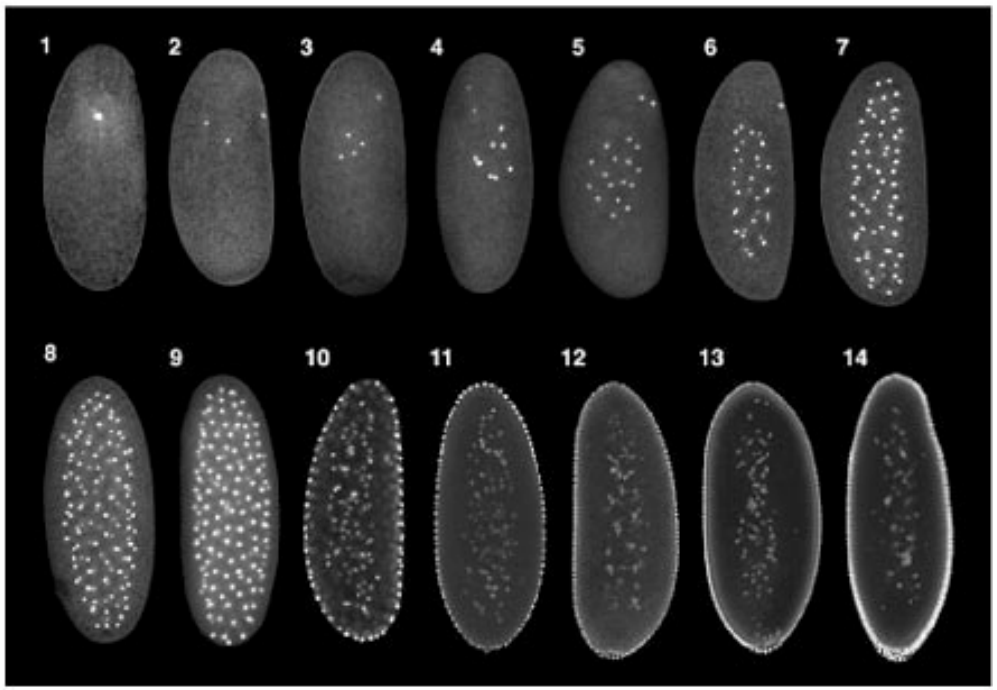


Figure 21-30. A Drosophila oocyte in its follicle. The oocyte is derived from a germ cell that divides four times to give a family of 16 cells that remain in communication with one another via cytoplasmic bridges (gray). One member of the family group becomes the oocyte, while the others become nurse cells, which make many of the components required by the oocyte and pass them into it via the cytoplasmic bridges. The follicle cells that partially surround the oocyte have a separate ancestry. As indicated, they are the sources of terminal and ventral egg-polarizing signals. (**From Bruce Albert Book)**

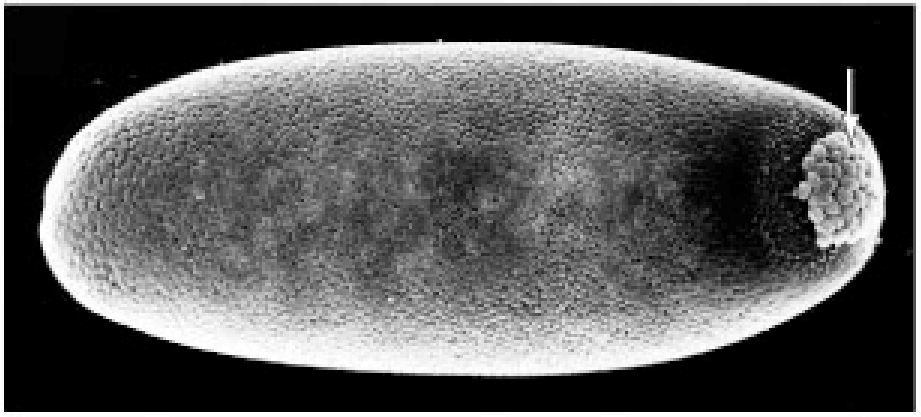




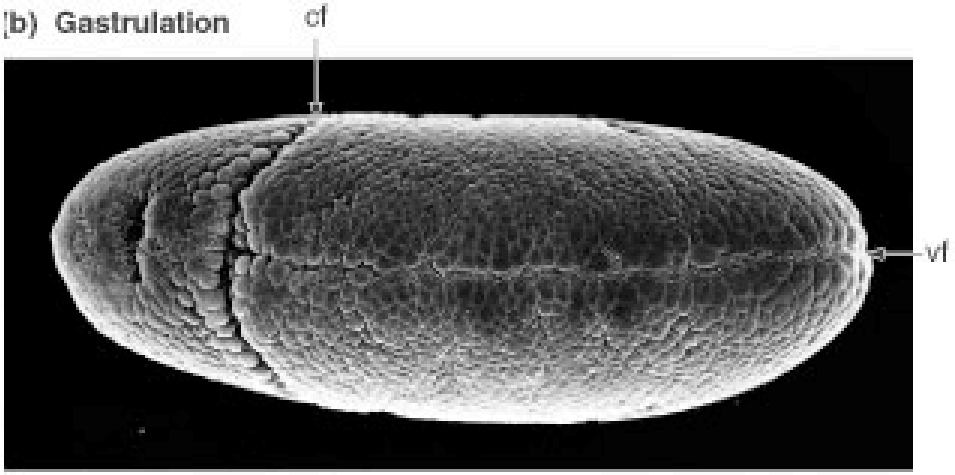
Drosophila Embryogenesis

Fig. D.18

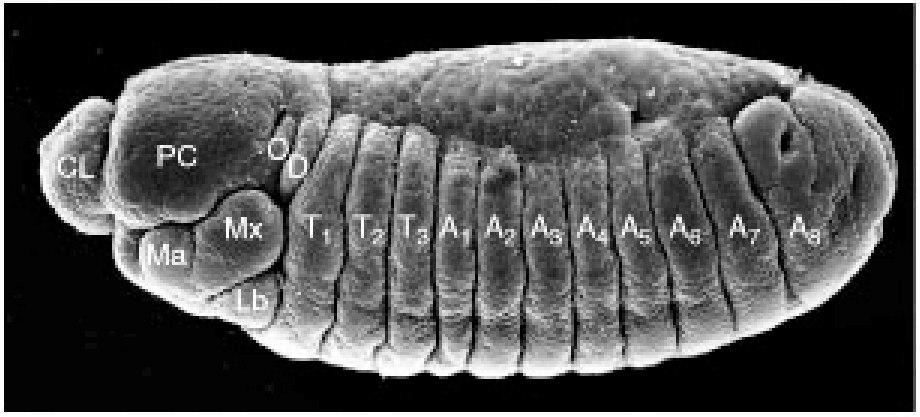
(a) Cellular blastoderm



(b) Gastrulation



(c) Segmentation



(d) Segment identity is preserved throughout development.

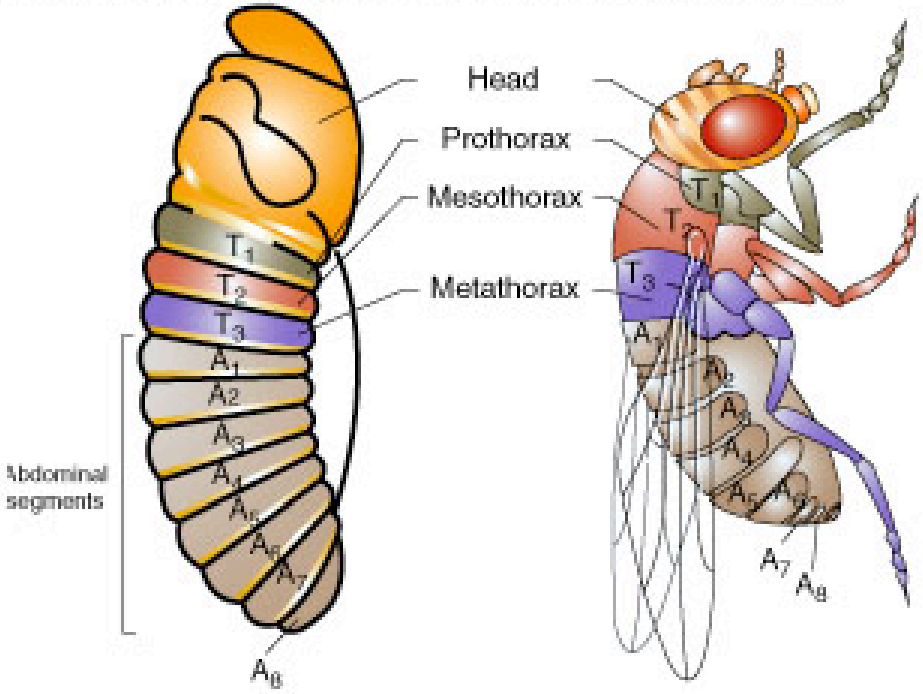
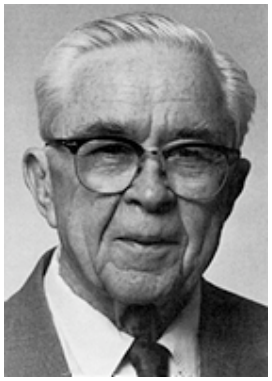


Fig. D.19

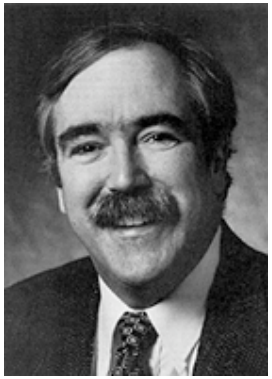
A parade of 1995 Nobels:

for their discoveries concerning the genetic control of early embryonic development



Edward B. Lewis

Christiane Nüsslein-Volhard

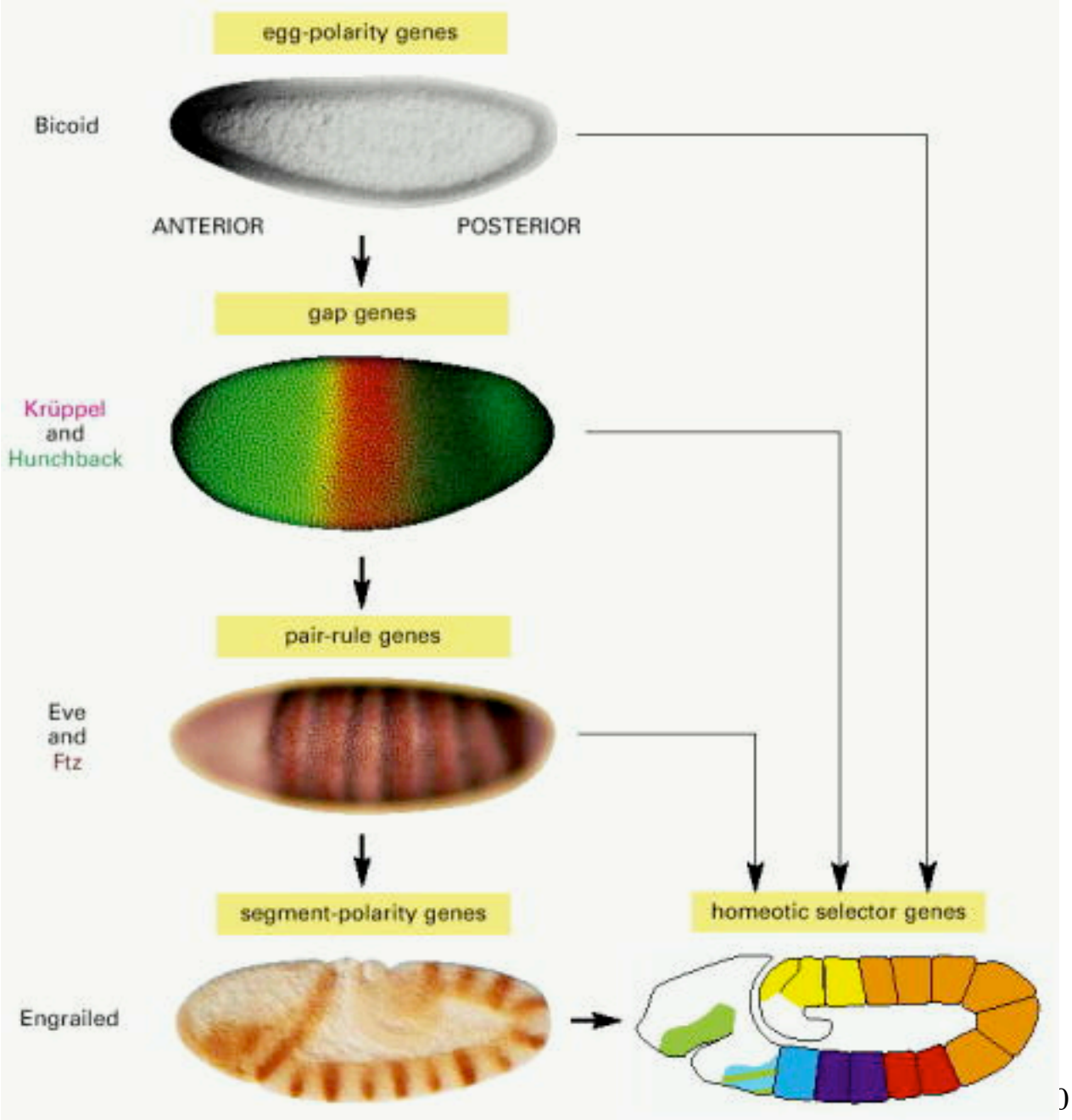


Eric F. Wieschaus

Four classes of genes responsible for formation of segments

- Maternal genes
- Gap genes
- Pair-rule genes
- Segmentation polarity genes
- Function in a hierarchy that progressively subdivides the embryo into successively smaller units

From Bruce Albert Book



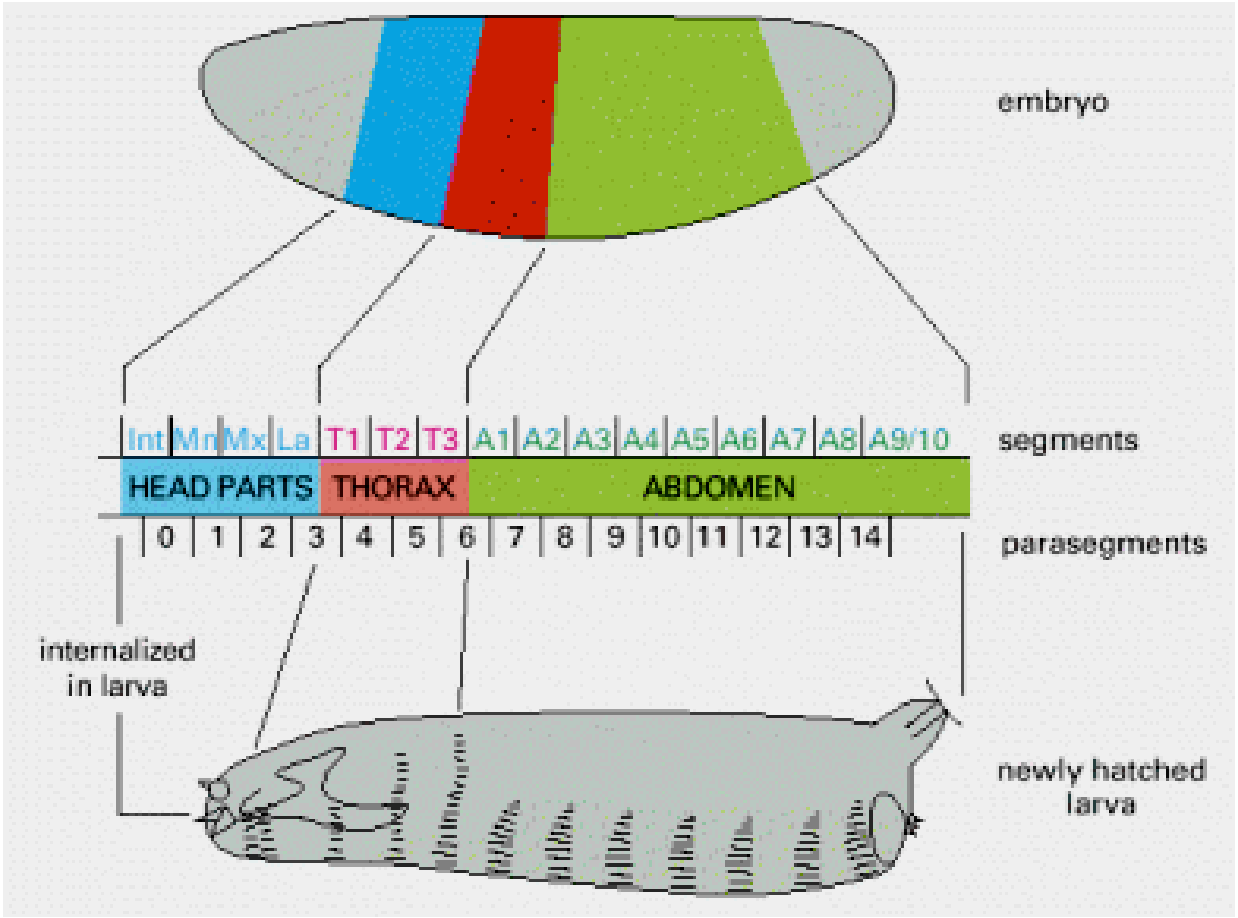


Figure 21-26. The segments of the Drosophila larva and their correspondence with regions of the blastoderm. The parts of the embryo that become organized into segments are shown in color. The two ends of the embryo, shaded gray, are not segmented and become tucked into the interior of the body to form the internal structures of the head and gut. (The future external, segmental structures of the adult head are also transiently tucked into the interior in the larva.) Segmentation in Drosophila can be described in terms of either segments or parasegments: the relationship is shown in the middle part of the figure. Parasegments often correspond more simply to patterns of gene expression. The exact number of abdominal segments is debatable: eight are clearly defined, and a ninth is present vestigially in the larva, but absent in the adult. **(From Bruce Albert Book)**

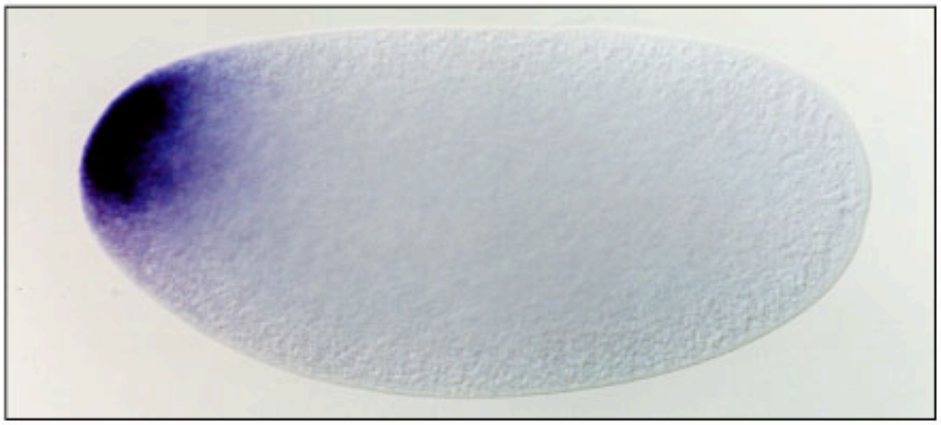
Morphogens: Substances that define different cell fate in a concentration-dependent manner

Klaus Sander proposed:

- Each pole of the egg produces a different substance
- These substance form the opposing gradients by diffusion
- Concentrations of these substances determine the type of structure produced at each position long the body axis

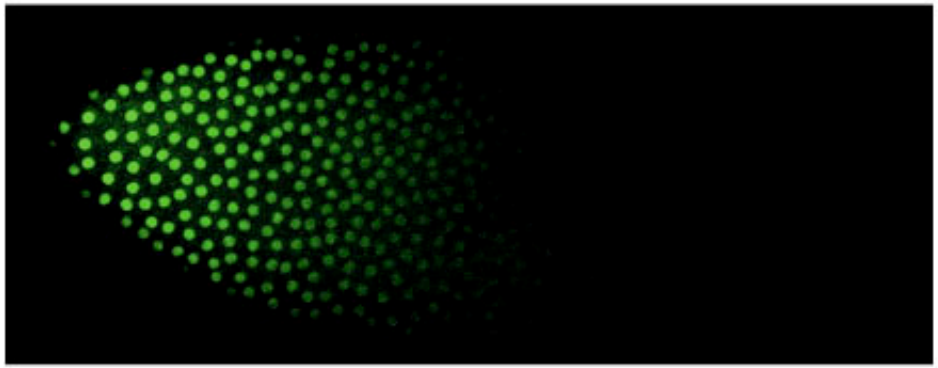
Bicoid (Bcd) is a morphogen

(a) Localization of *bicoid* mRNA



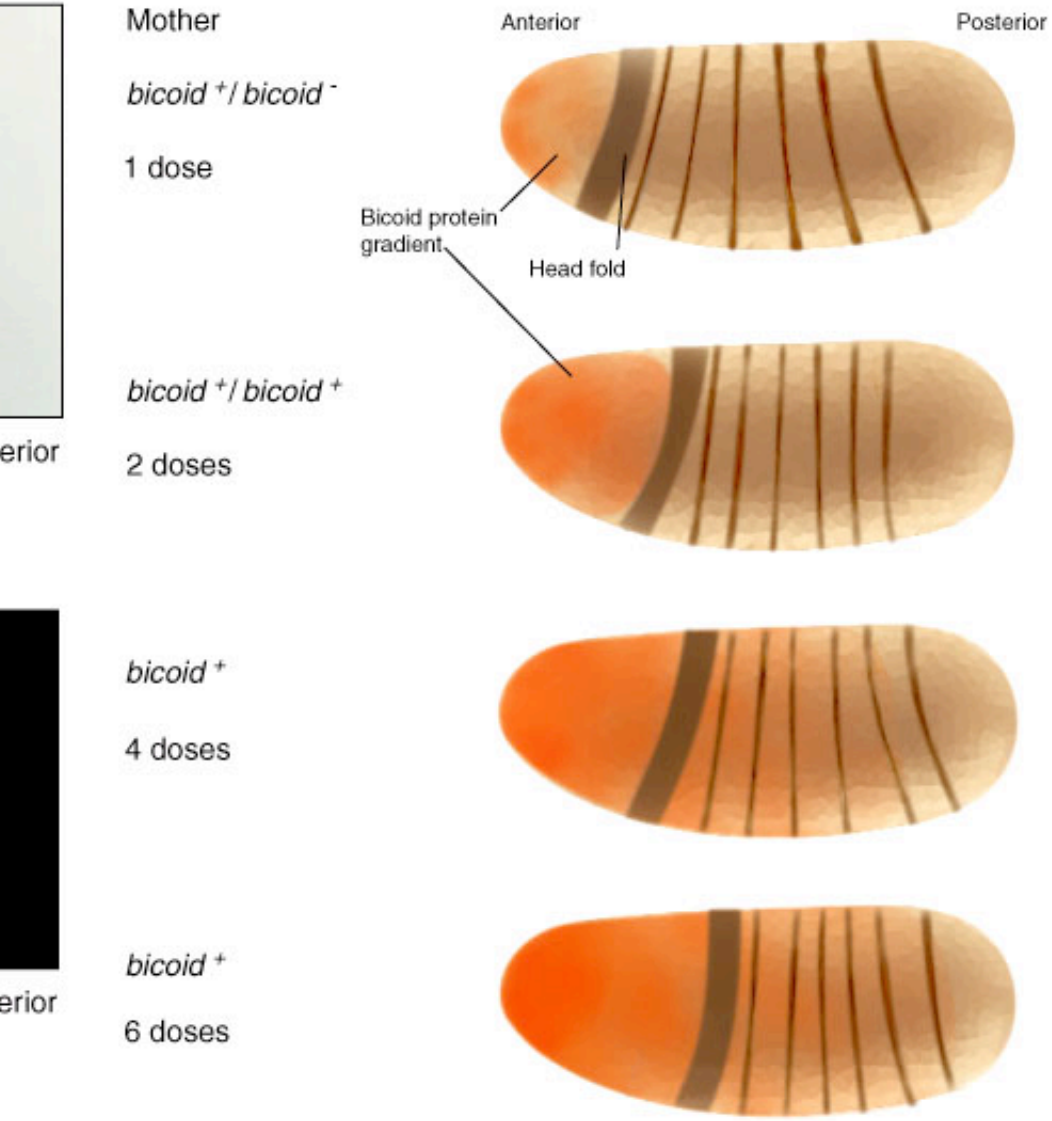
Anterior Posterior

(b) A gradient of Bicoid protein

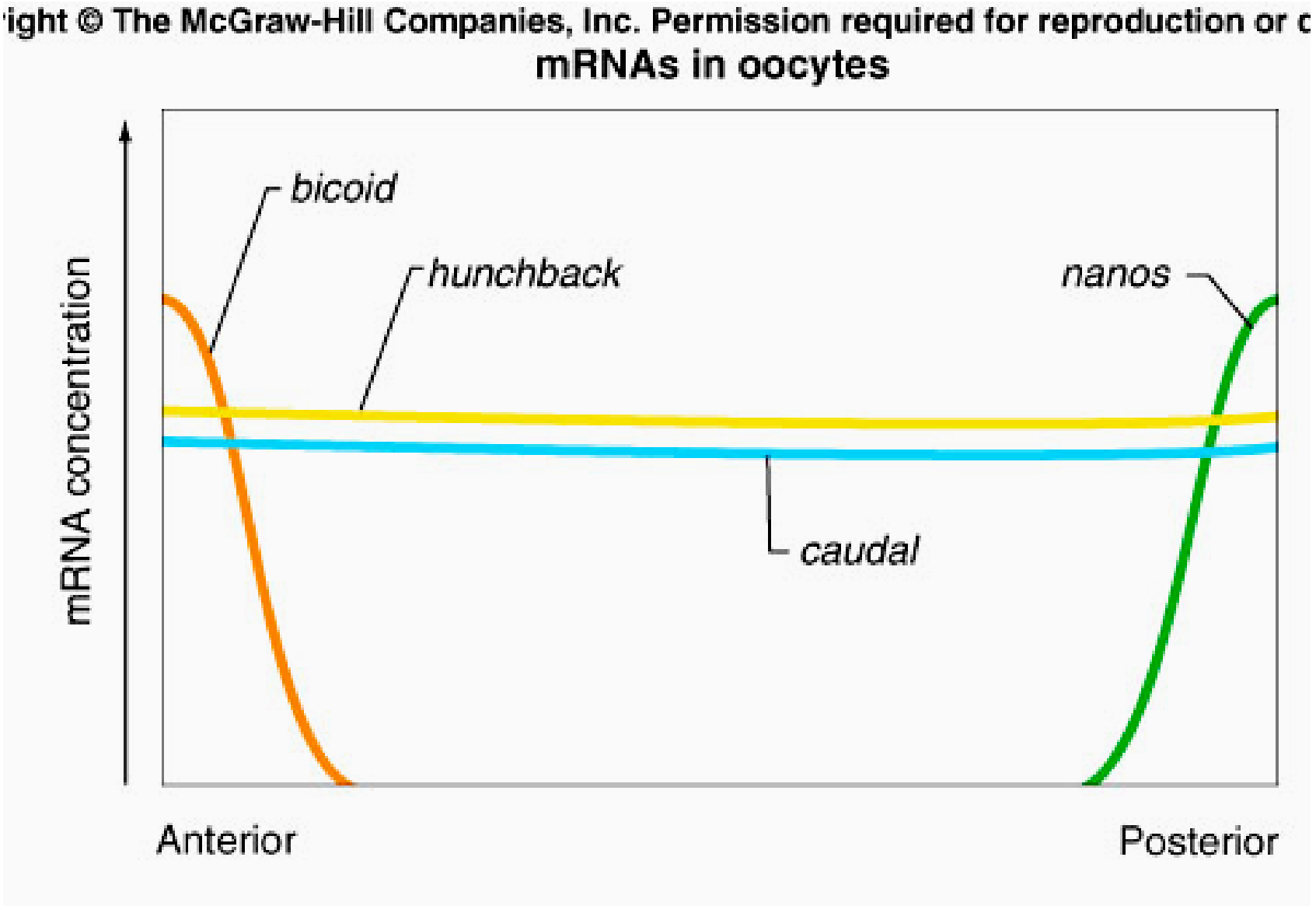


Anterior Posterior

(c) Bicoid protein is a morphogen.



How Bcd protein works



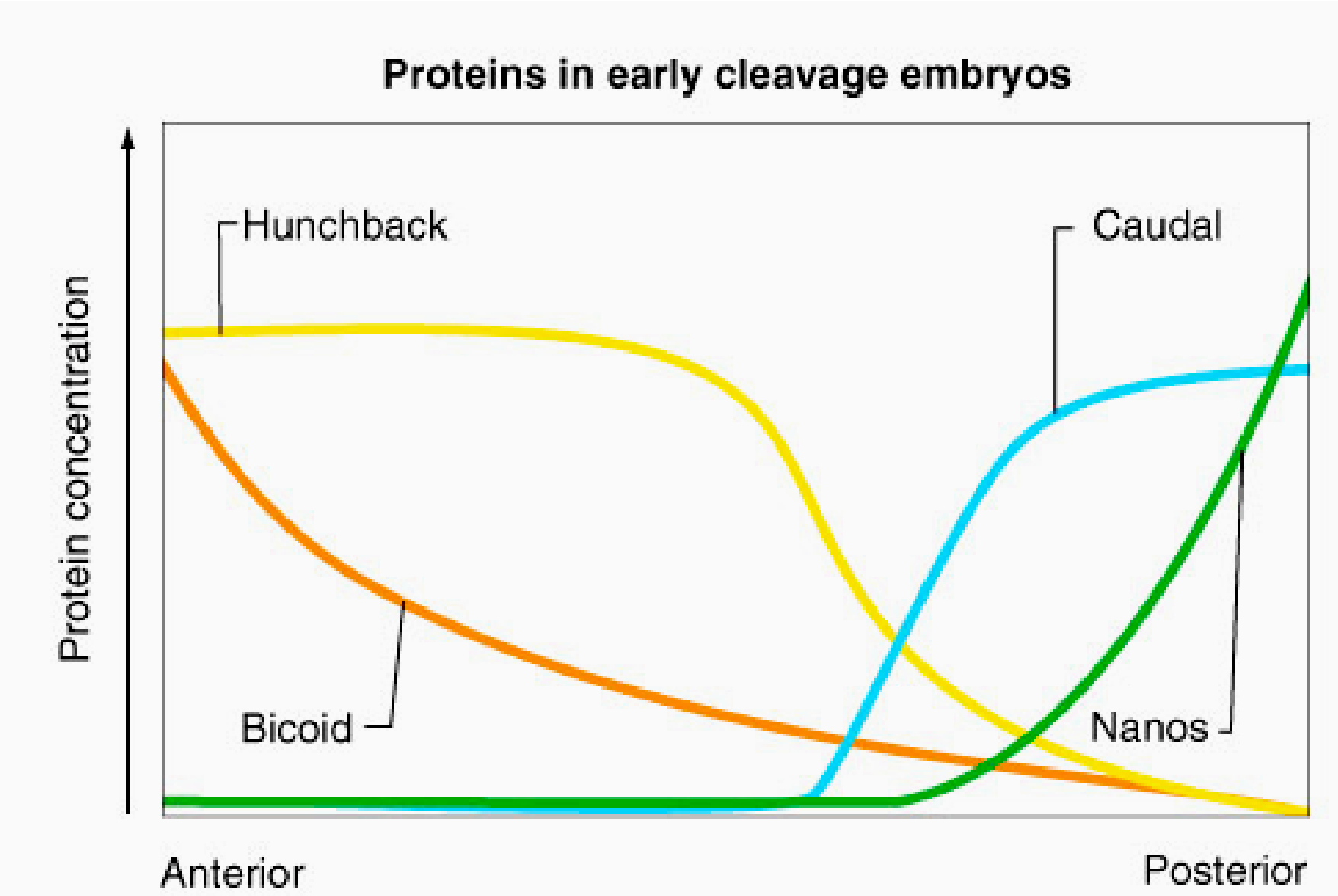


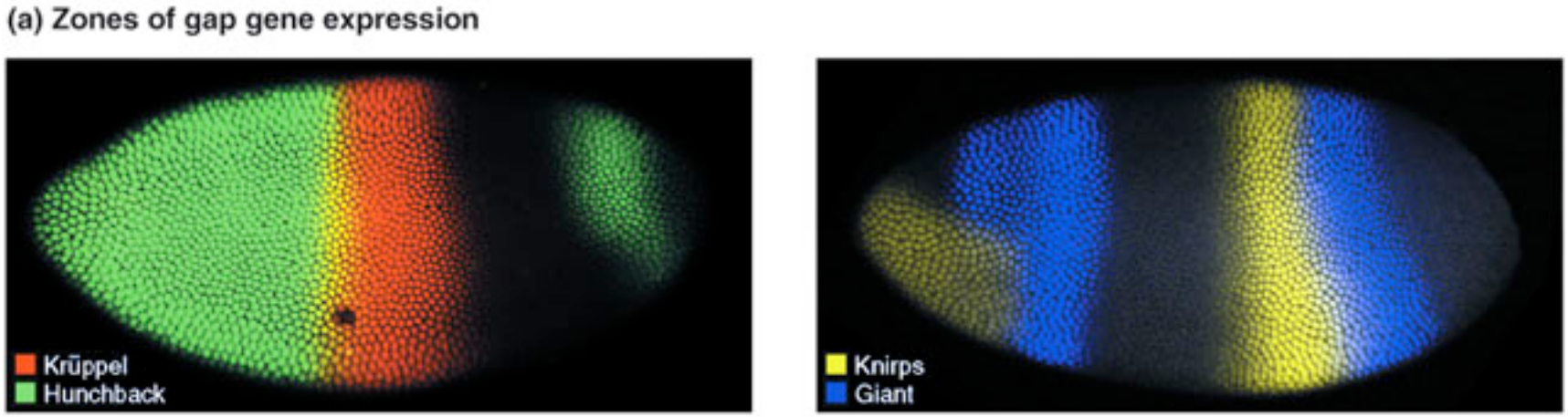
Fig. D.21 bottom

Maternal genes interact to produce morphogen gradients

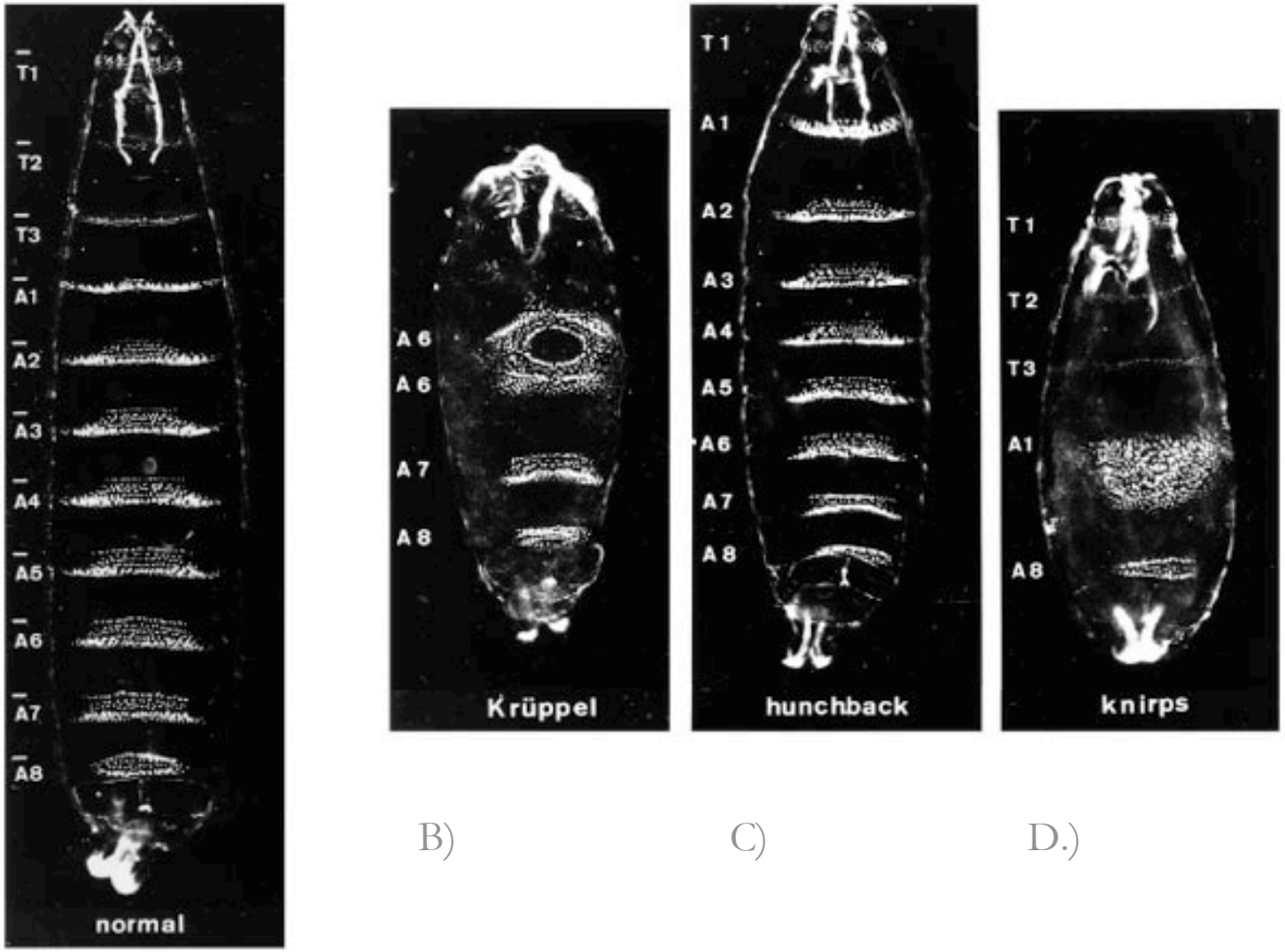
- **Maternal-effect mutations**
  - **Recessive mutations in maternal genes that influence embryonic development**
- **Maternally supplied components account for formation of body plan between fertilization and end of 13 syncytial divisions**
- **Nusslein-Volhard and Wieschaus screened thousands of mutagen treated chromosomes by examining phenotypes of embryos from homozygous mutant mothers**
- **Focuses on stocks with homozygous mutant sterile females**
- **Identified large number of maternal genes**
- **Nobel Prize in medicine**

Gap genes

Zones of expression of four gap genes: *hunchback*, *Kruppel*, *knirps*, and *giant* in late syncytial blastoderm embryos



Defects in segmentation from mutations in gap genes



A) B) C) D.)

Fig. D.22b

Mutations in gap gene result in loss of segments corresponding to zone of expression

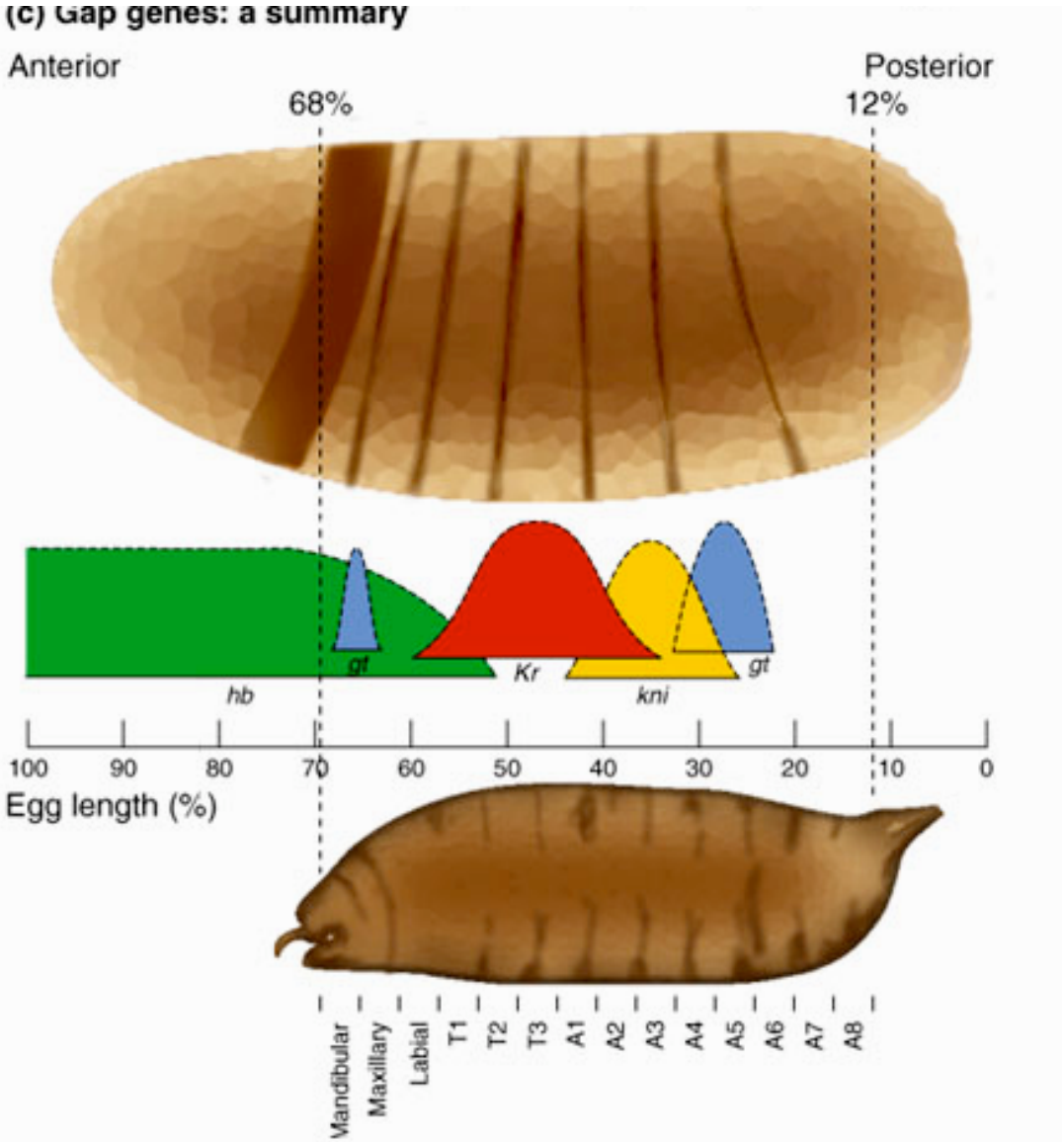
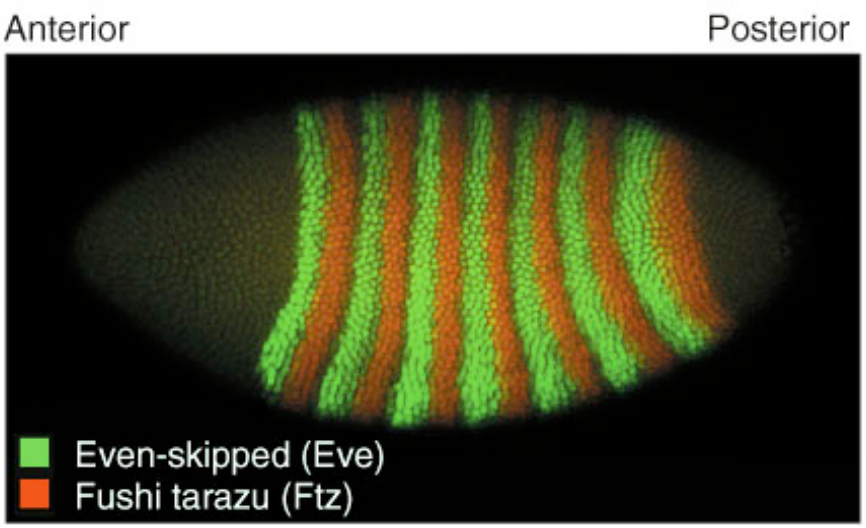


Fig. 22 c

- Gap genes
  - Gap mutants show a gap in segmentation pattern at positions where particular gene is absent
  - Binding sites in promoter have different affinities for maternal transcription factors
  - Gap genes encode transcription factors that influence expression of other gap genes

Pair-rule genes



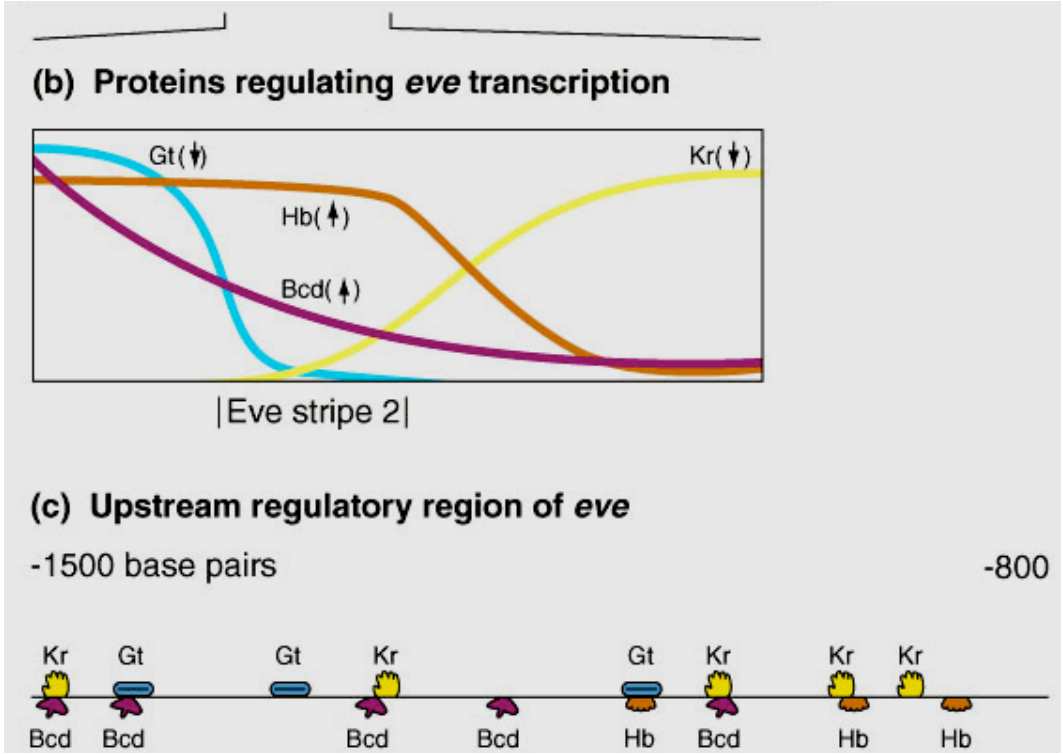
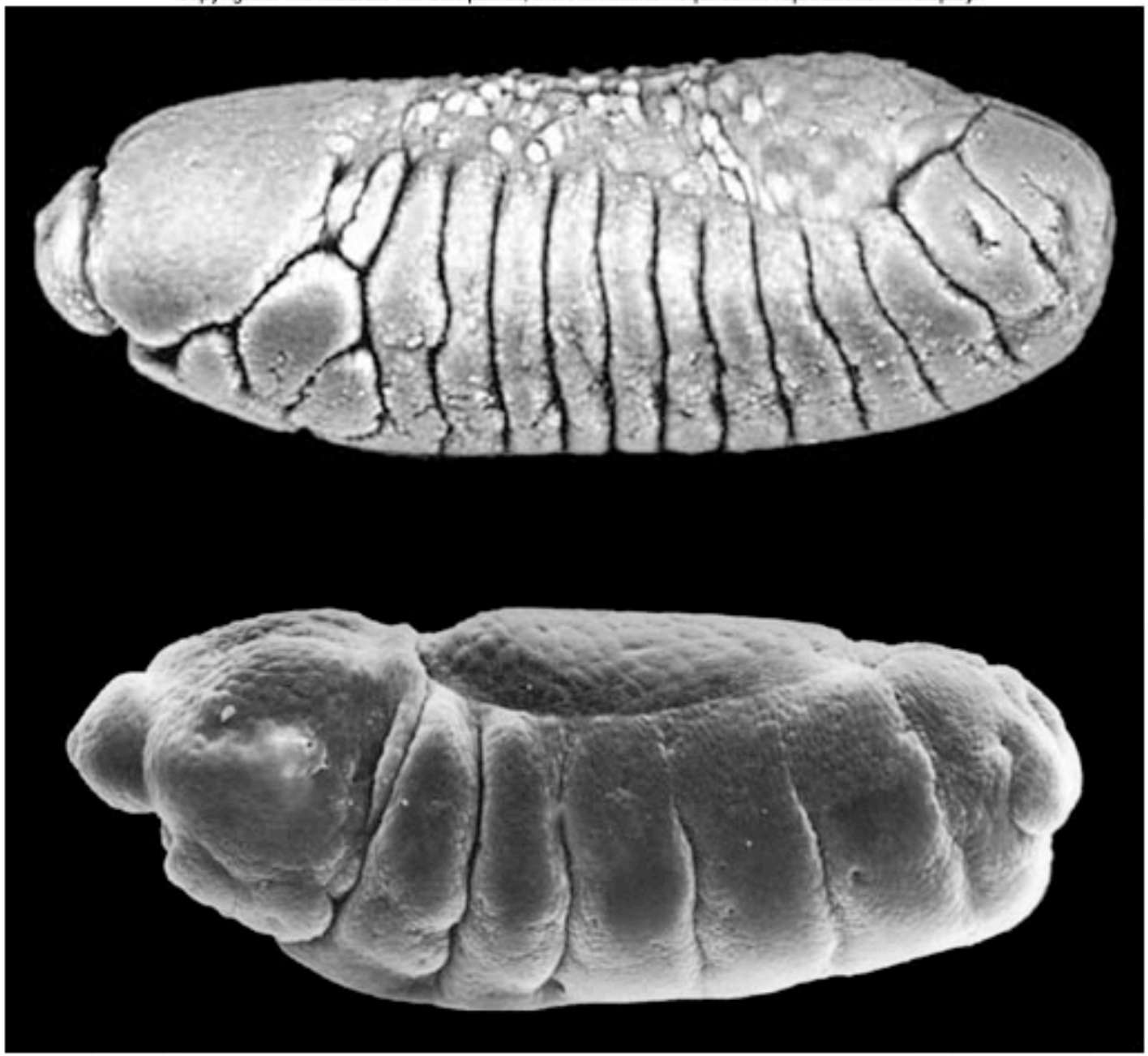


Fig. D.23

Fig. 19.2



Ftz
mutant

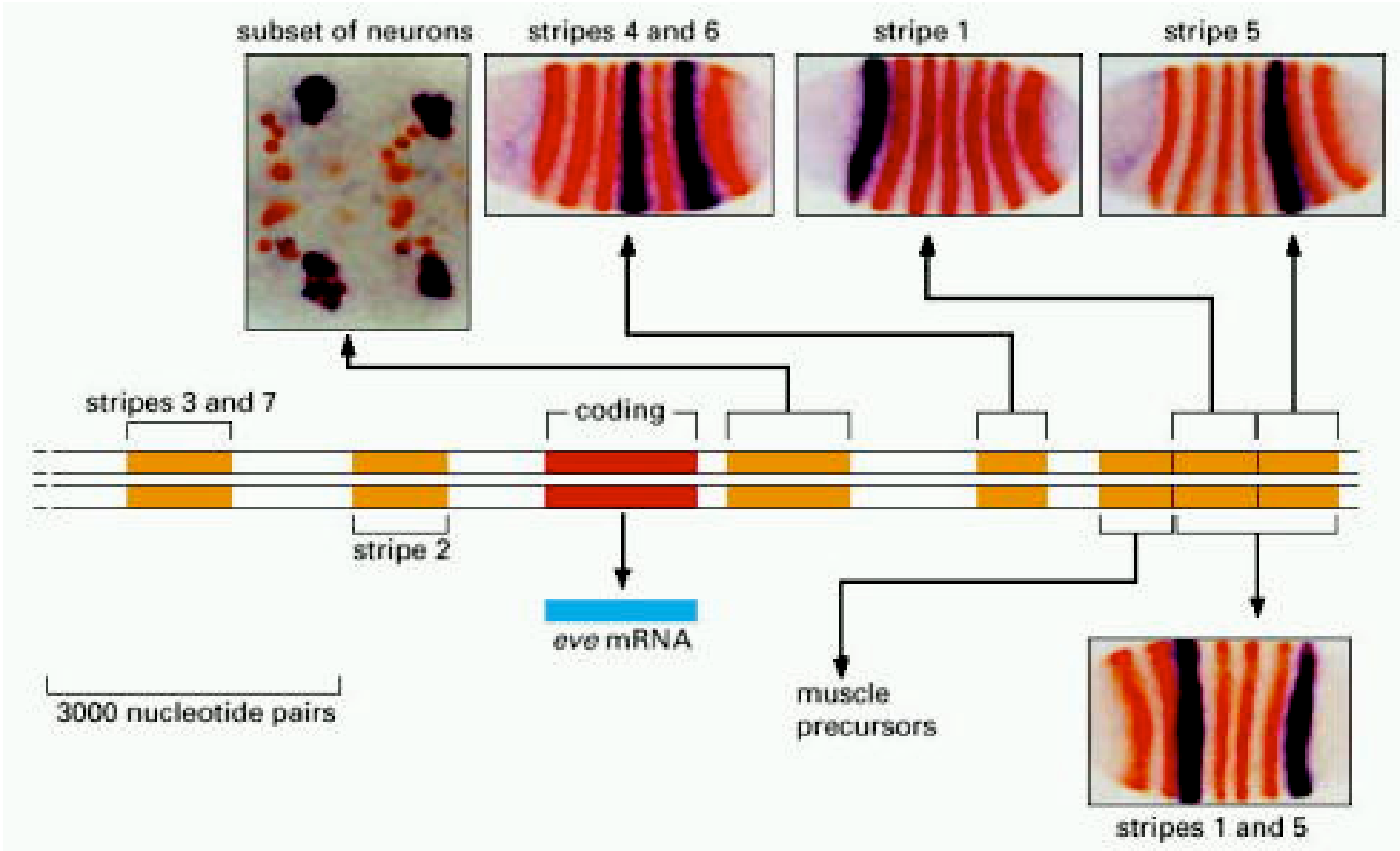


Figure 21-38. Modular organization of the regulatory DNA of the eve gene. In the experiment shown, cloned fragments of the regulatory DNA were linked to a LacZ reporter (a bacterial gene). Transgenic embryos containing these constructs were then stained by in situ hybridization to reveal the pattern of expression of LacZ (blue/black), and counterstained with an anti-Eve antibody (orange) to show the positions of the normal eve expression stripes. Different segments of the eve regulatory DNA (ochre) are thus found to drive gene expression in regions corresponding to different parts of the normal eve expression pattern. Two segments in tandem drive expression in a pattern that is the sum of the patterns generated by each of them individually. Separate regulatory modules are responsible for different times of gene expression, as well as different locations: the leftmost panel shows the action of a module that comes into play later than the others illustrated and drives expression in a subset of neurons. **(From Bruce Albert Book)**

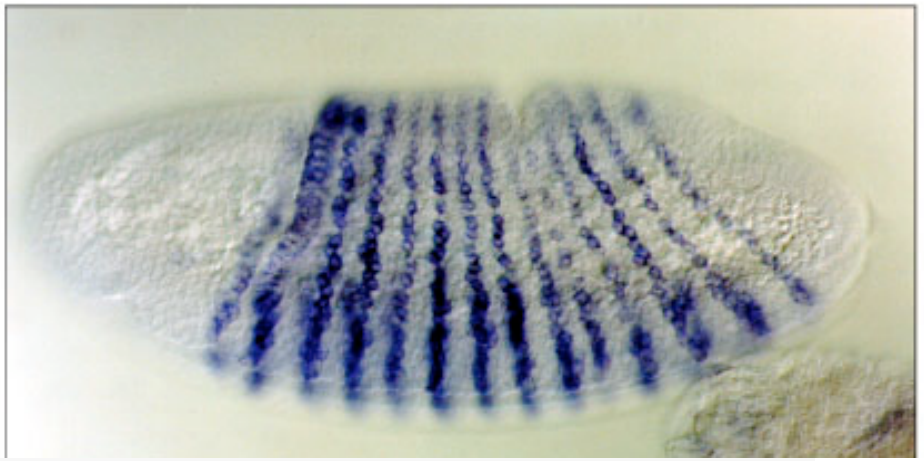
Pair-rule genes

- (a) zones of expression at beginning of blastoderm stage
  - Each gene expressed in seven stripes

- (b) formation of Eve stripe 2 requires activation by Bcd and Hb proteins and repression by Gt and Kr proteins

Segment polarity genes

(a) Distribution of Engrailed protein



(b) Segment polarity genes establish compartment borders.

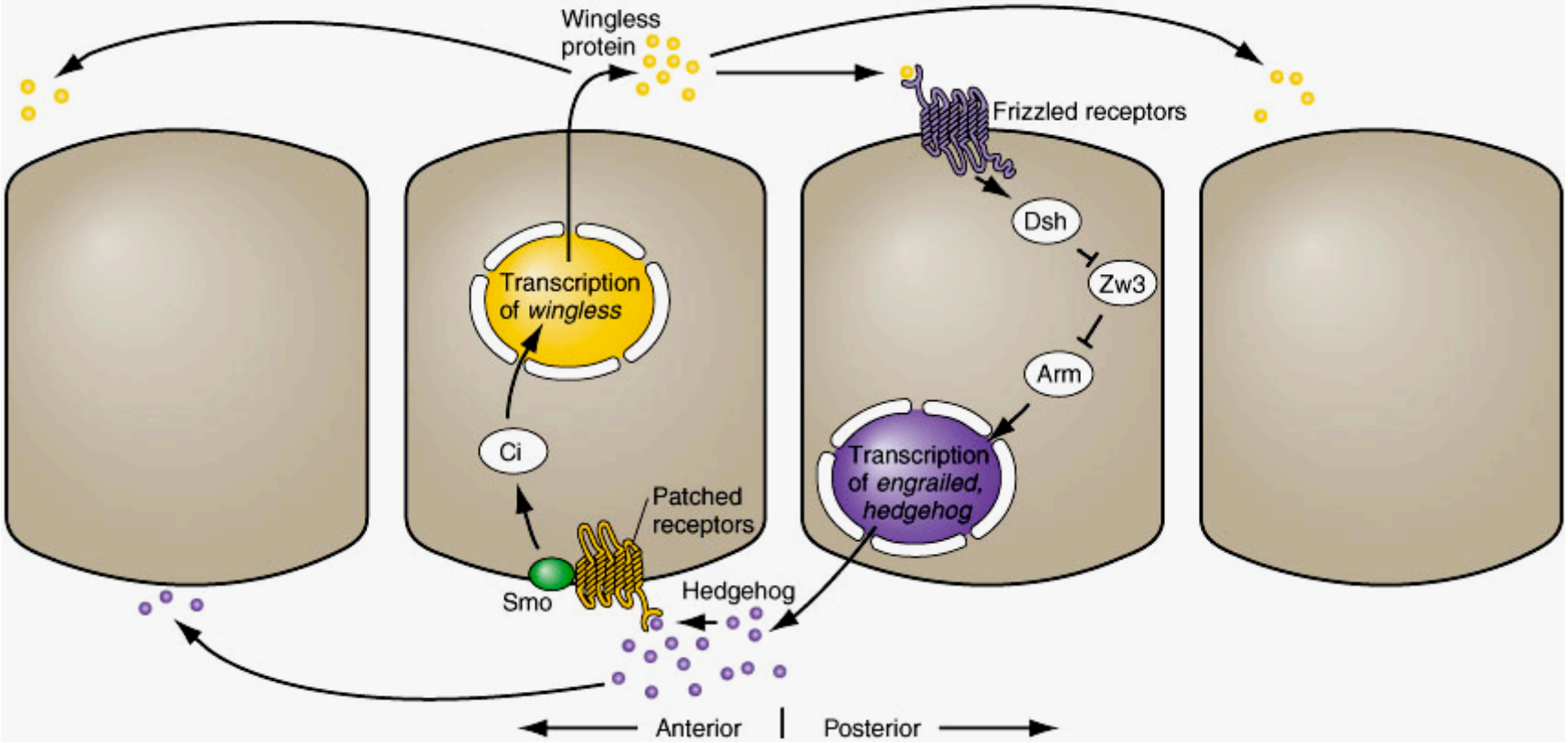


Fig. D.24

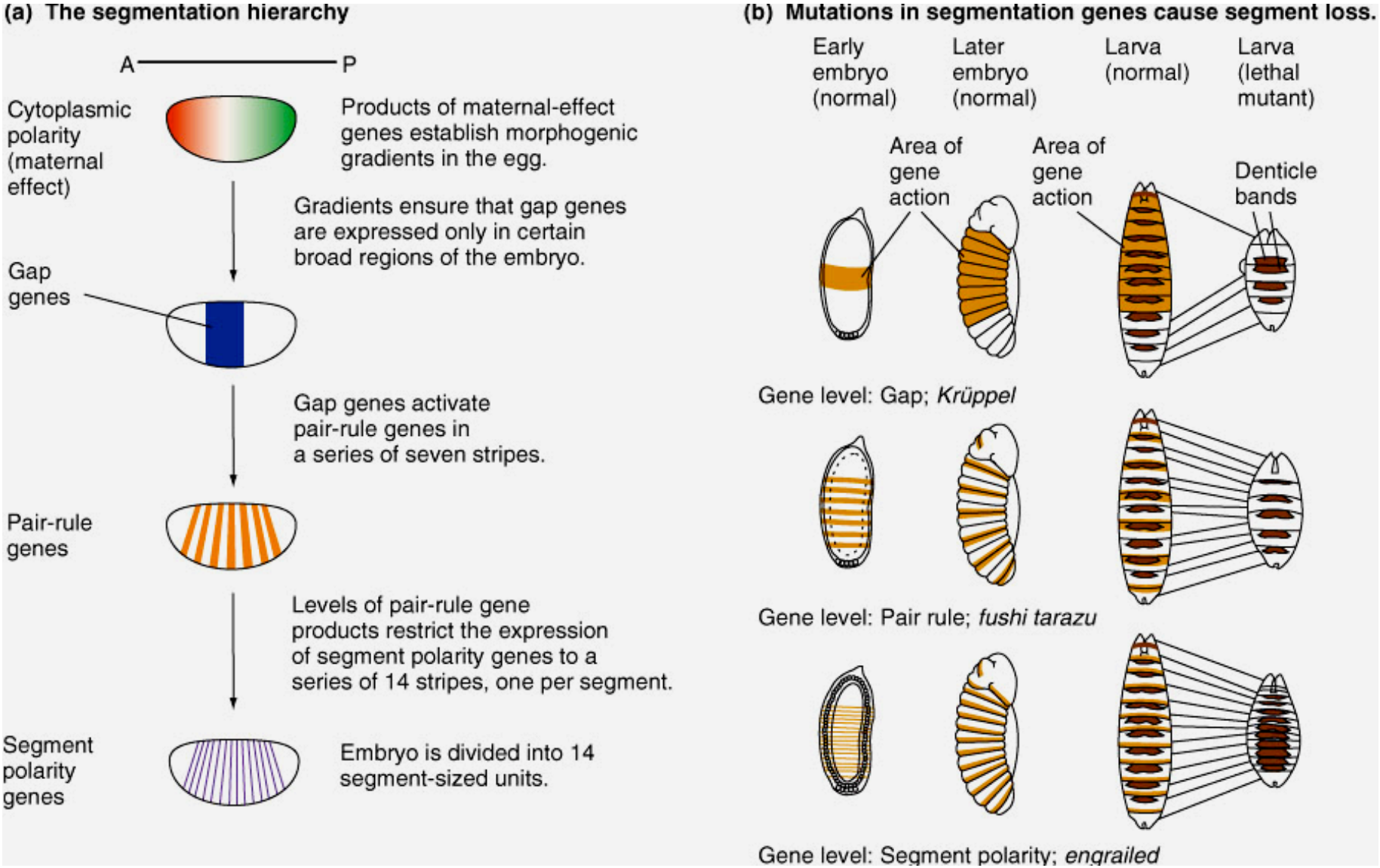

(a) The segmentation hierarchy
A
P
Cytoplasmic polarity (maternal effect)
Products of maternal-effect genes establish morphogenic gradients in the egg.
Gradients ensure that gap genes are expressed only in certain broad regions of the embryo.
Gap genes
Gap genes activate pair-rule genes in a series of seven stripes.
Pair-rule genes
Levels of pair-rule gene products restrict the expression of segment polarity genes to a series of 14 stripes, one per segment.
Segment polarity genes
Embryo is divided into 14 segment-sized units.
(b) Mutations in segmentation genes cause segment loss.
Early embryo (normal)
Later embryo (normal)
Larva (normal)
Larva (lethal mutant)
Area of gene action
Area of gene action
Denticle bands
Gene level: Gap; Krüppel
Gene level: Pair rule; fushi tarazu
Gene level: Segment polarity; engrailed

Fig. D.25

Segment polarity genes are lowest level of segmentation hierarchy

- Mutations in segment polarity genes cause deletion of part of each segment and its replacement by mirror image of different part of next segment

- Regulatory system complex
  - Transcription factors encoded by pair-rule genes initiate pattern by regulating segment polarity genes
  - Interactions between cell polarity genes maintain periodicity later in development