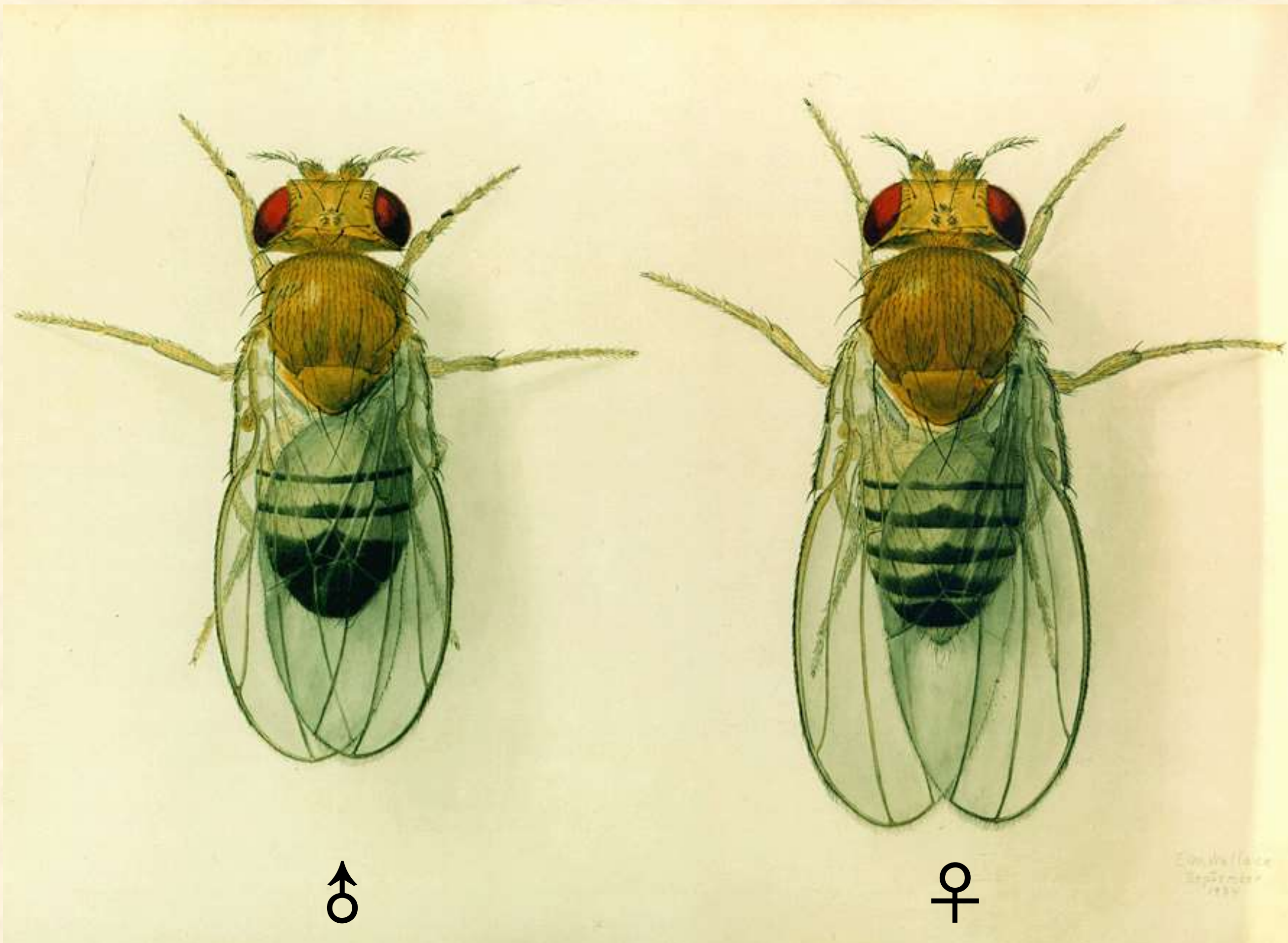
Drosophila melanogaster



Drosophila

means “dew-loving”

Latin： *drósos* *phílos*

English： dew loving

露水

also called: fruit flies

reason: linger around overripe or rotting fruits, in particular, grapes.

Drosophila

about 1,500 species totally

found all around the world, in deserts, tropical rainforest, cities, and alpine zones

more species in the tropical regions

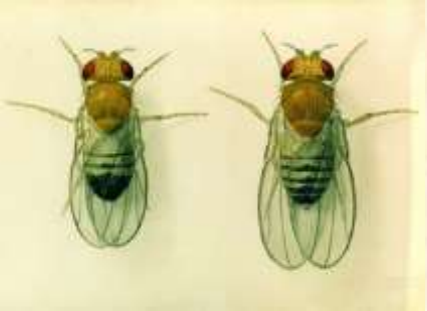
493 species in China

Food: fruit, decaying plant, flowers, fungal and mushrooms

Drosophila melanogaster

Scientific classification

Kingdom:	Animalia	动物界
Phylum:	Arthropoda	节肢动物门
Class:	Insecta	昆虫纲
Order:	Diptera	双翅目
Family:	Drosophilidae	果蝇科
Genus:	Drosophila	果蝇属
Species:	Drosophila melanogaster	黑腹果蝇



Drosophila melanogaster

The most important model organism for studies in Genetics and Developmental Biology

Small size：	5 mm	
A short generation time：	10 days	
Large number of offspring：	a female lays 50 - 80 eggs everyday	
Life span:	60 - 90 days	
Compact genome:	sex chromosome	1 pair
	autosome	3 pairs
Easy to obtain mutant animals:	X-ray, chemical mutagen (EMS),	
	transposable element	
Genetic manipulation is easy：	100 years of genetics	
Easily cultured and Inexpensive:	fruits or medium	
Genome:	sequenced in 2000, about 15000 genes	
	77% of human disease genes (714/929 genes)	

The Nobel Prize in Physiology or Medicine 1933

"for his discoveries concerning the role played by the chromosome in heredity "

Thomas Hunt Morgan

(1866 –1945)

1906, began his work on D. melanogaster at Columbia University

1910, reported the white eyed mutant – the first gene (white) identified

1933, rewarded Nobel Prize in Medicine

Table 1: Expected Mendelian Ratios versus Morgan's Actual Results

Cross	Outcome	
	Expected Phenotypes	**Observed Phenotypes**
P_1 Red ♀ × P_1 White ♂	F_1 = All Red	F_1 = All Red*
F_1 Red ♀ × F_1 Red ♂	75% Red ♀ and ♂ 25% White ♀ and ♂	50% Red ♀ 25% Red ♂ 25% White ♂

♀ w^+/w^+

♂ w^-/Y

P1

X

♀ w^+/w^-

♂ w^+/Y

F1

X

F2

♀ w^+/w^+

♀ w^+/w^-

♂ w^+/Y

♂ w^-/Y

♀ w^+/w^+

♂ w^-/Y

P1

X

♀ w^+/w^-

♂ w^+/Y

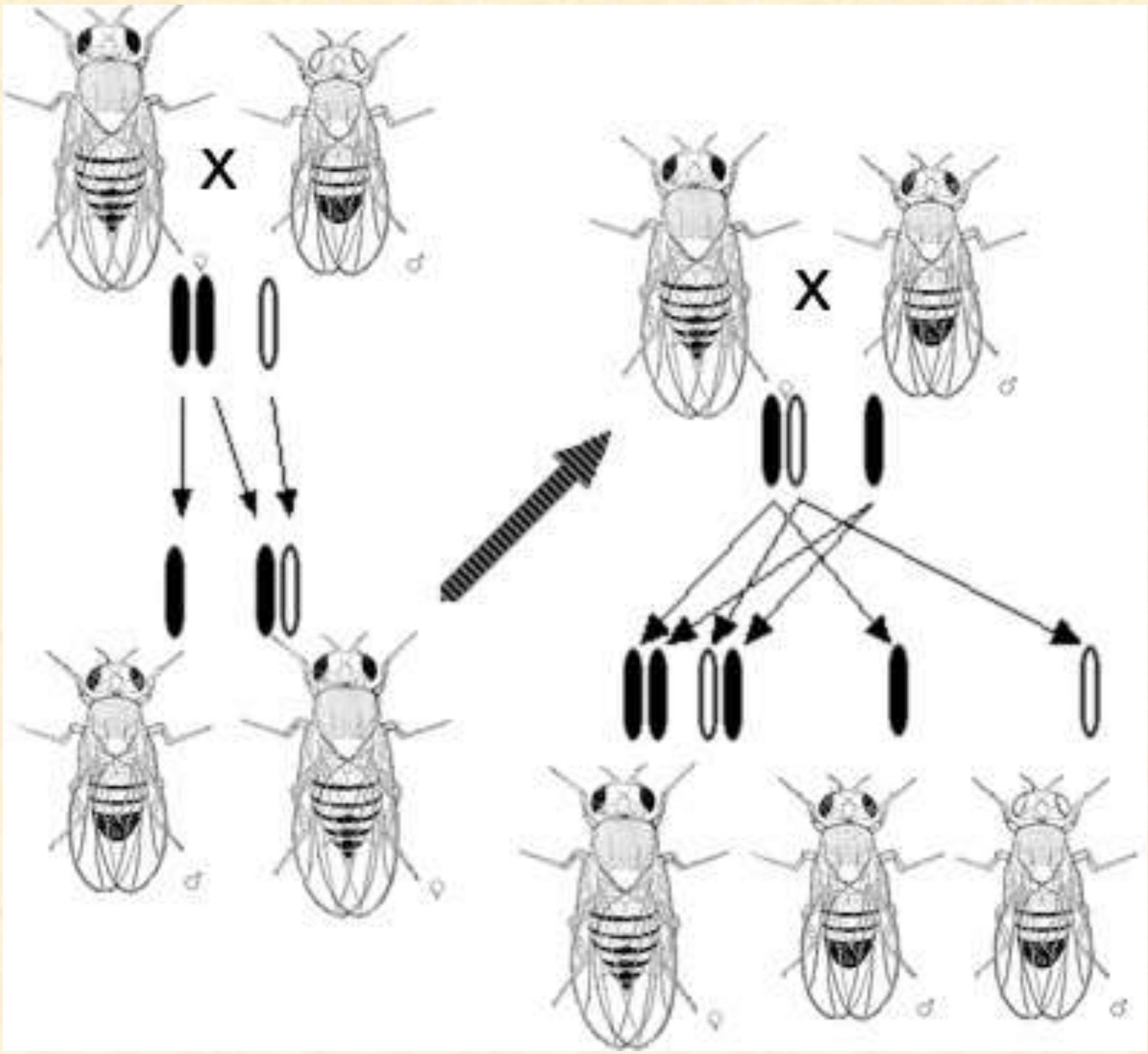
F1

♀ w^+/w^-

♀ w^-/w^-

♂ w^+/Y

♂ w^-/Y


X
X

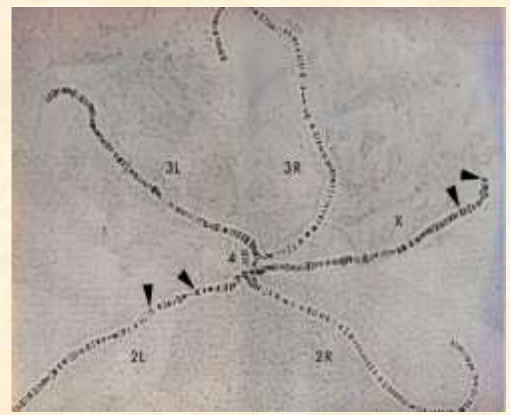
Alfred Sturtevant

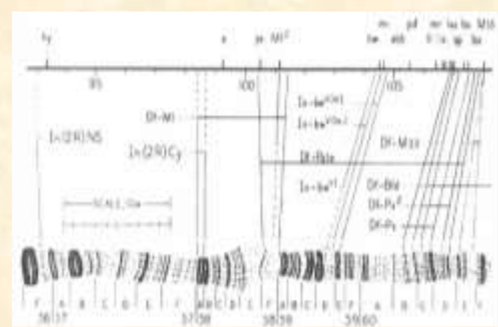
Identified chromosomes as the carriers of the hereditary material as a undergraduate student of Morgan in 1911

Thomas Morgan

Calvin Bridges

Ph.D. thesis - the 1st paper in the 1st issue of *Genetics* in 1916





Polytene chromosome and banding pattern

Alfred Sturtevant

Thomas Morgan

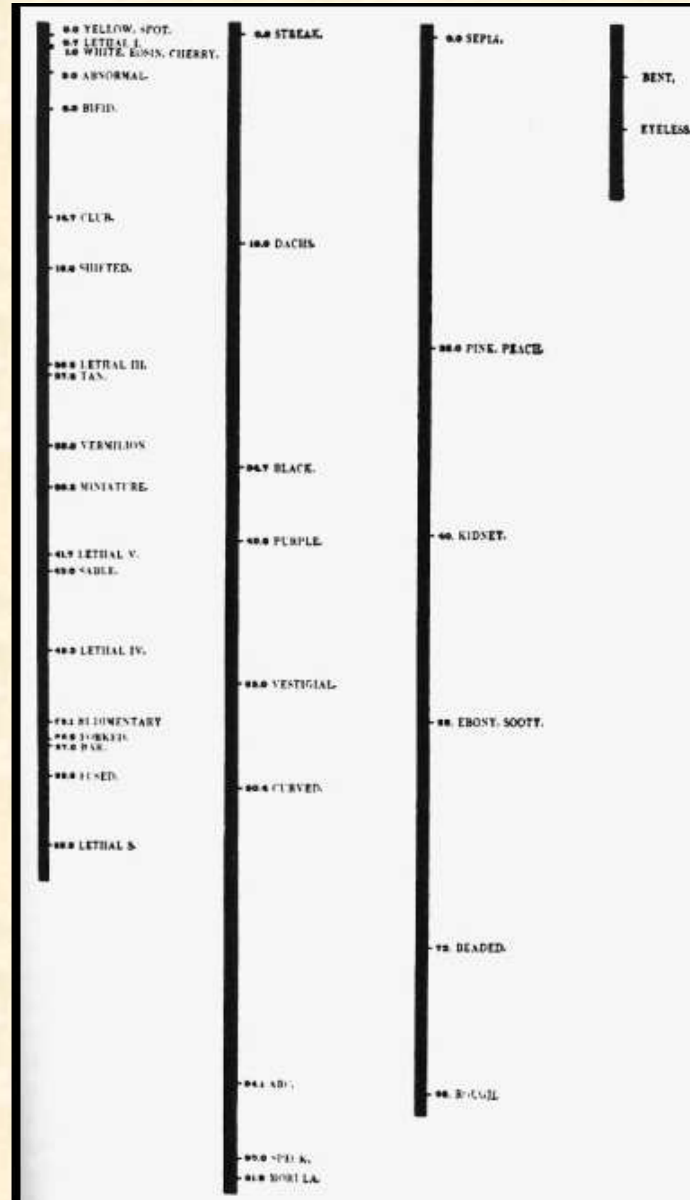
Calvin Bridges

Ph.D. thesis - the 1st paper

in the 1st issue of *Genetics* in 1916

Chromosome

X 2 3 4

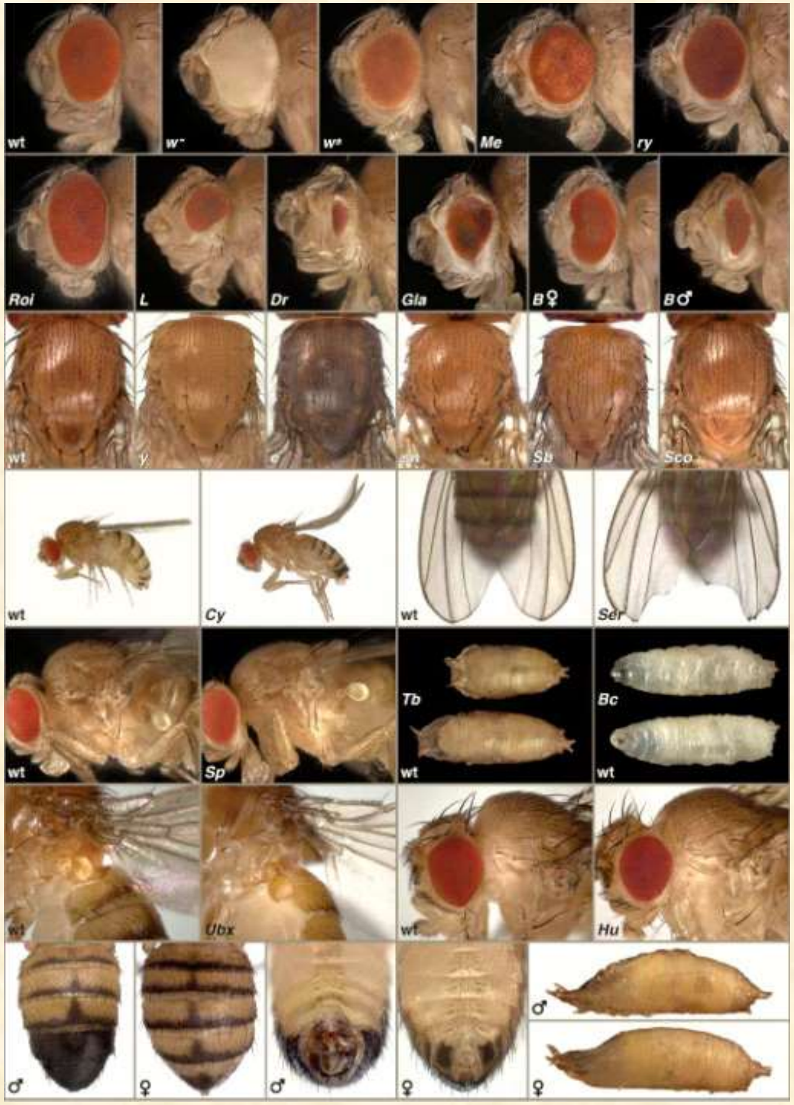


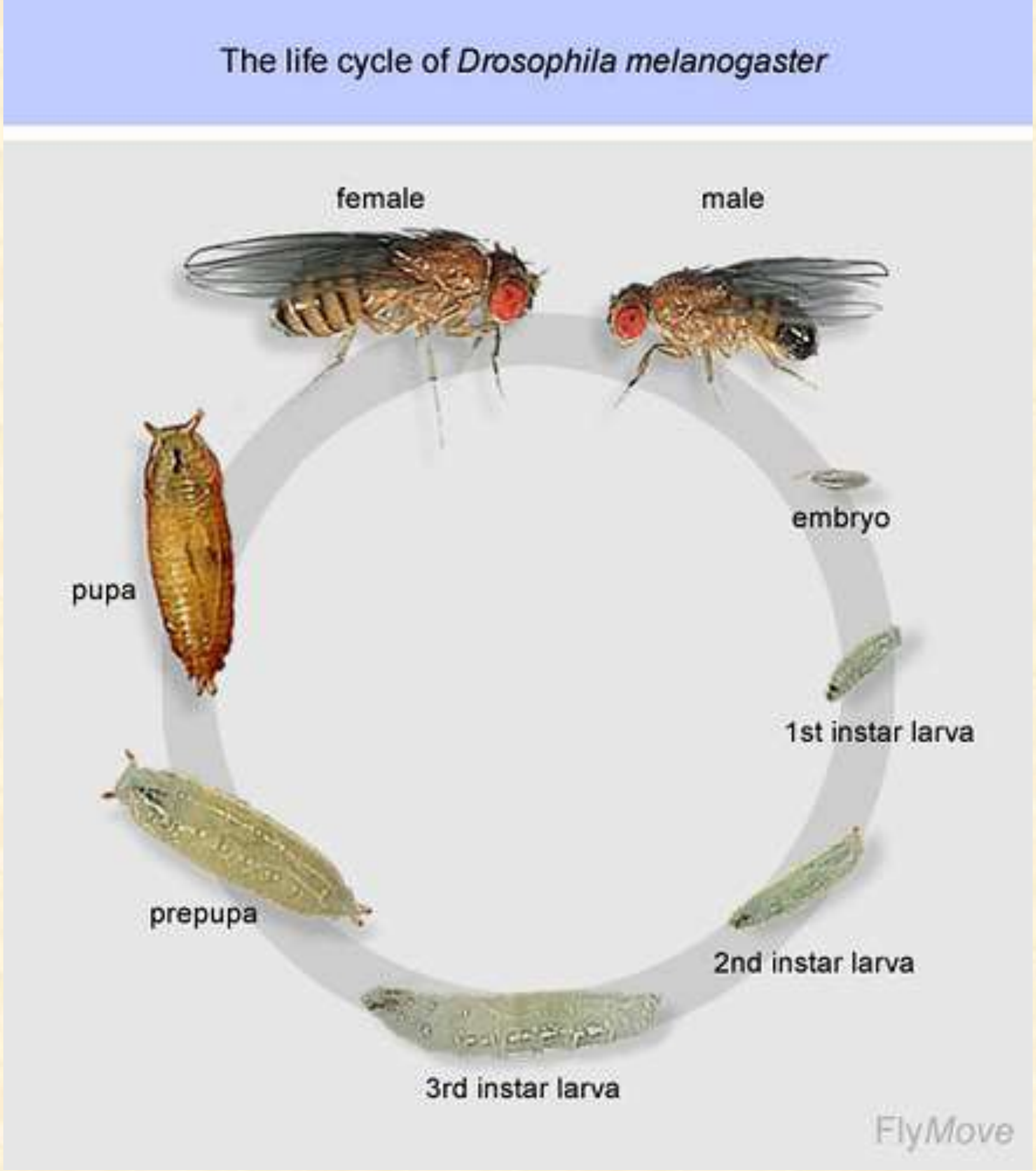
The Nobel Prize in Physiology or Medicine 1946

"for the discovery of the production of mutations by means of X-ray irradiation "

Hermann Joseph Muller

(1890 –1967)




The life cycle of *Drosophila melanogaster*
female
male
embryo
1st instar larva
2nd instar larva
3rd instar larva
prepupa
pupa
FlyMove

Drosophila oocyte

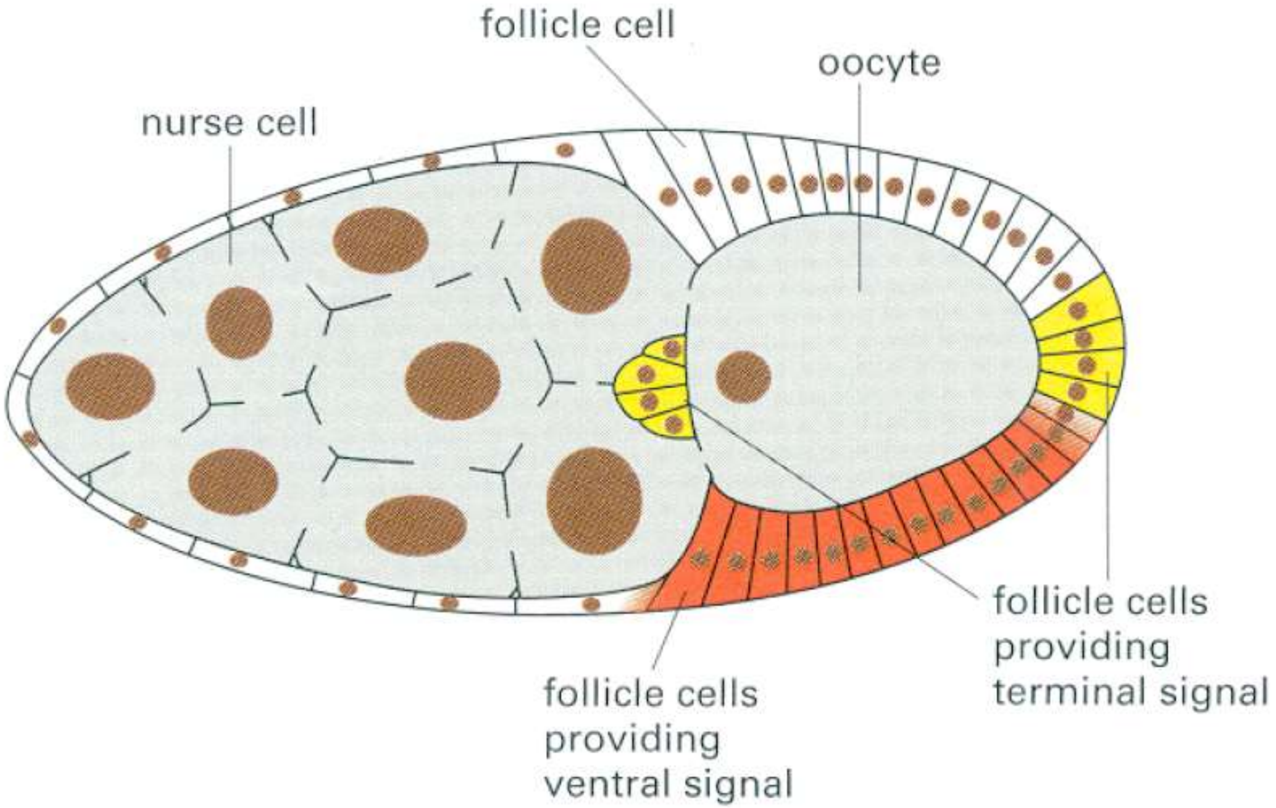
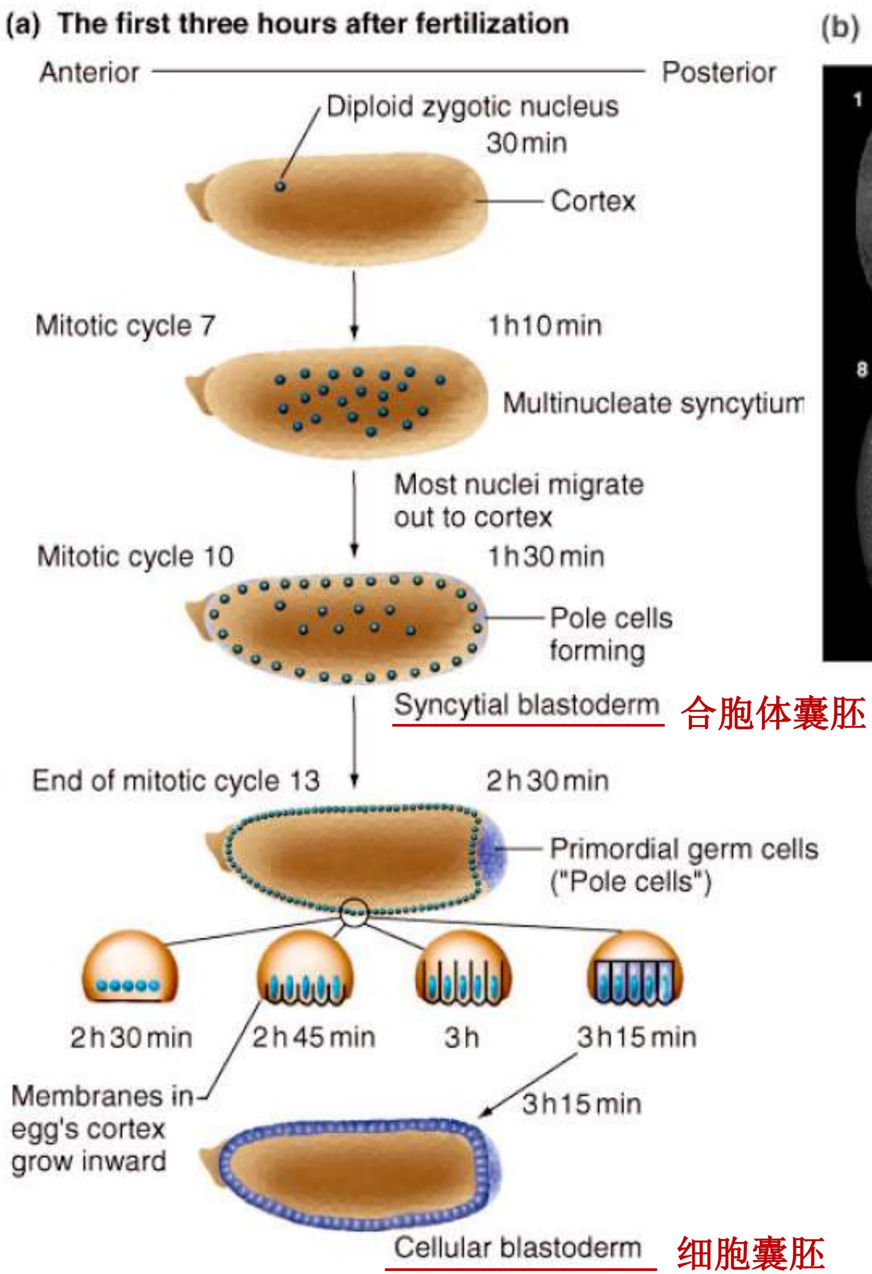
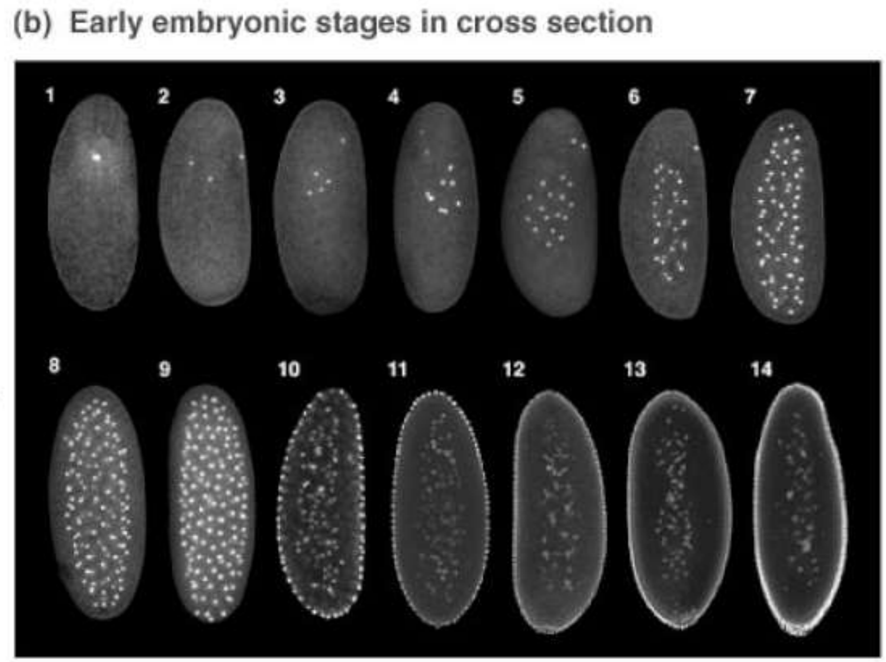


Figure 21-30. A Drosophila oocyte in its follicle. The oocyte is derived from a germ cell that divides four times to give a family of 16 cells that remain in communication with one another via cytoplasmic bridges (gray). One member of the family group becomes the oocyte, while the others become nurse 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**)

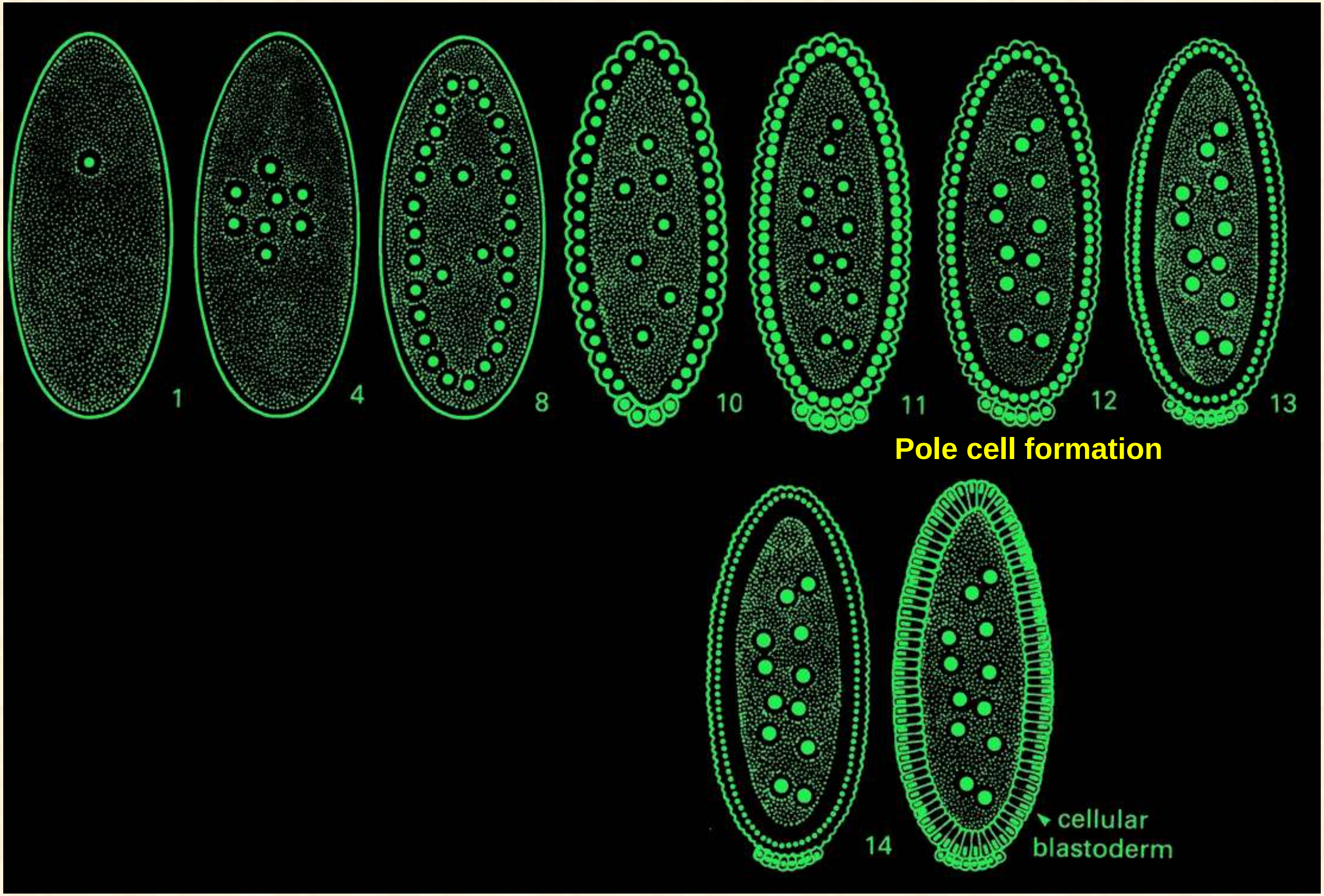




Drosophila Embryogenesis

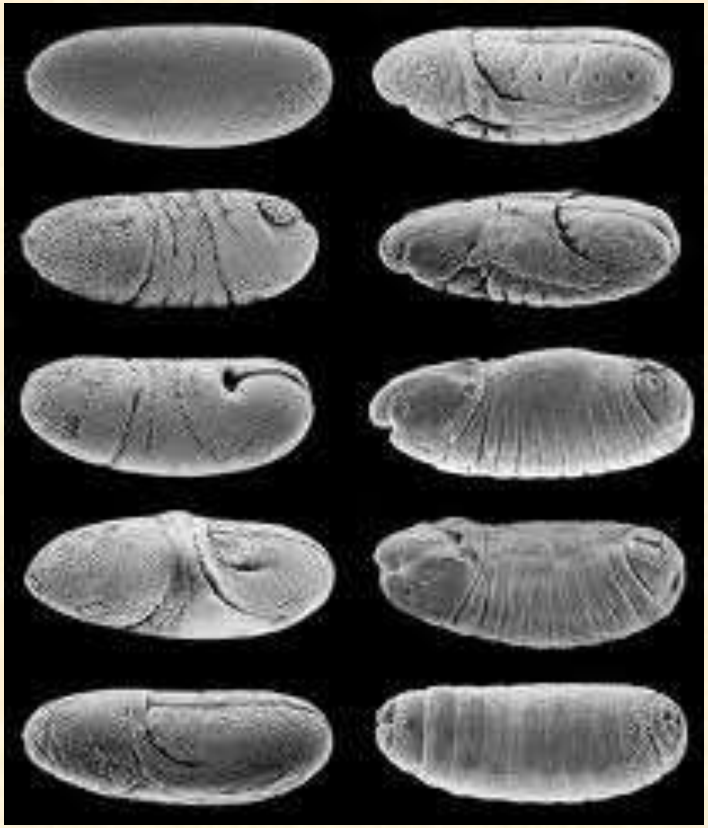
Fig. D.18

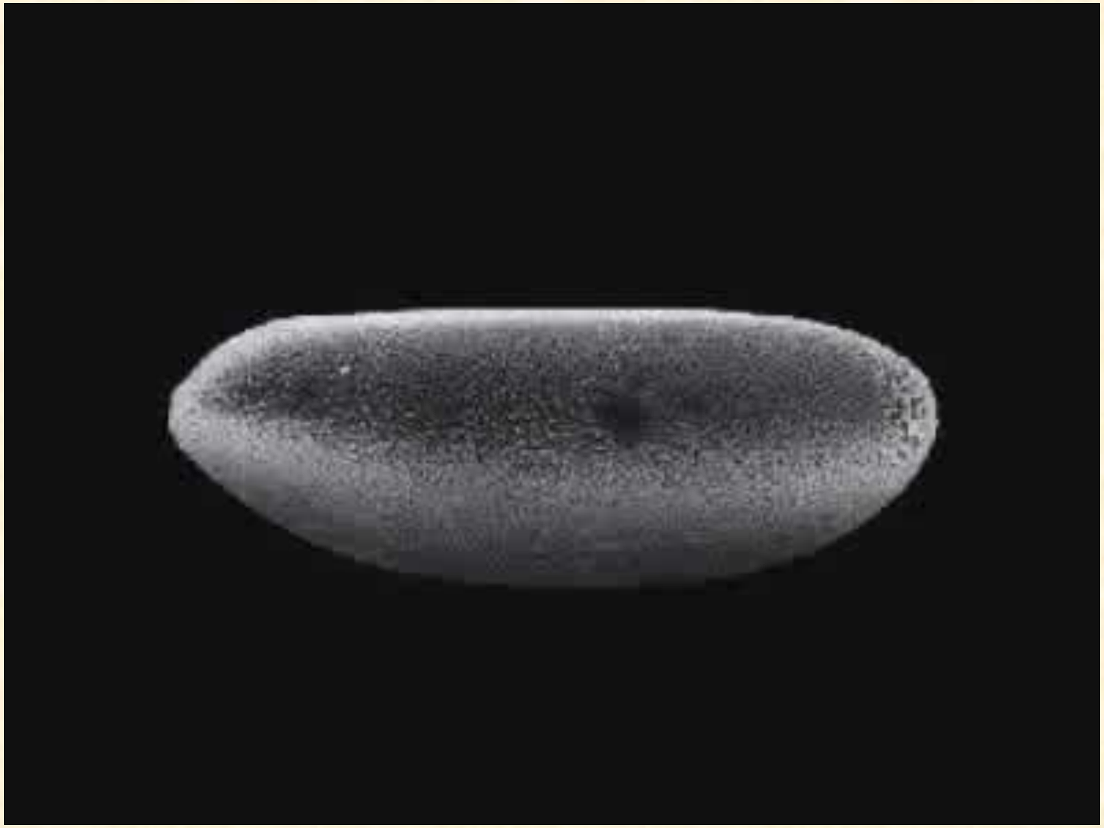
syncytial blastoderm



Drosophila embryogenesis

Dorsal

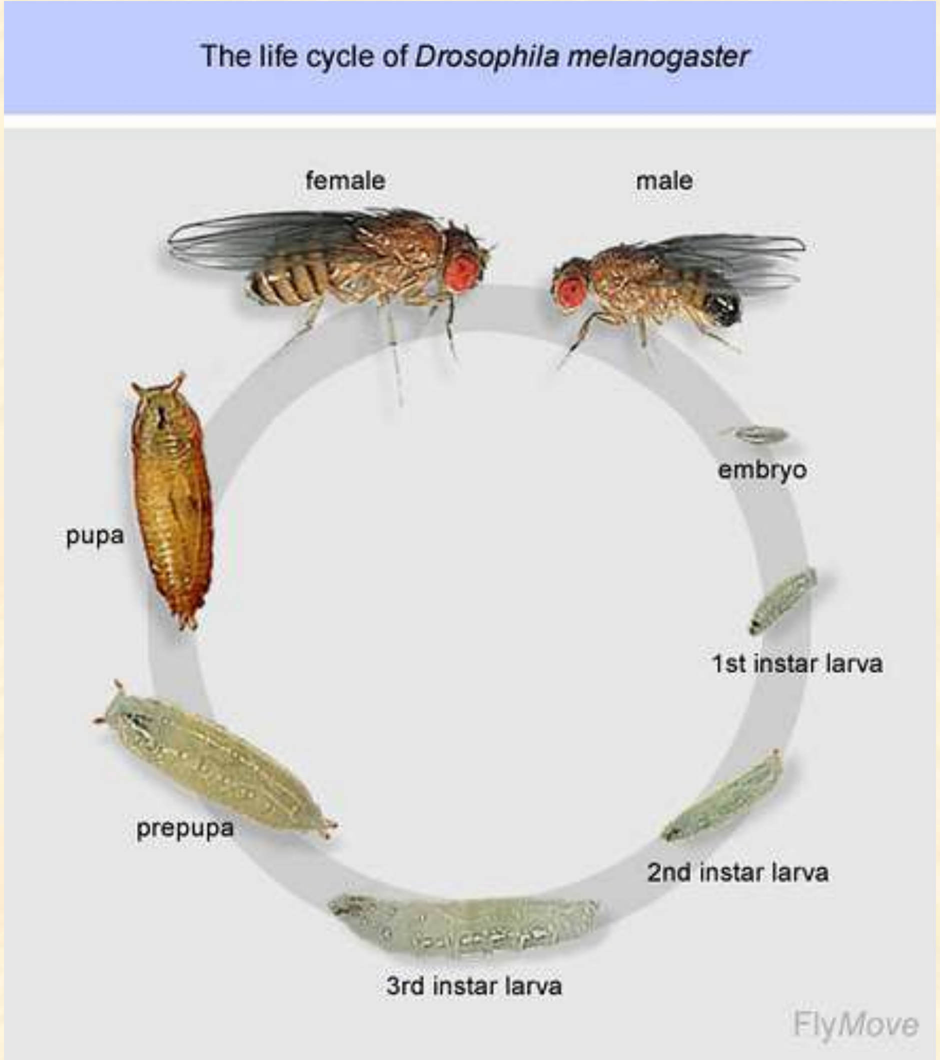


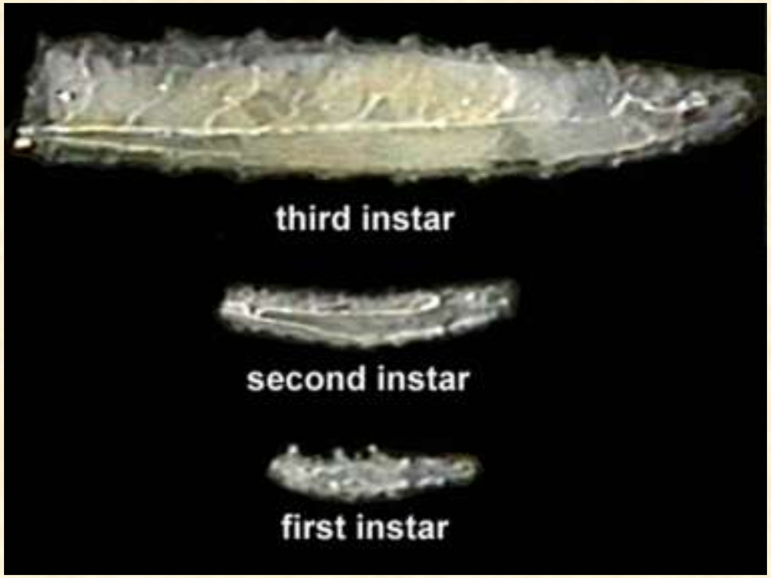


Ventral

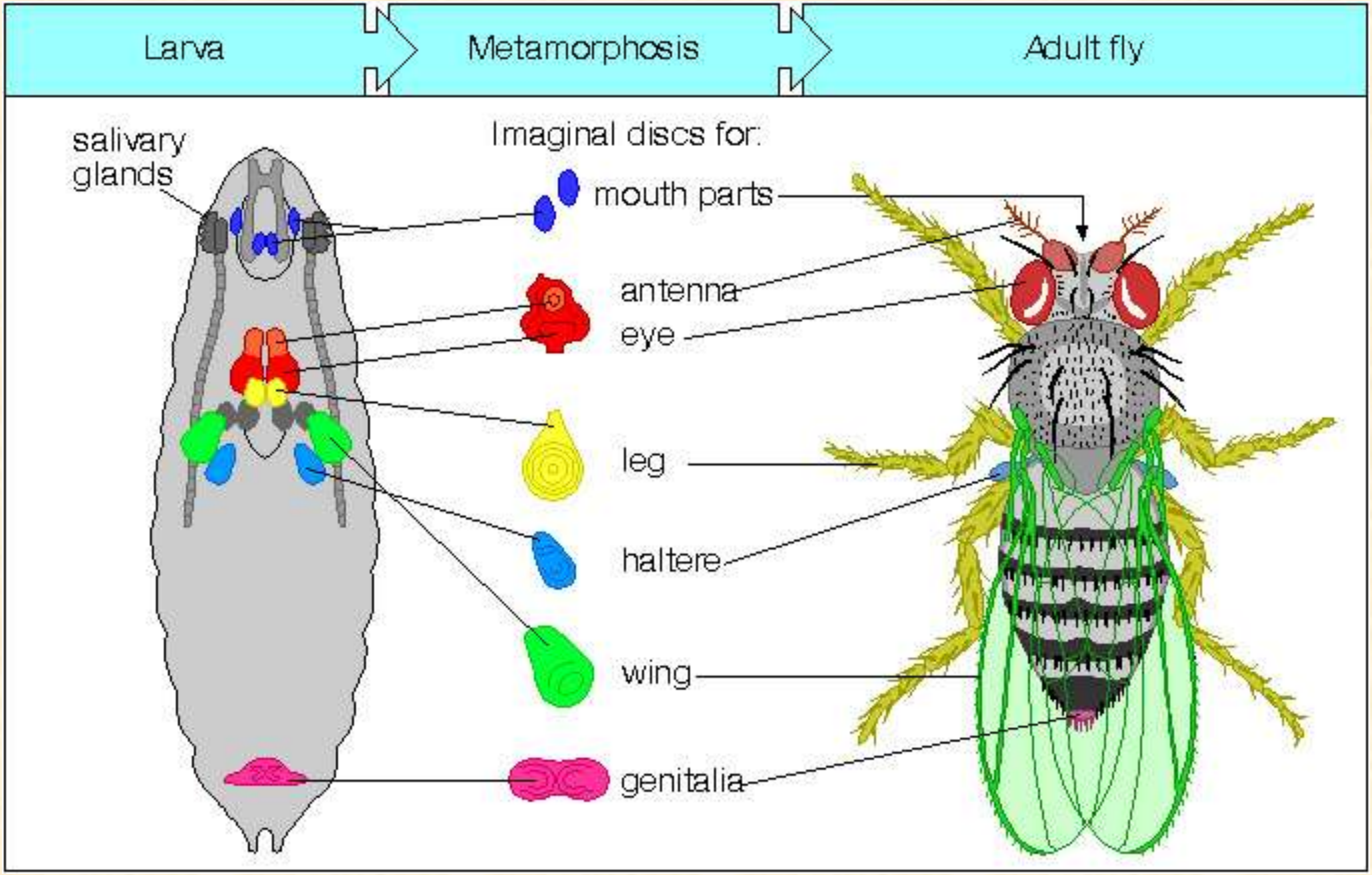
Drosophila embryogenesis

Drosophila embryo morphogenesis is the process from which a fertilized single cell egg becomes a multicellular embryo with structured tissues and specialized cells/organs. This process occurs through many complex cell shape changes and movements, including the formation of cellular blastoderm, gastrulation, and germ band elongation/retraction.


The life cycle of *Drosophila melanogaster*
female
male
embryo
pupa
1st instar larva
prepupa
2nd instar larva
3rd instar larva
FlyMove

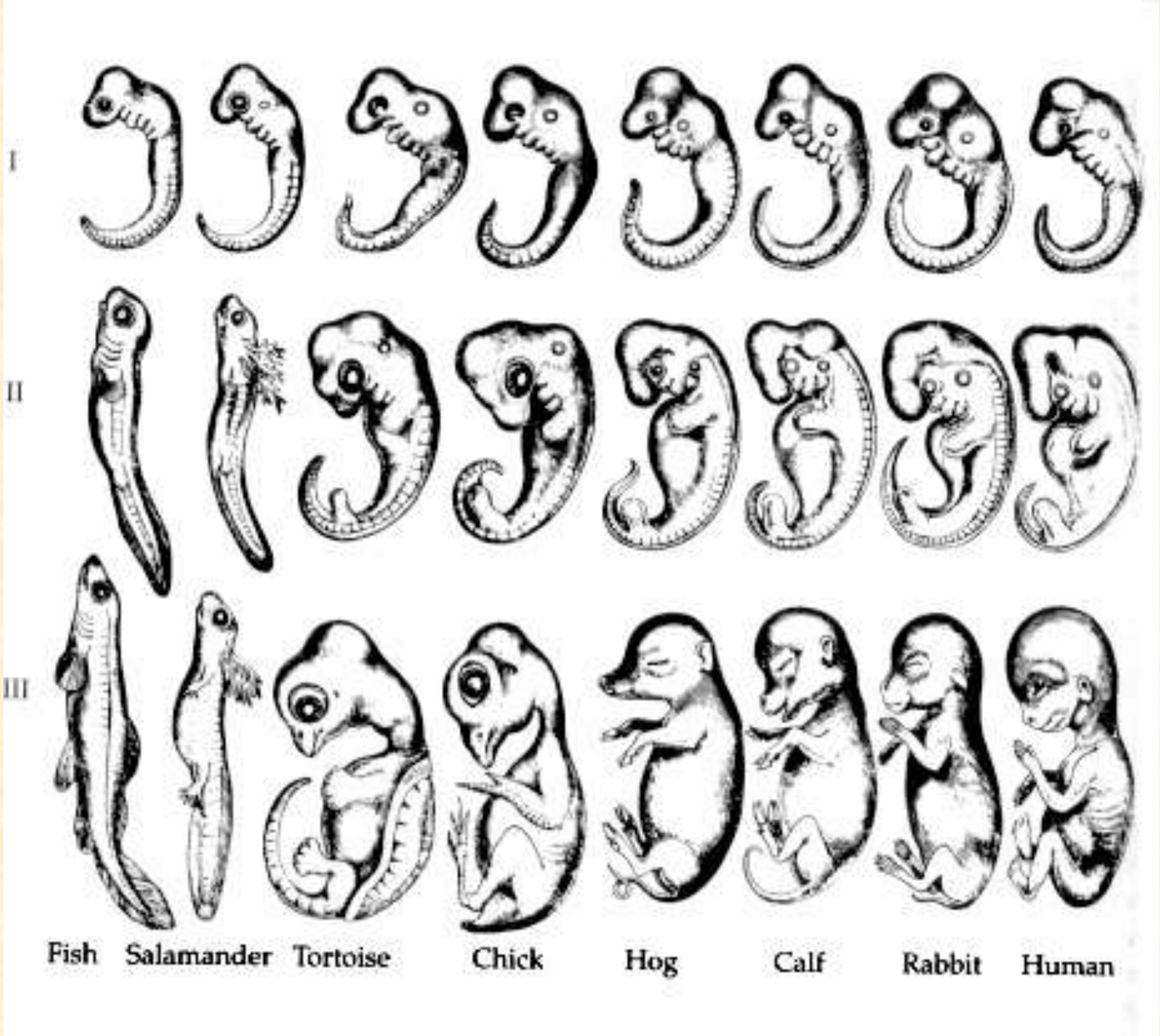

third instar
second instar
first instar

Drosophila Development

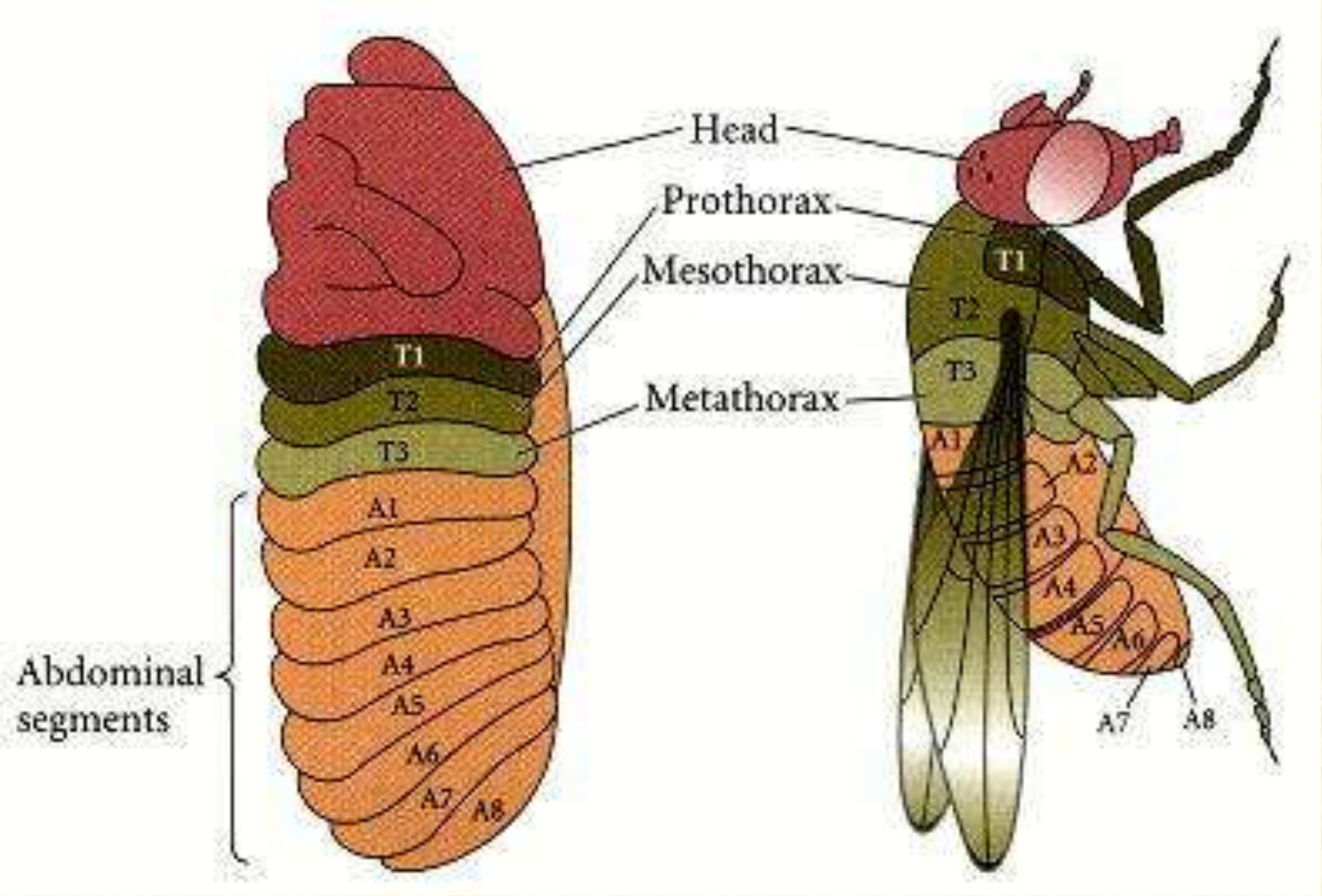


Haeckel's 1874 version of vertebrate embryonic development.

Drosophila



Segmentation in *Drosophila*



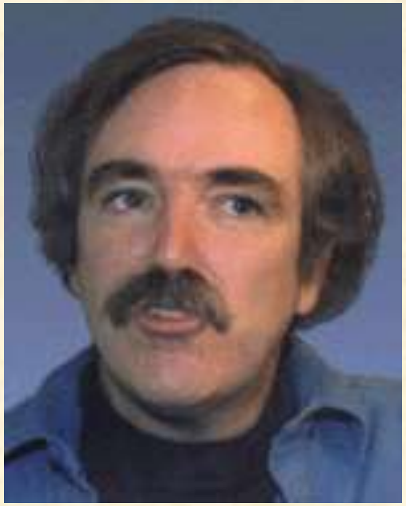
Developmental Biology S. F. Gilbert

The Nobel Prize in Physiology or Medicine 1995

"for their discoveries concerning the genetic control of early embryonic development "

Edward B. Lewis

Christiane Nüsslein-Volhard



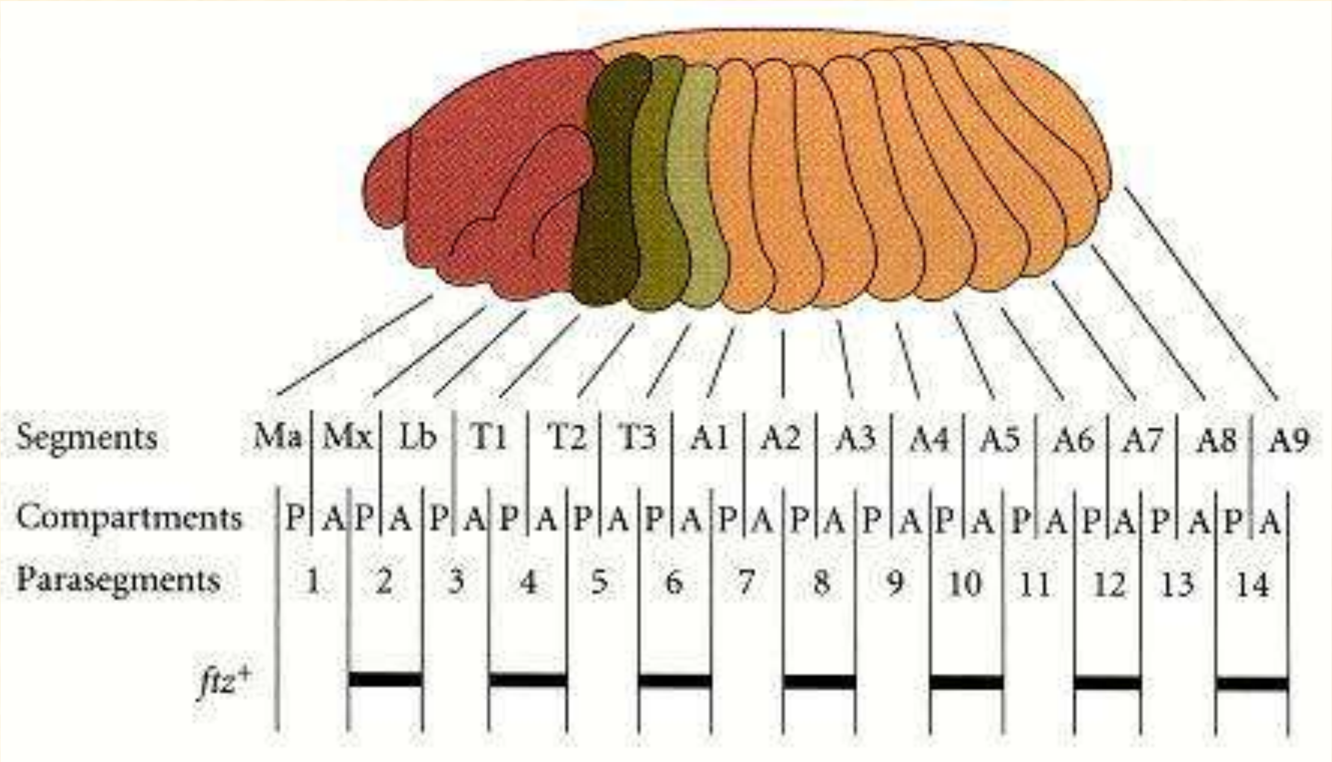
Eric Wieschaus

Segmentation genes

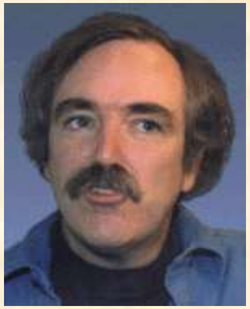
the segmentation genes divide the embryo into 14 parasegments

which include the posterior part of an anterior segment

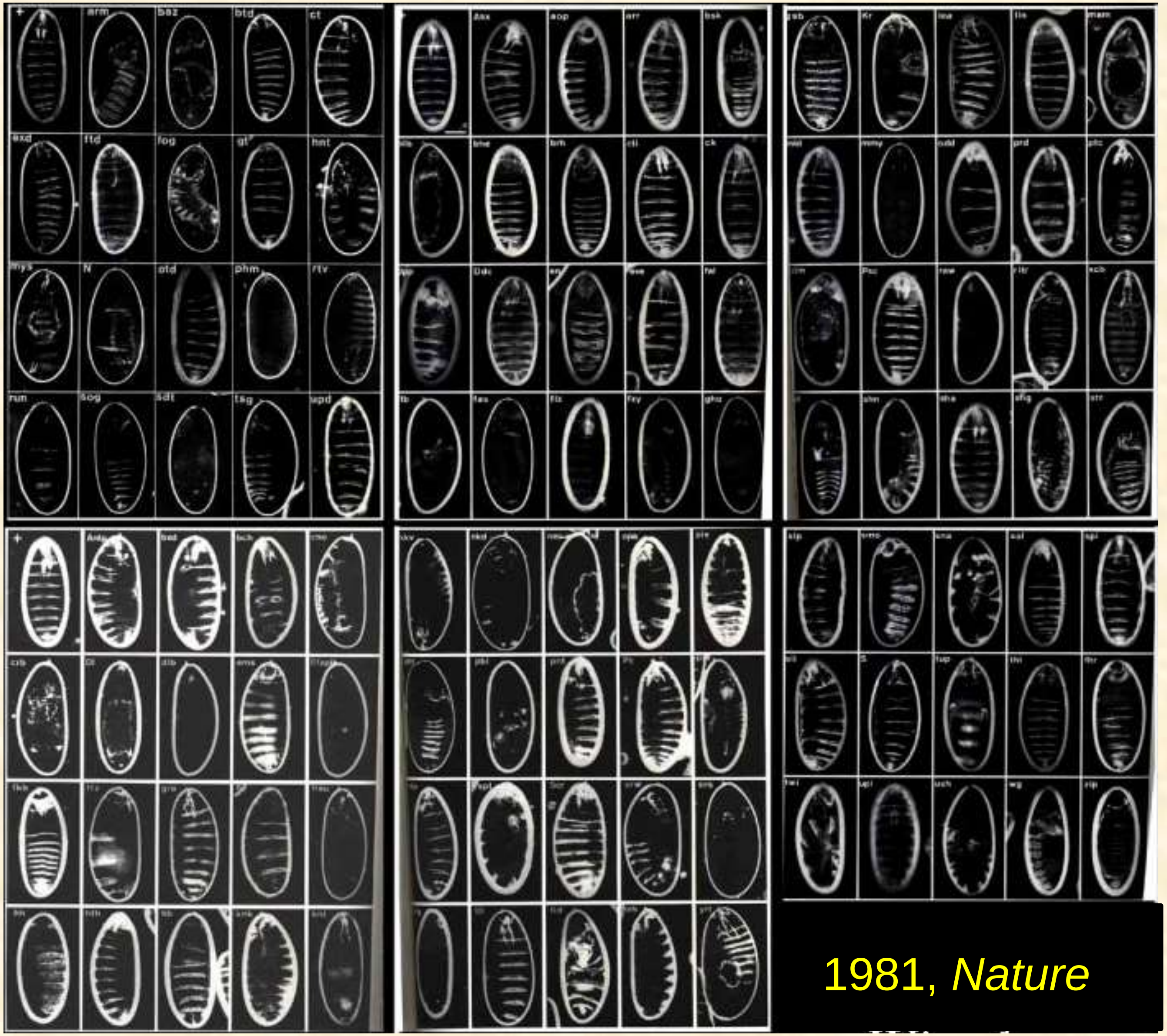
and the anterior portion of the segment behind it



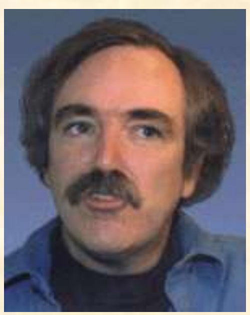
Christiane Nüsslein-Volhard



Eric Wieschaus



Christiane Nüsslein-Volhard

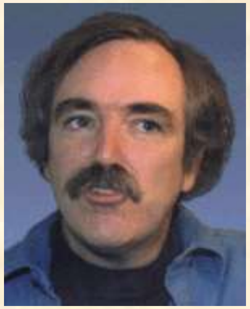


Eric Wieschaus

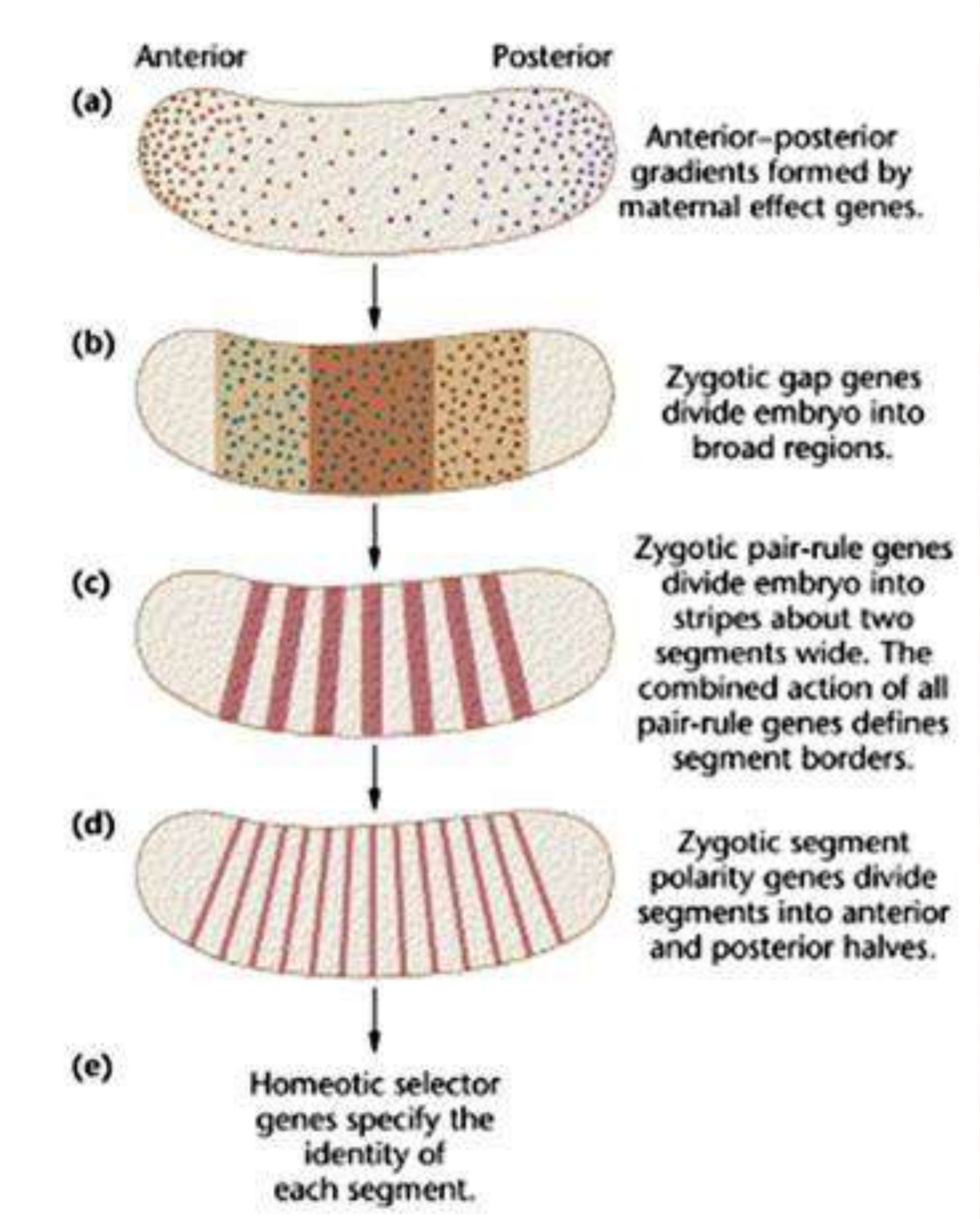
Four classes of genes responsible for formation of segments

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

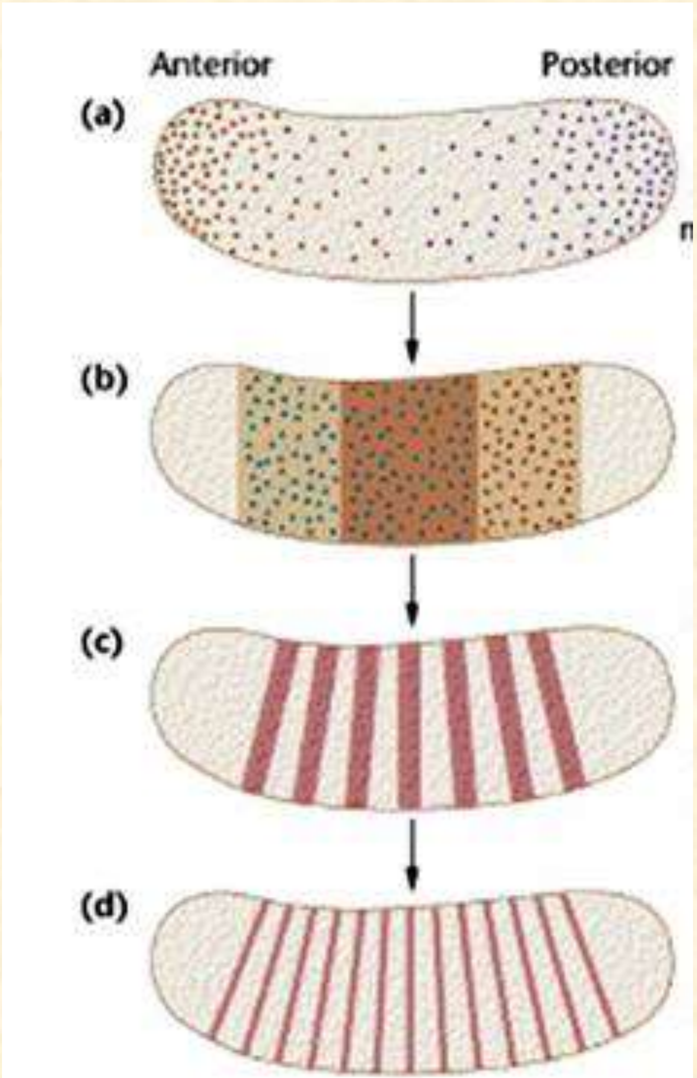
Christiane Nüsslein-Volhard

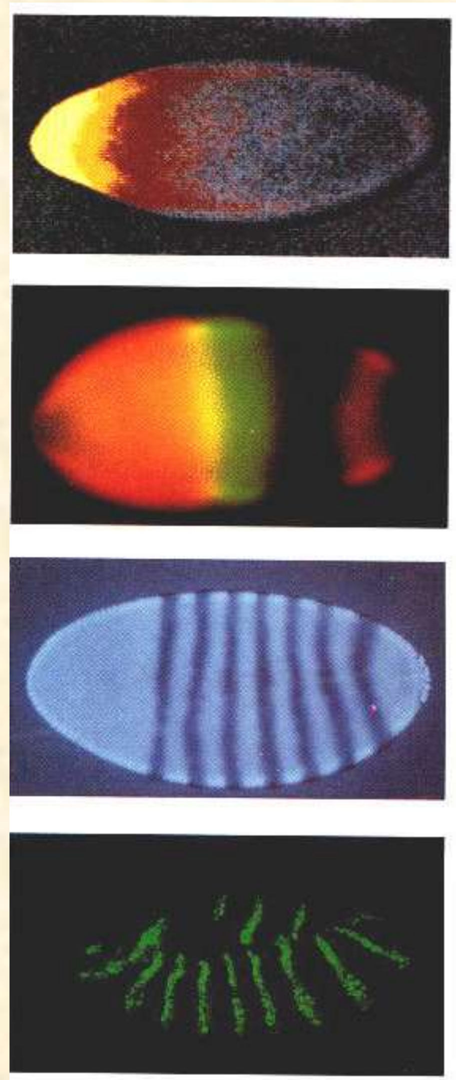


Eric Wieschaus



Anterior-posterior (A/P) polarity and Segmentation





bicoid

Maternal gene

Hunchback (red)

kruppel (green)

Gap gene

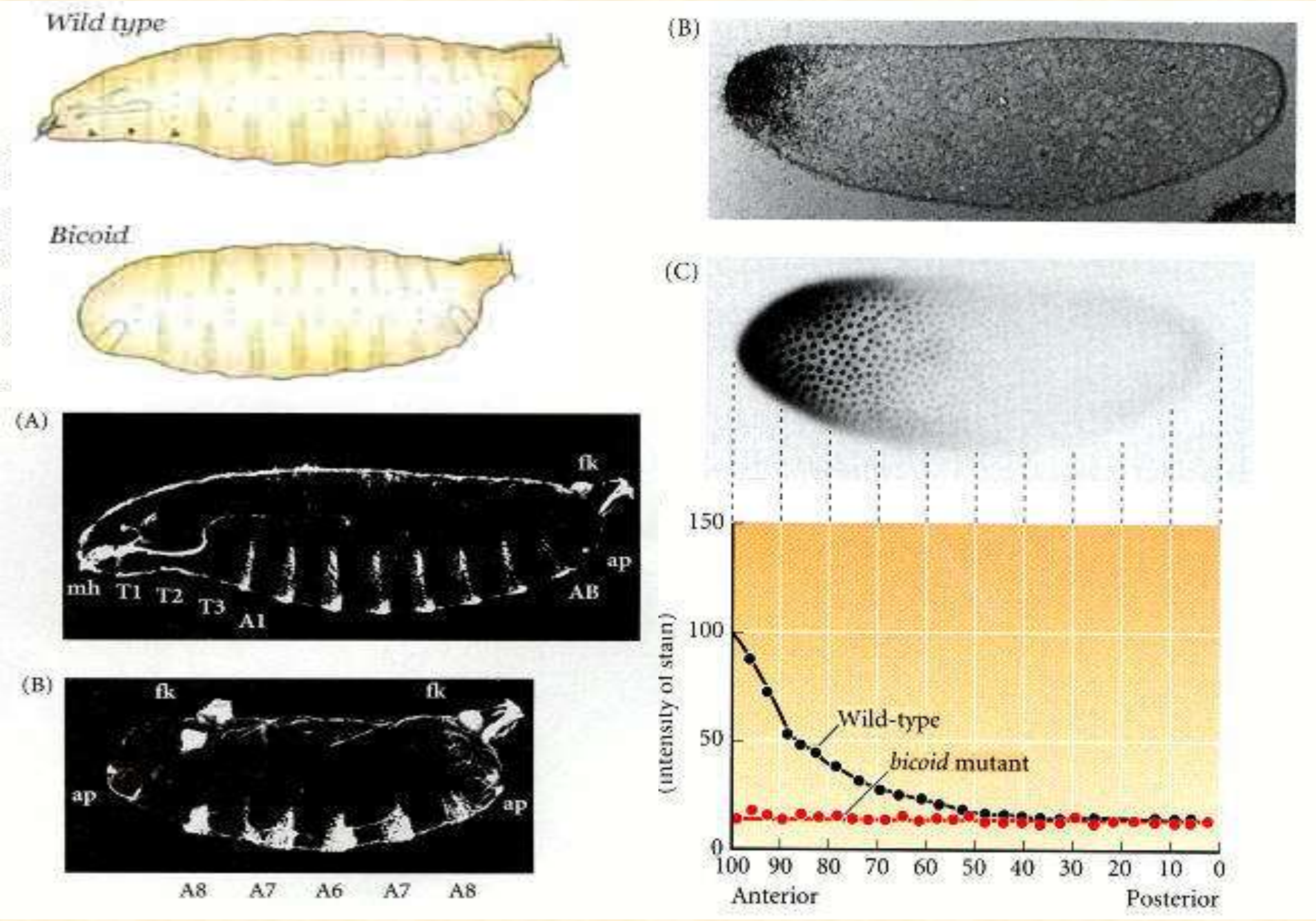
fushi tarazu

Pair-rule gene

engrailed

Segment polarity gene

Maternal effect gene *bicoid* control anterior structures



Morphogen Theory

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

Klaus Sander proposed:

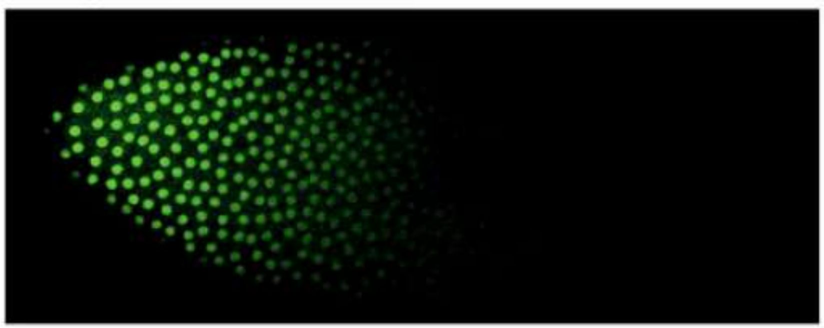
- Each pole of the egg produces a different substance
- These substance form the opposing gradients by diffusion
- Concentrations of these substances determine the type of structure produced at each position long the body axis

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.

Mother

bicoid $^{+}$/ *bicoid* $^{-}$

1 dose

bicoid $^{+}$/ *bicoid* $^{+}$

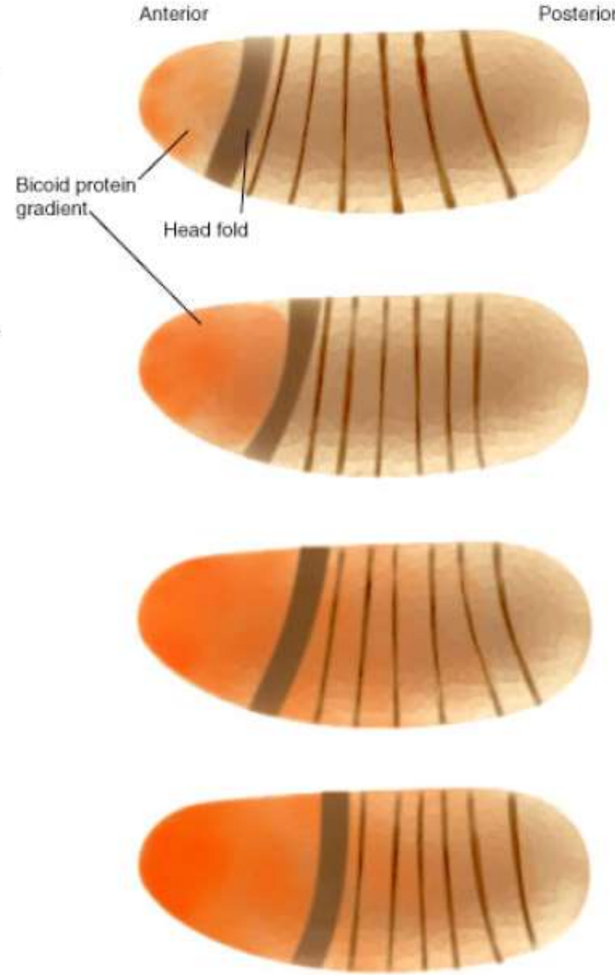
2 doses

bicoid $^{+}$

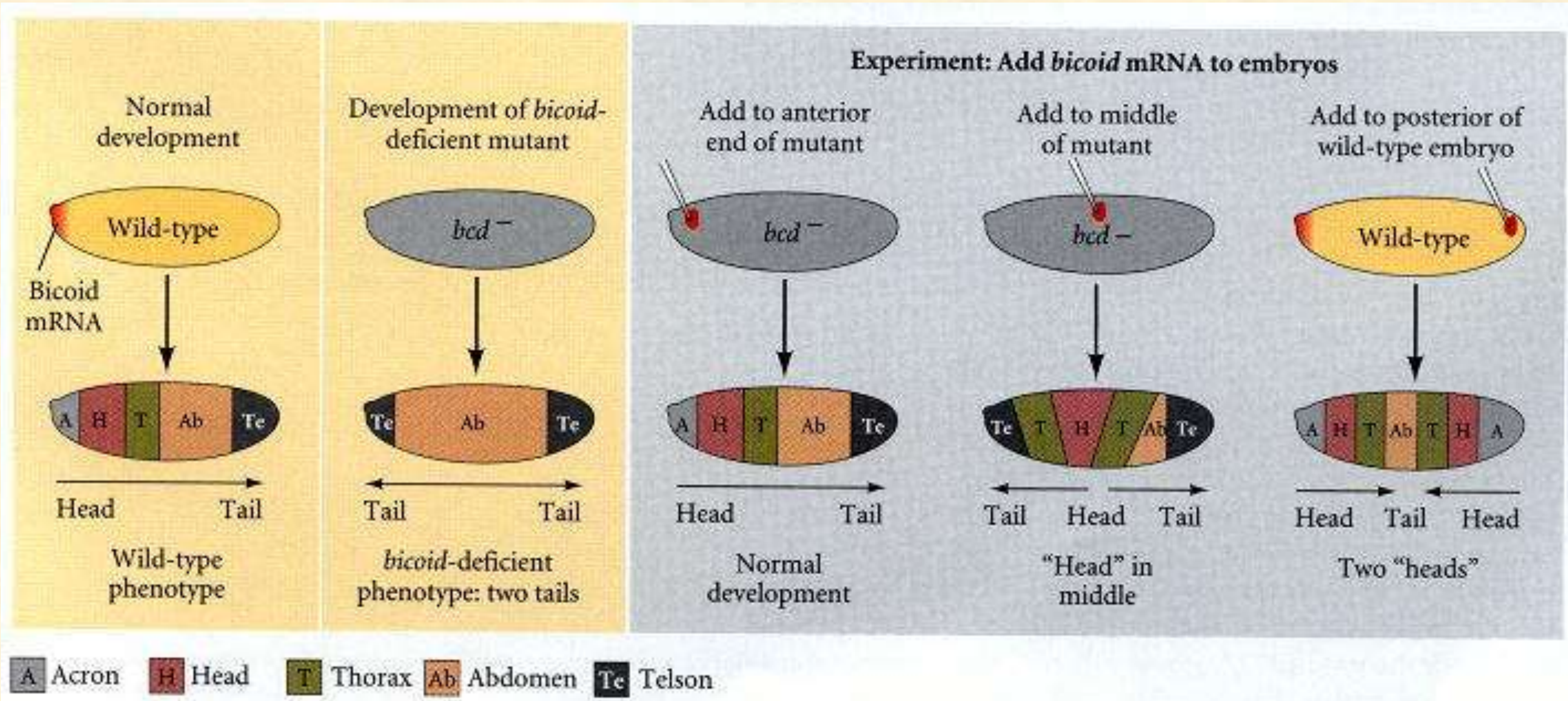
4 doses

bicoid $^{+}$

6 doses



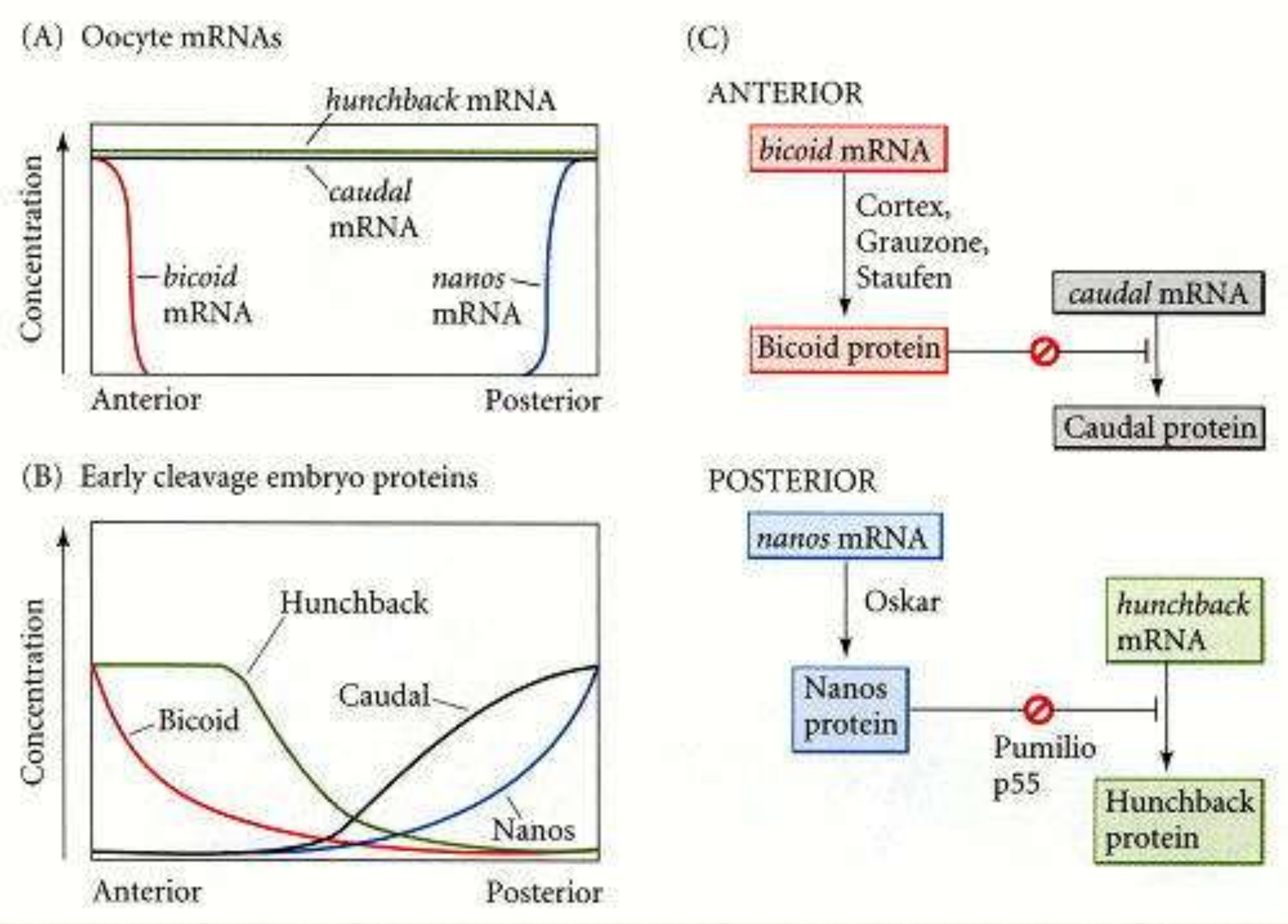
Maternal effect gene *bicoid* control anterior structures

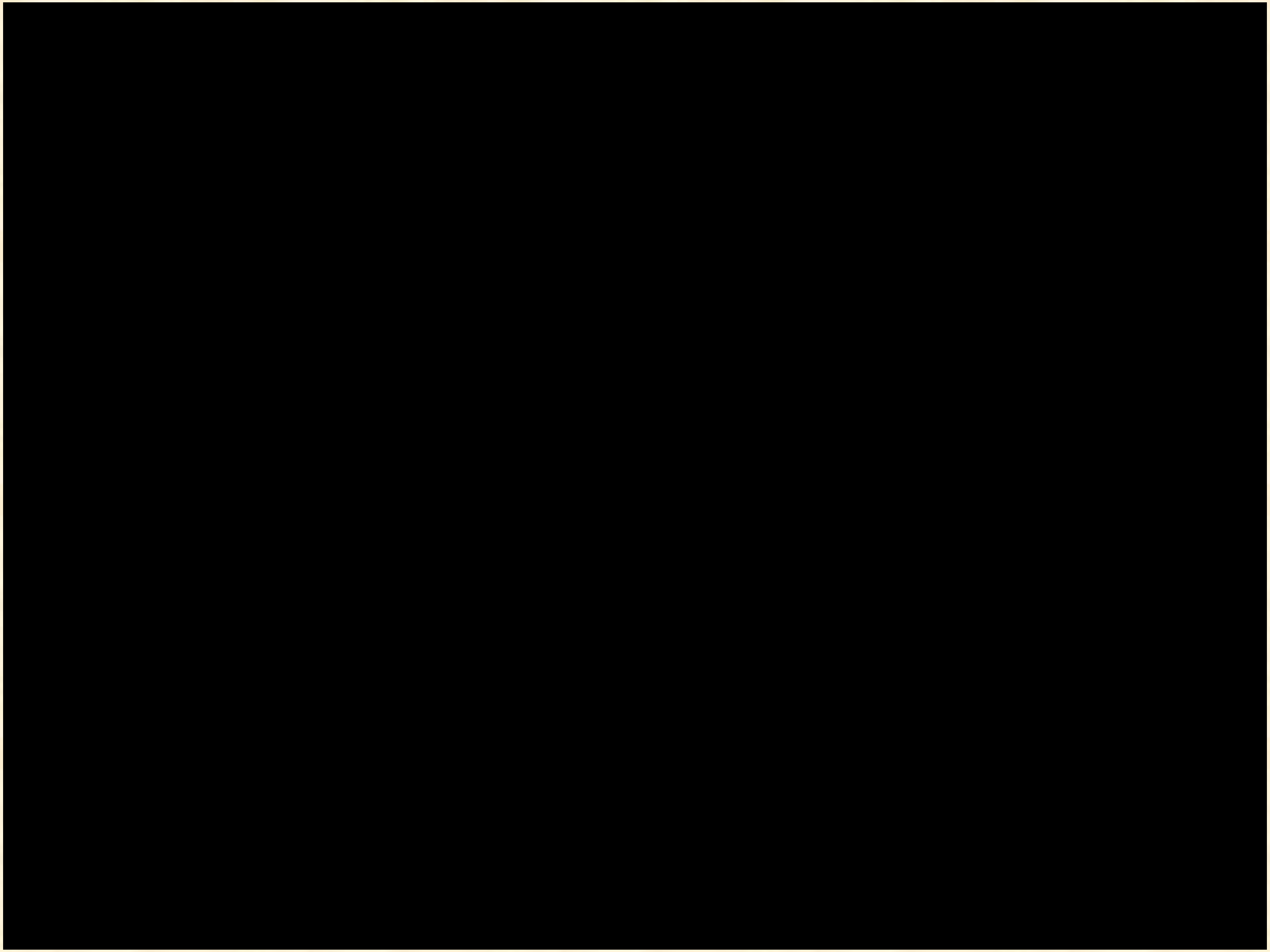


顶节

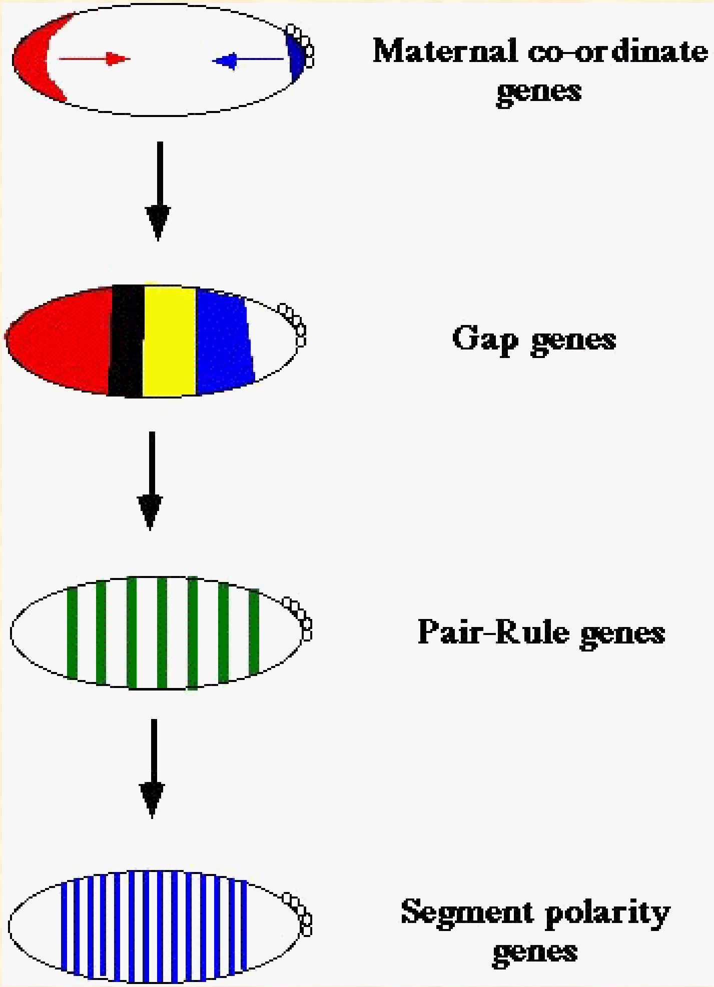
尾节

Maternal Effect Genes





Anterior-posterior (A/P) polarity and Segmentation

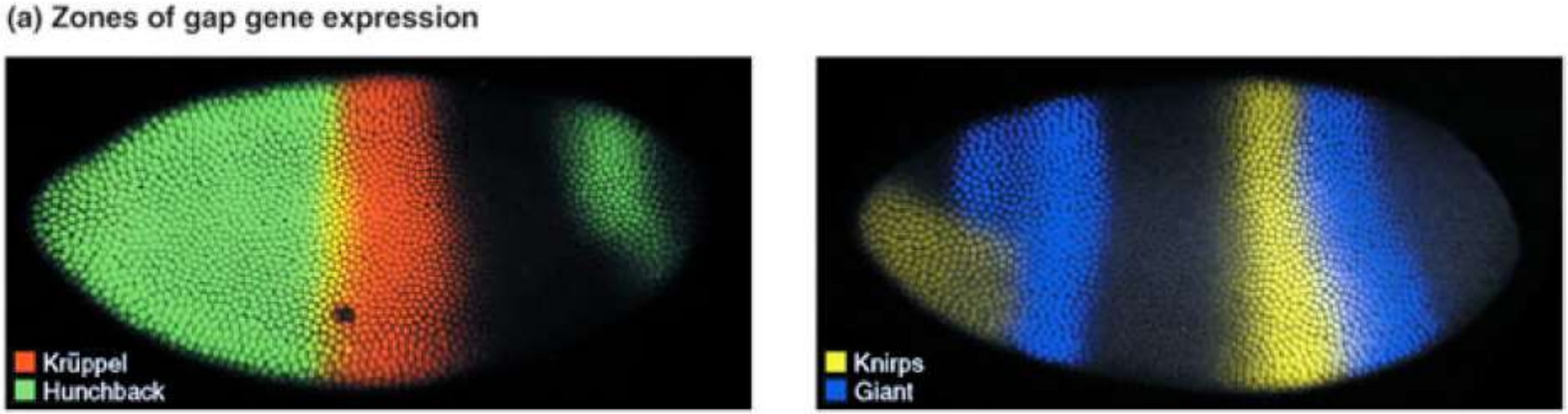


Gap genes

- 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

Gap genes

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



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

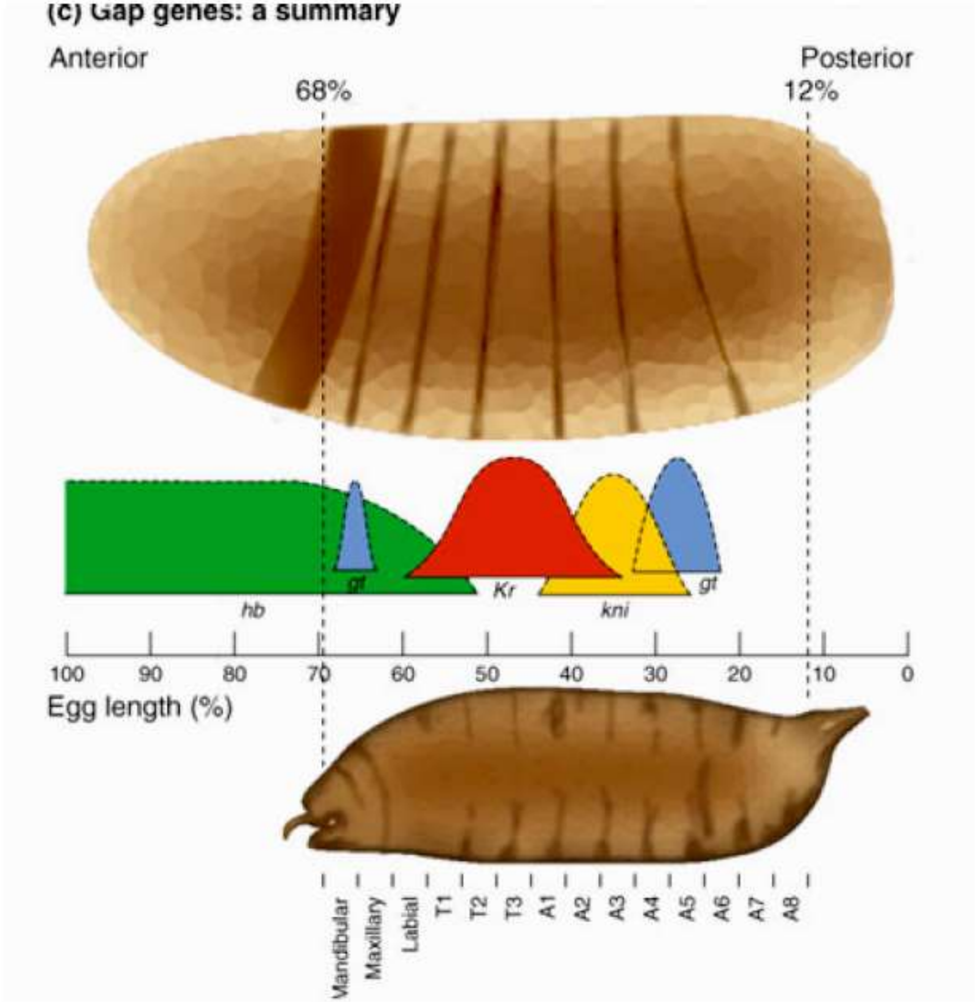
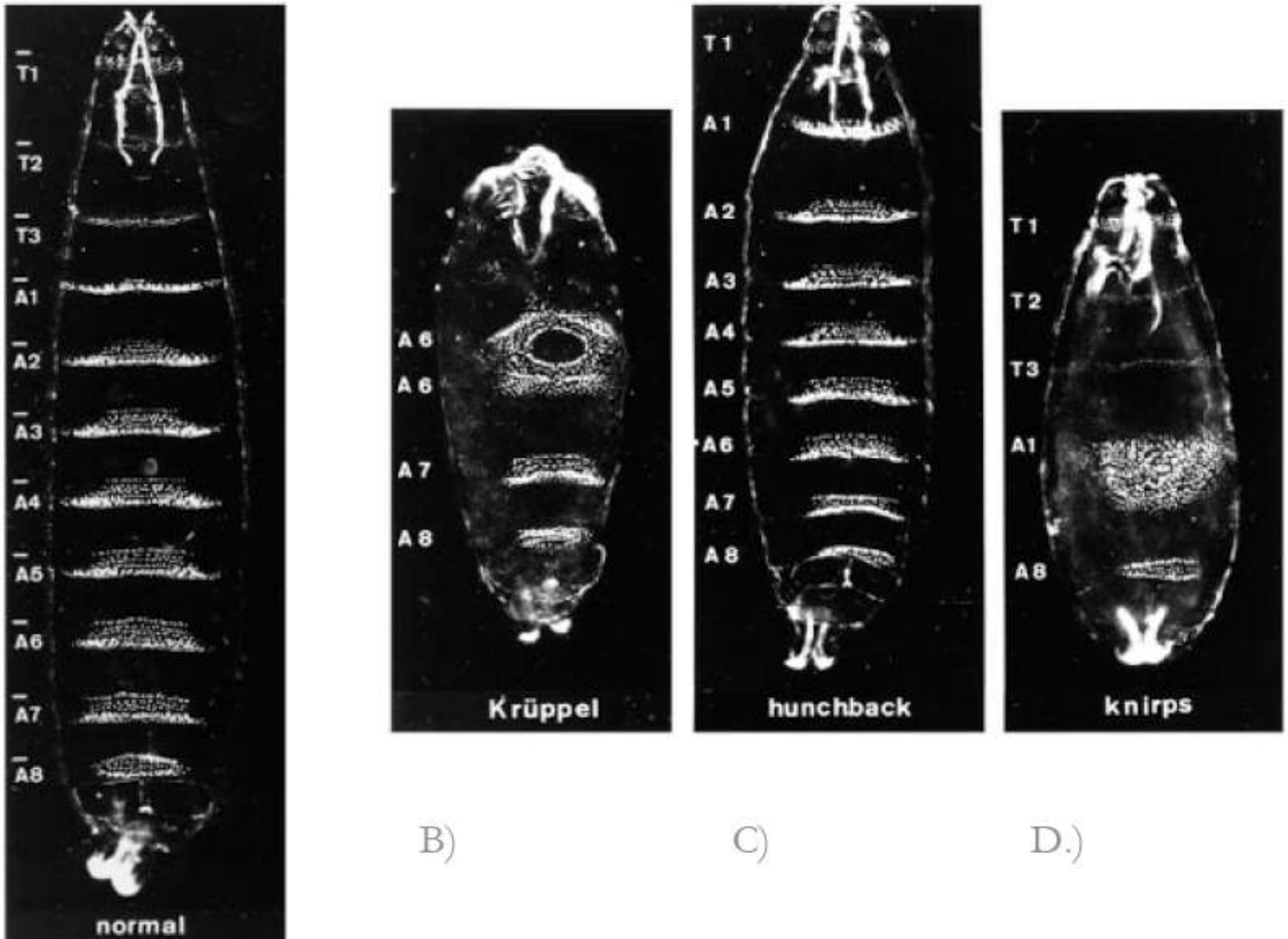


Fig. 22 c

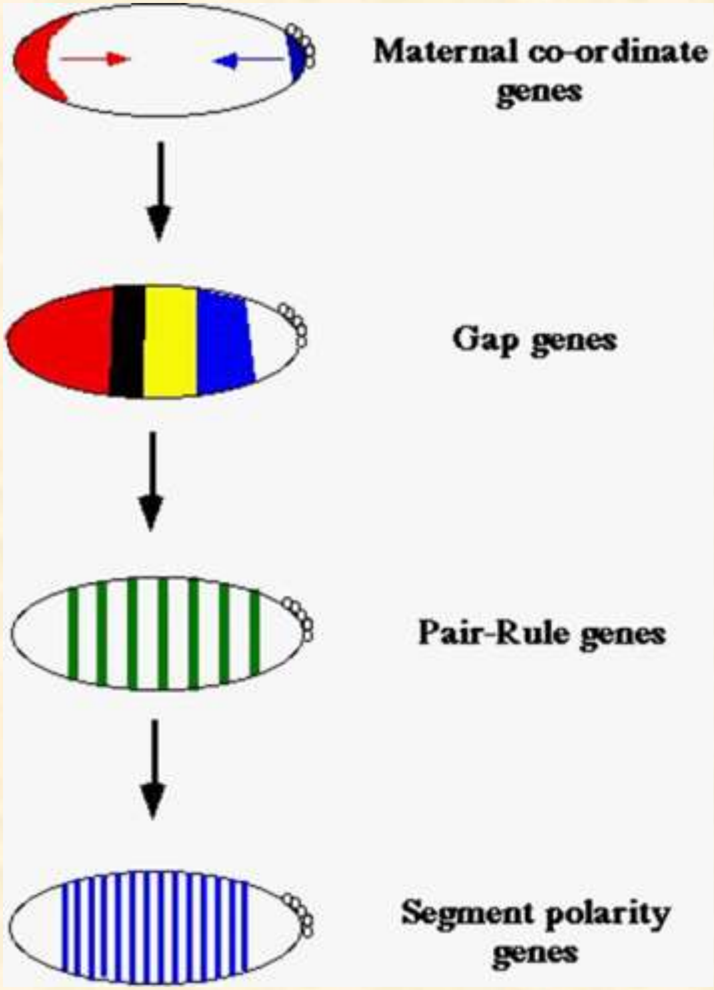
Defects in segmentation from mutations in gap genes

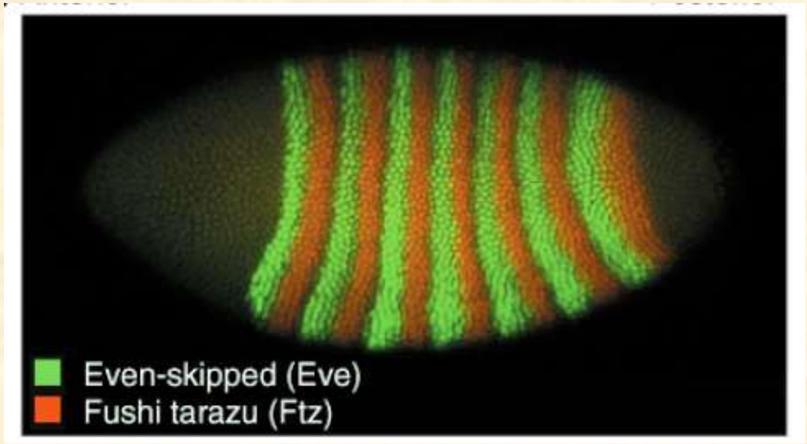


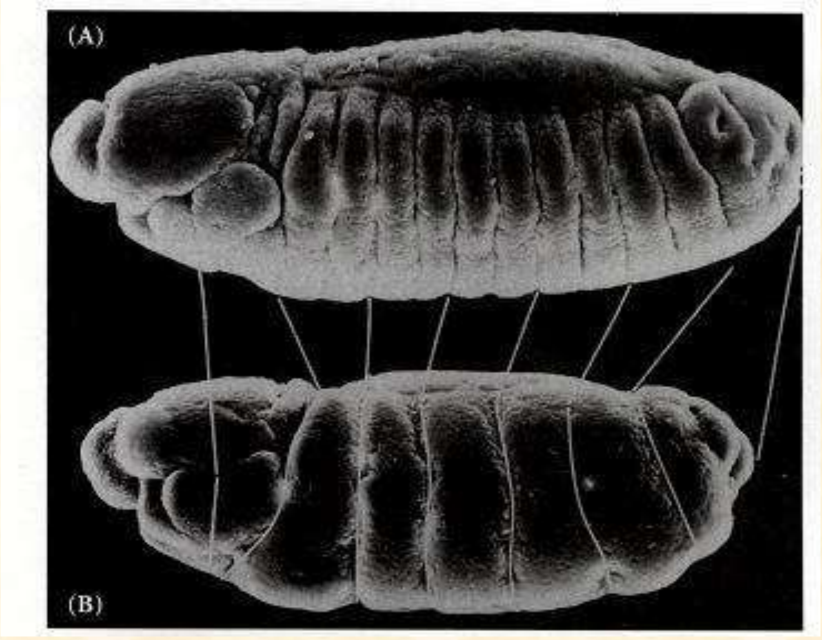
A) B) C) D.)

Fig. 18.22b

Pair-rule Genes

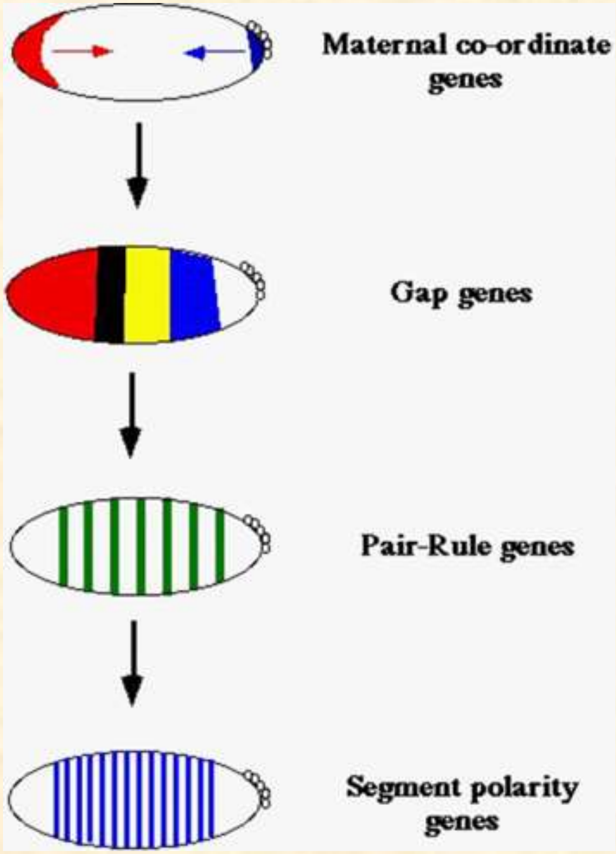


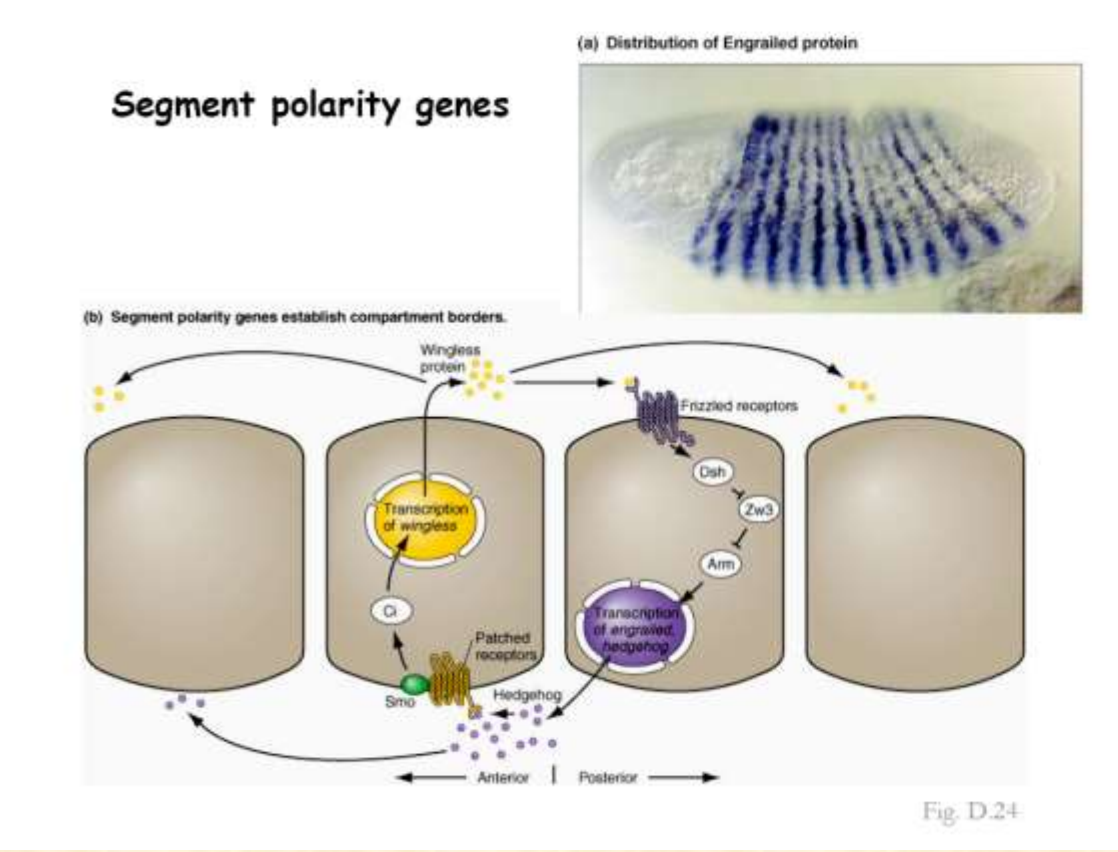




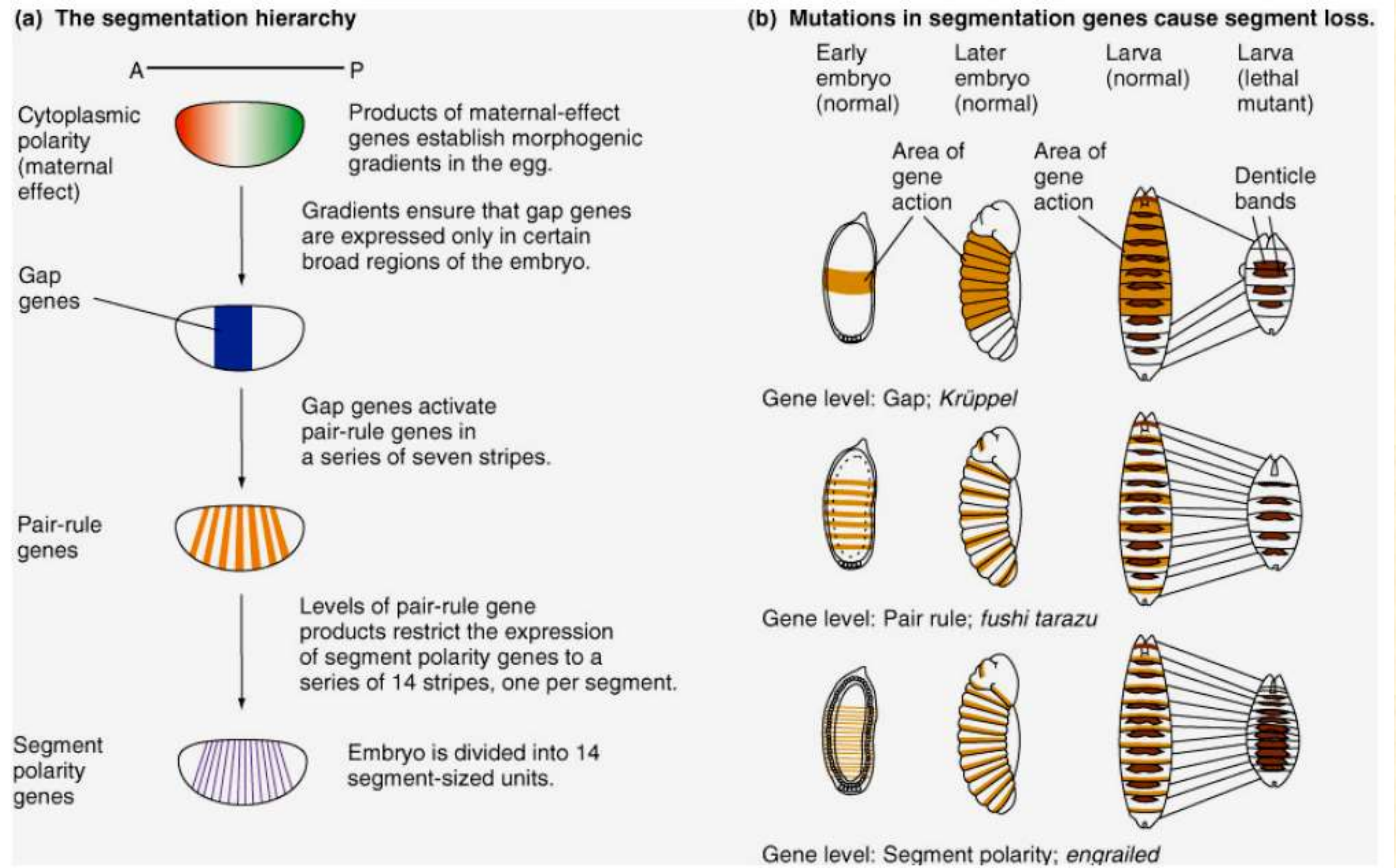
Segment polarity genes are lowest level of segmentation hierarchy

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

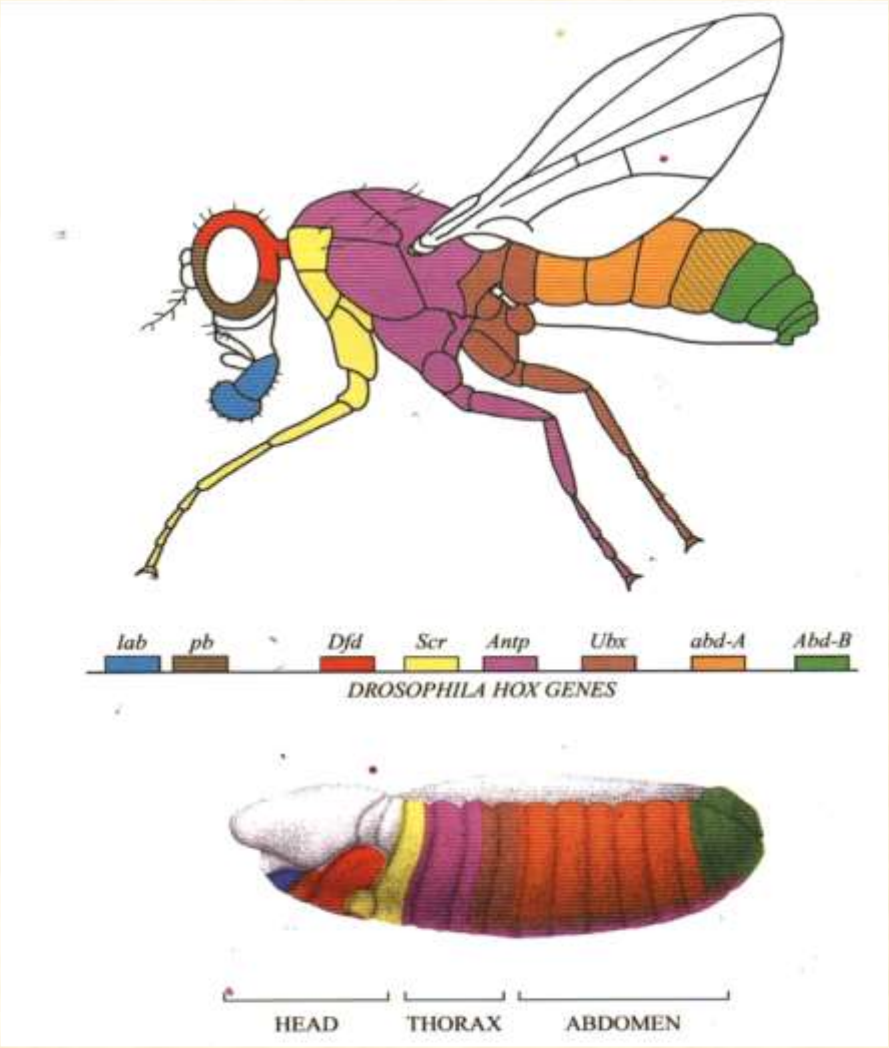


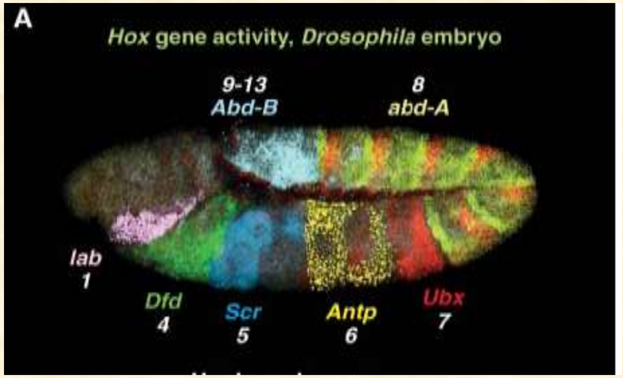


Drosophila embryogenesis: Segmentation genes



Homeotic selector genes: determine the fate of each segment

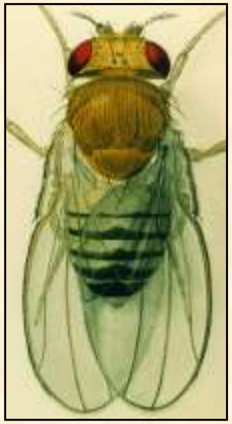


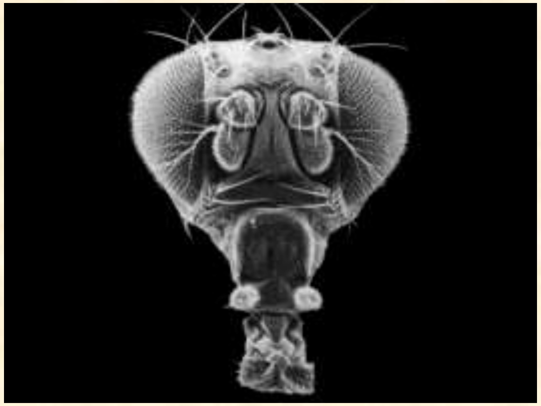


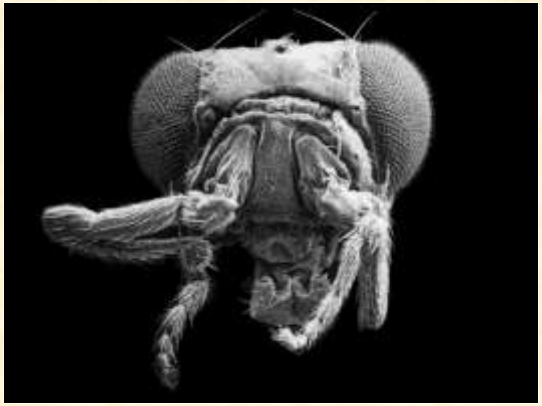
Drosophila Homeotic mutants

Edward B. Lewis

Wild type



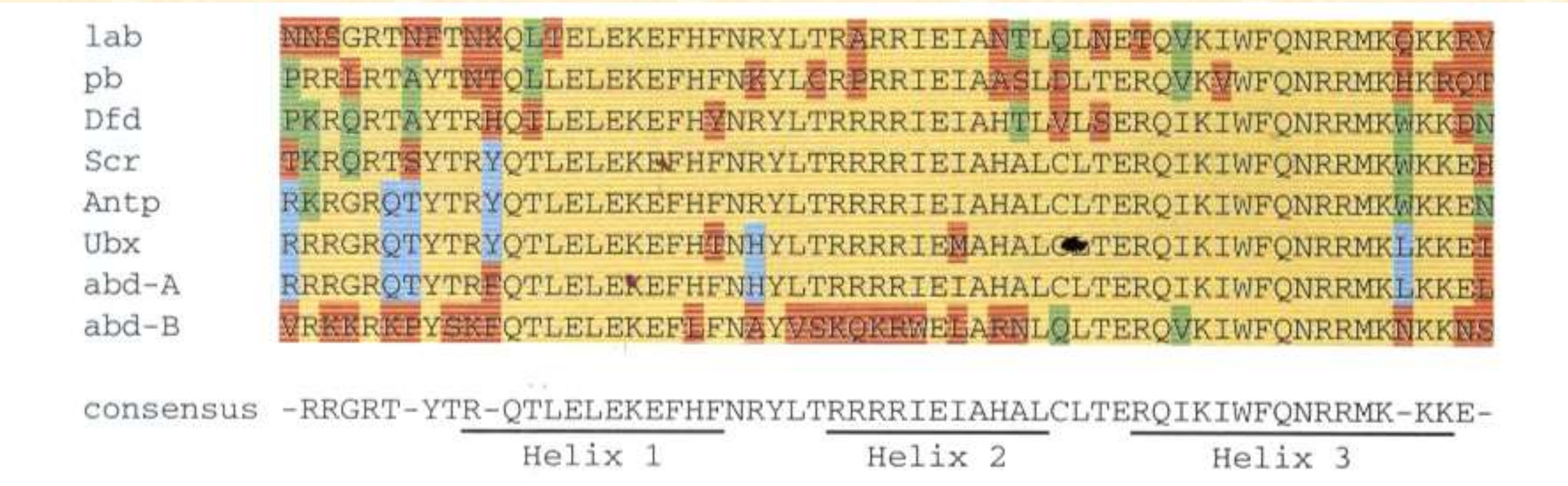




Ubx

Antp

The homeotic genes contain a highly conserved homeobox (Hox)

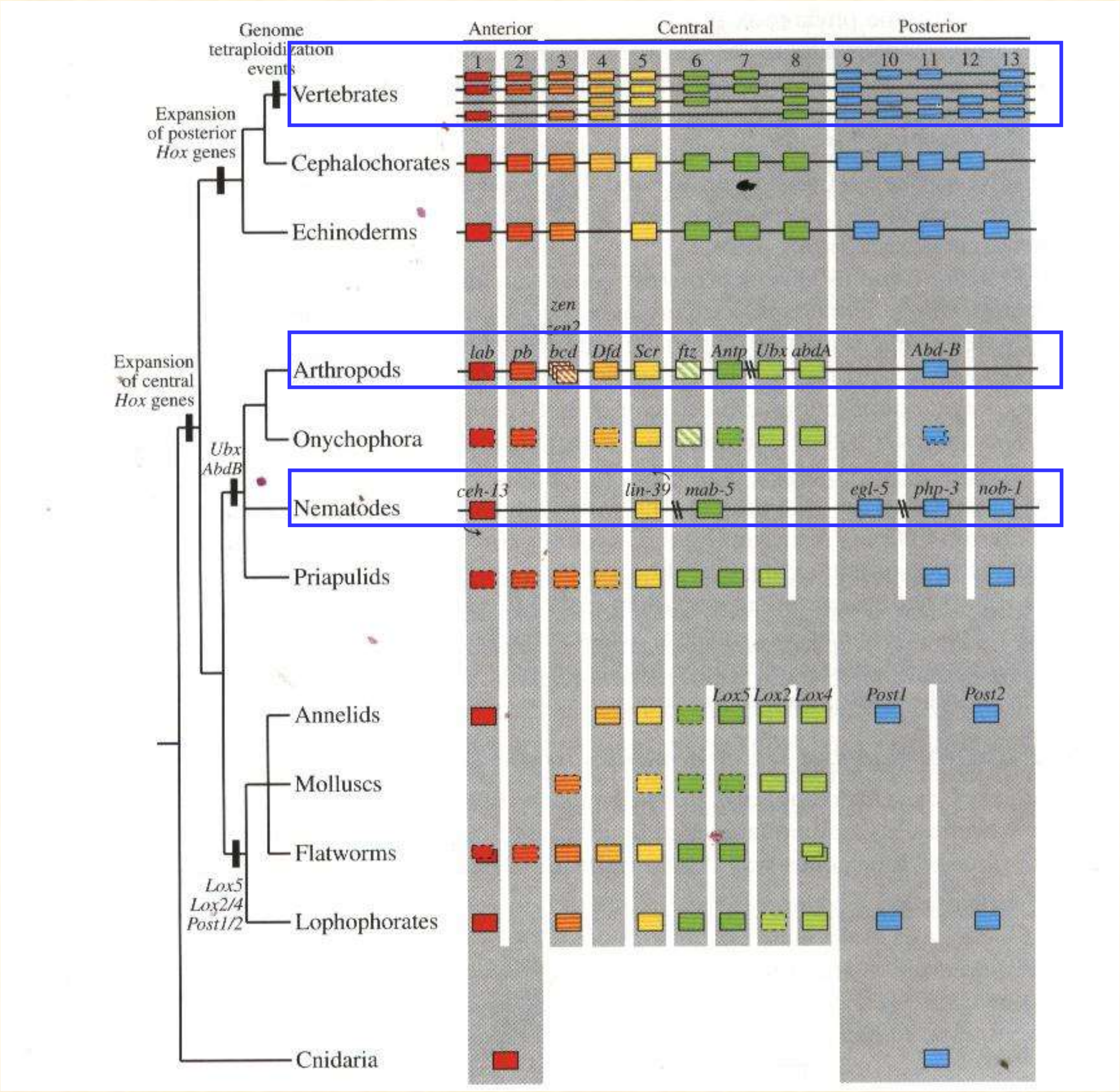


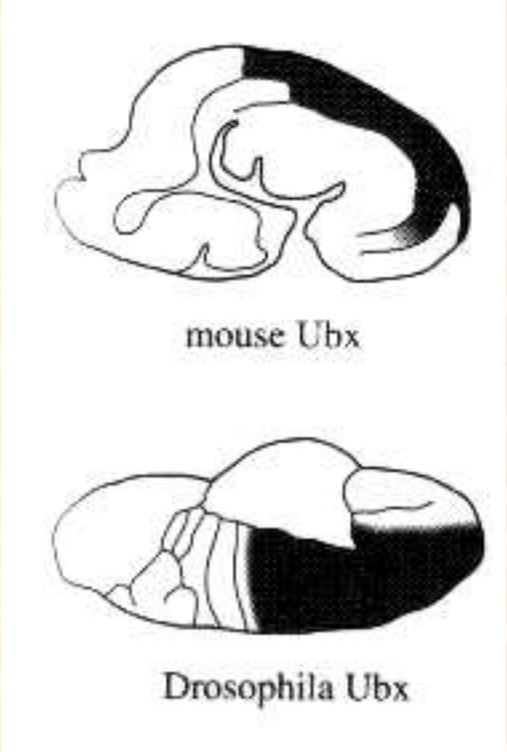
The Homeobox (*Hox)* genes are transcription regulators

the Homeobox encodes a Homeodomain

Which is the first known DNA-binding domain

Evolution of Metazoan *Hox* genes





The Nobel Prize in Physiology or Medicine 2011

"for their discoveries concerning **the activation of innate immunity**"

Jules Hoffmann

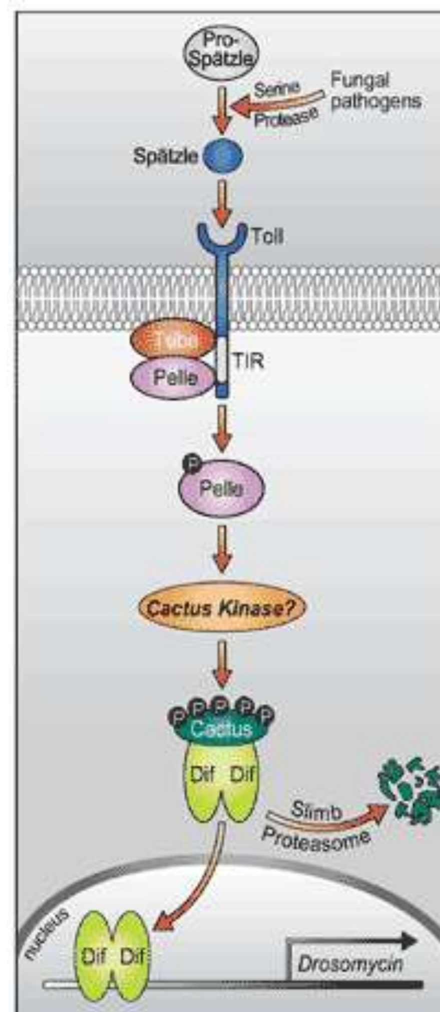
Toll/NF-κB 信号通路

调控先天免疫

Cell, Vol. 86, 973–983, September 20, 1996, Copyright ©1996 by Cell Press

The Dorsoventral Regulatory Gene Cassette *spätzle/Toll/cactus* Controls the Potent Antifungal Response in Drosophila Adults

Bruno Lemaitre, Emmanuelle Nicolas, Lydia Michaut,
Jean-Marc Reichhart, and Jules A. Hoffmann



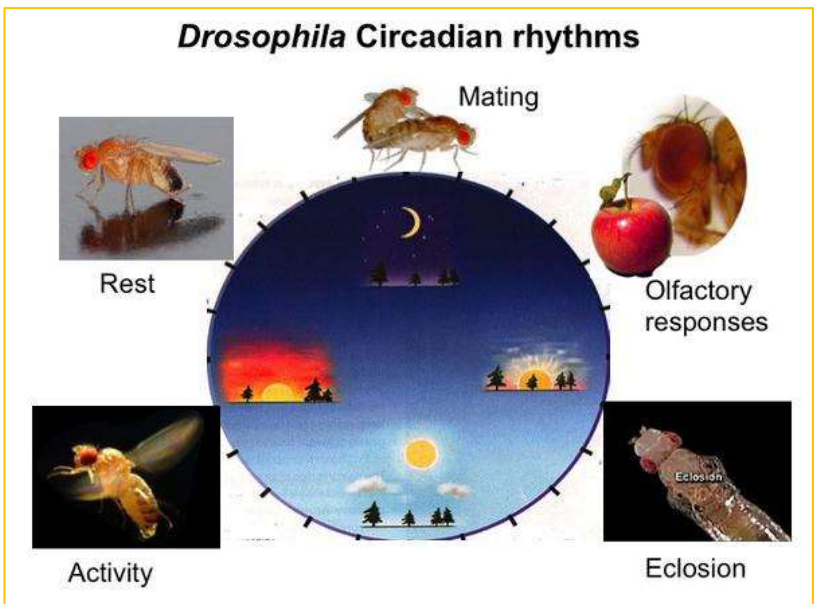
The Nobel Prize in Physiology or Medicine 2017

"for their discoveries of molecular mechanisms controlling the circadian rhythm"

Jeffrey C. Hall

Michael Rosbash

Michael W. Young



Seymour Benzer

1921 - 2007

Ronald Konopka

1947 - 2015

Proc. Nat. Acad. Sci. USA
Vol. 68, No. 9, pp. 2112–2116, September 1971

Clock Mutants of *Drosophila melanogaster*

(eclosion/circadian/rhythms/X chromosome)

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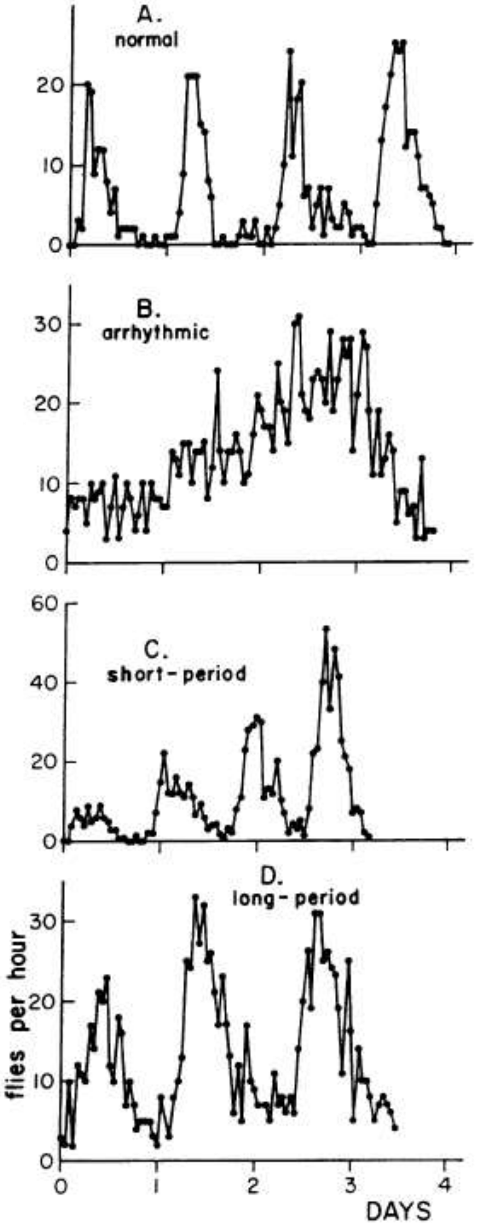
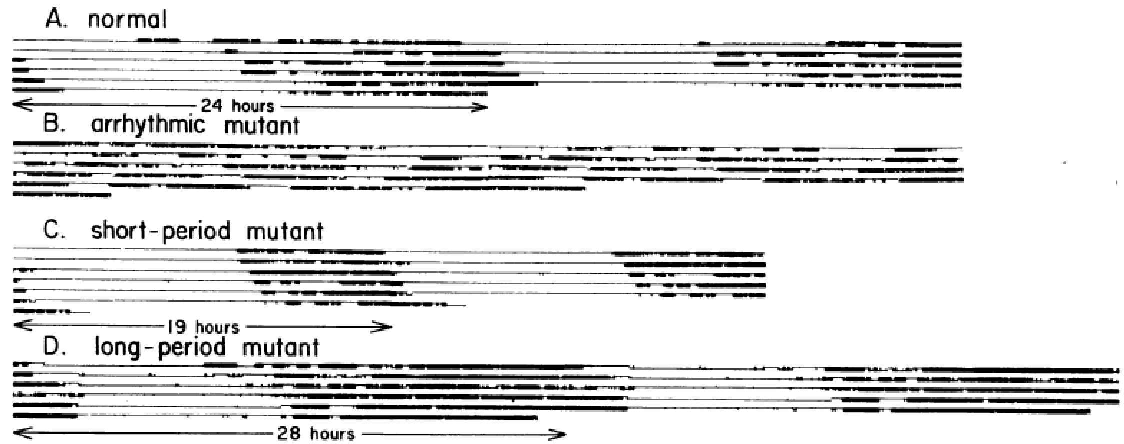
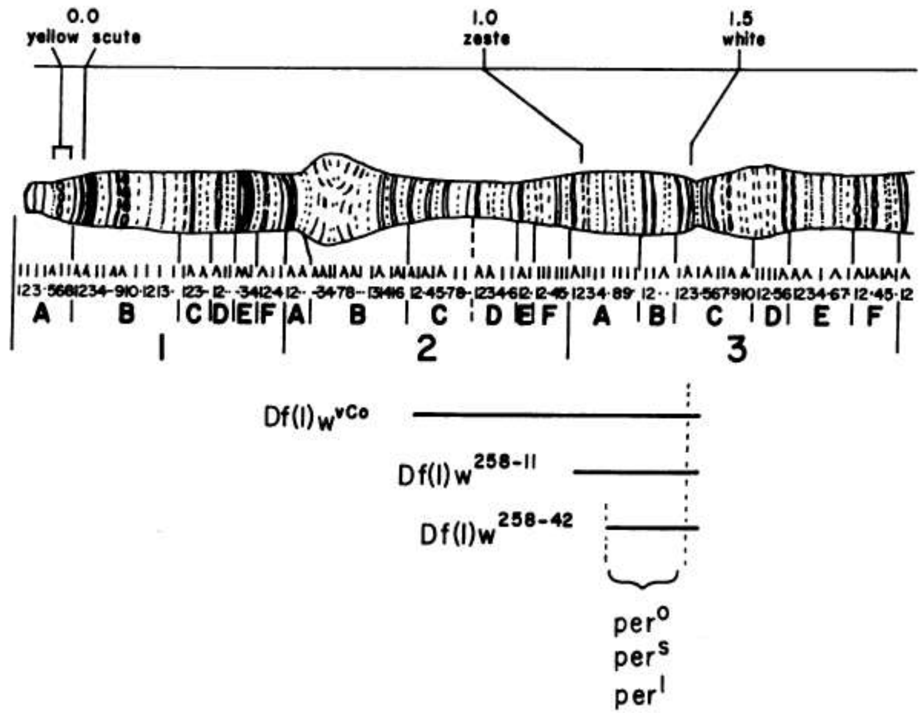
ABSTRACT Three mutants have been isolated in which the normal 24-hour rhythm is drastically changed. One mutant is arrhythmic; another has a period of 19 hr; a third has a period of 28 hr. Both the eclosion rhythm of a population and the locomotor activity of individual flies are affected. All these mutations appear to involve the same functional gene on the X chromosome.

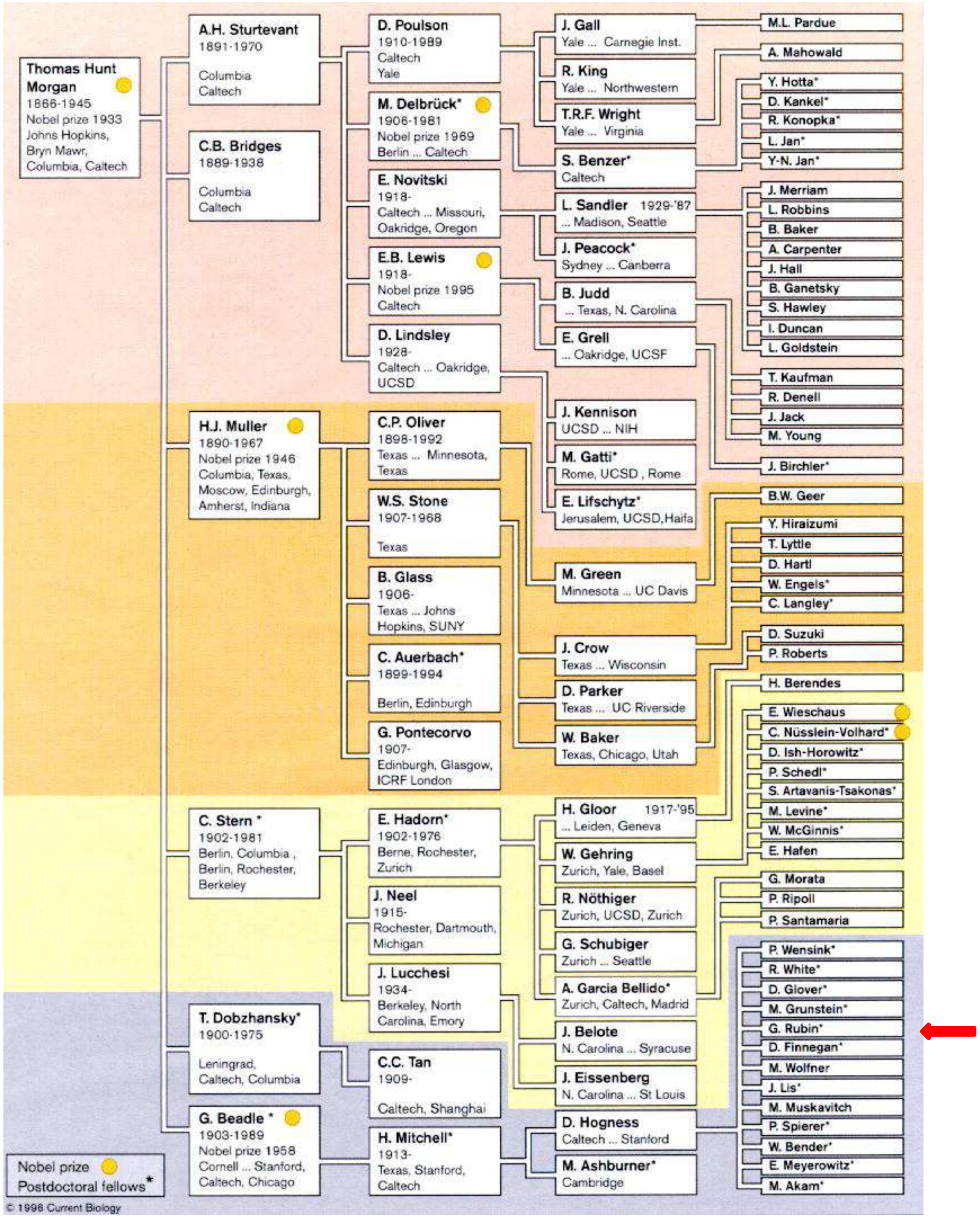


Eclosion rhythms, in constant darkness,

Locomotor activity rhythms,







The Morgan pedigree

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CLOCKWORK
GENES
DISCOVERIES IN
BIOLOGICAL TIME
Howard Hughes
Medical Institute
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