

Mutations affecting  
segment number and  
polarity in *Drosophila*

Christiane Nüsslein-Volhard and Eric Wieschaus

*Nature* (1980)

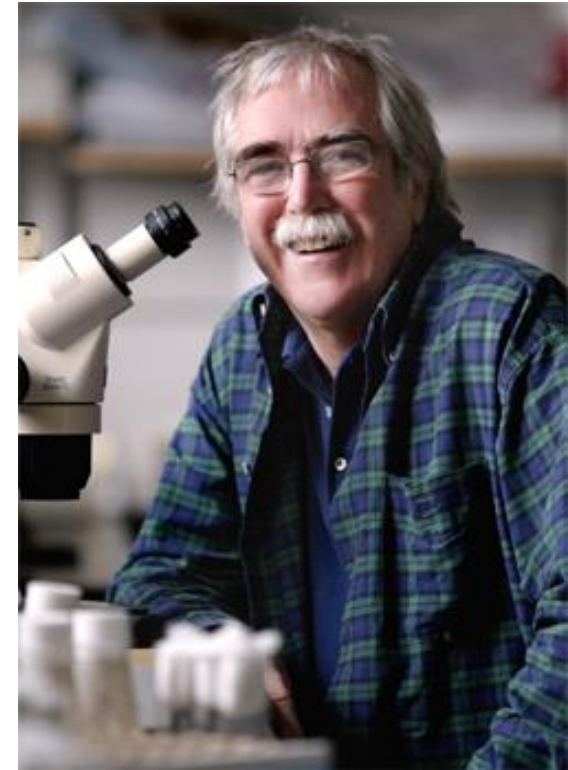
# Christiane Nüsslein-Volhard

- Born October 20, 1942 in Magdeburg Germany
- Bachelors in Biology, Chemistry and Physics from Johann-Wolfgang-Goethe-University in 1964. Degree in biochemistry (1968) and a PhD in biology and genetics in 1973 from Eberhard-Karl University in Tübingen
- Post-doc in Basel and Freiburg
- Became a group leader at the European Molecular Biology Laboratory (Heidelberg, Germany) in 1978
- Moved to the Max Planck Institute in 1981, and became director of genetics from 1985-2014



# Eric Wieschaus

- Born June 8, 1947 in South Bend, Indiana
- B.S. in Biology from Notre Dame (1969) and PhD in Biology from Yale (1974) while studying maternal effect genes
- Post-doc under Rolf Nöthiger in Zurich studying segmentation development in flies
  - Met Nüsslein-Volhard while in Zurich
- Moved with Nüsslein-Volhard to EMBL to collaborate in 1978
- After publication, moved to a faculty position at Princeton in 1981 where he remains today



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# **Mutations affecting segment number and polarity in *Drosophila***

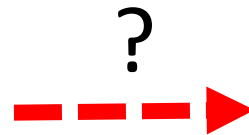
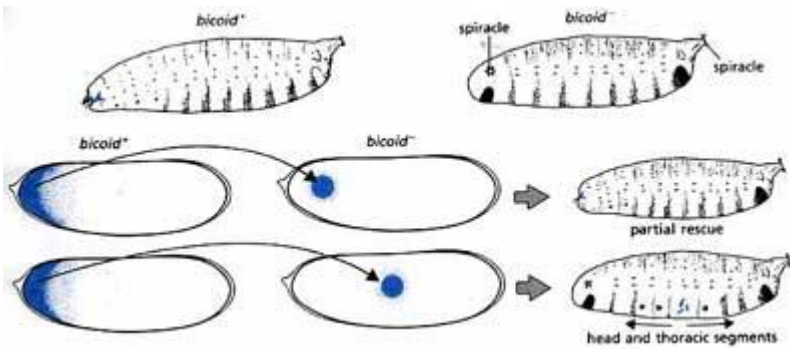
**Christiane Nüsslein-Volhard & Eric Wieschaus**

European Molecular Biology Laboratory, PO Box 10.2209, 69 Heidelberg, FRG

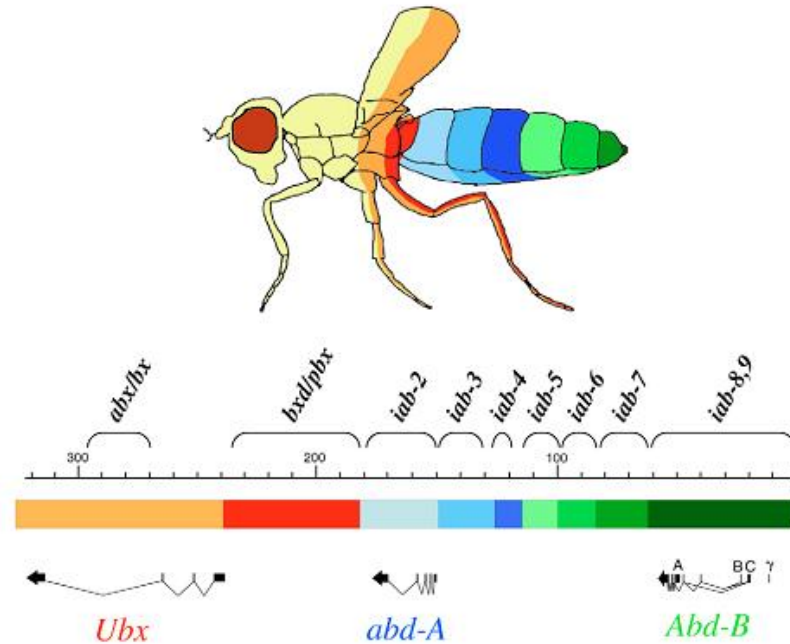
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# Genes already known to affect fly development

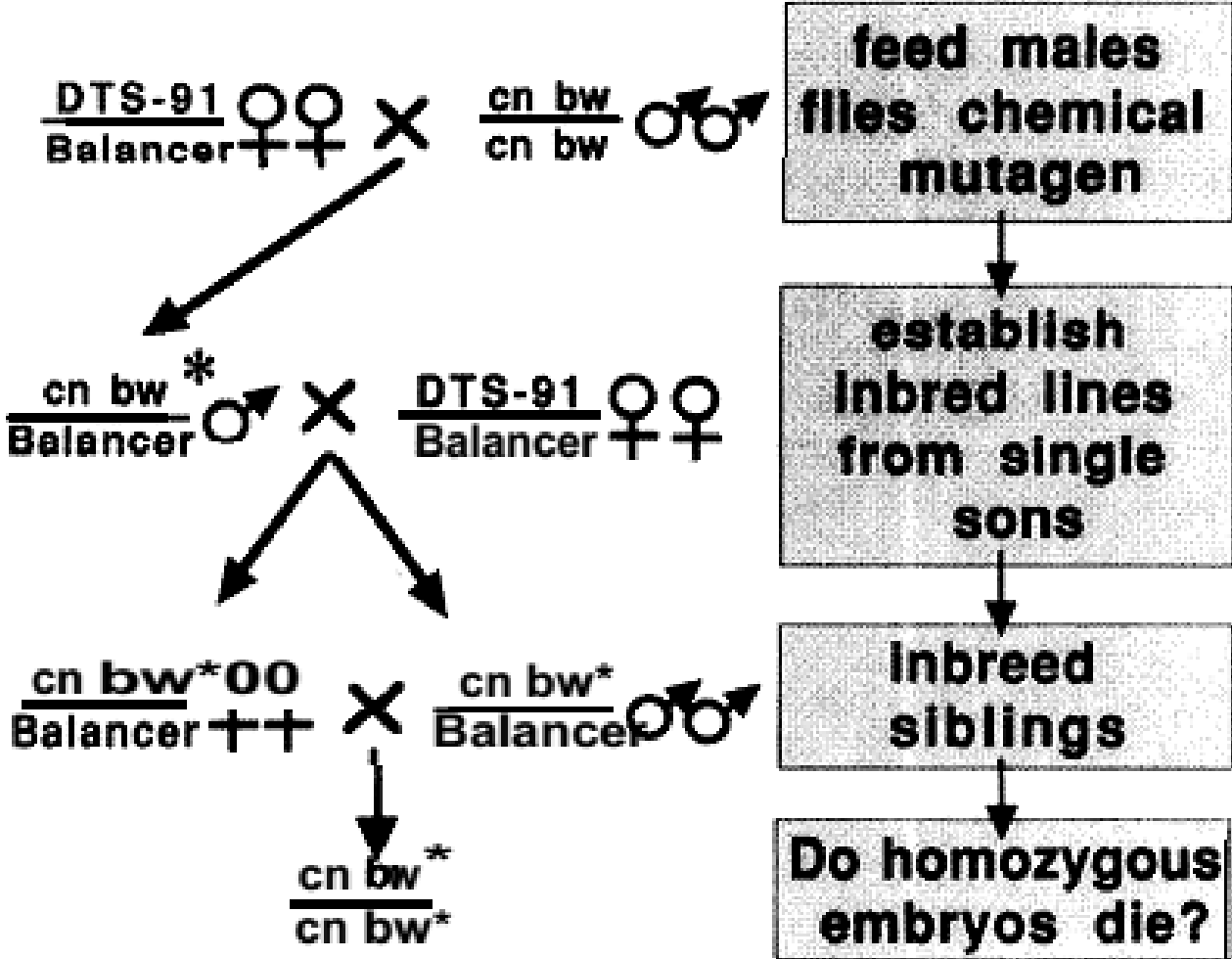
## Early antero-posterior signaling



## Genes affecting late development



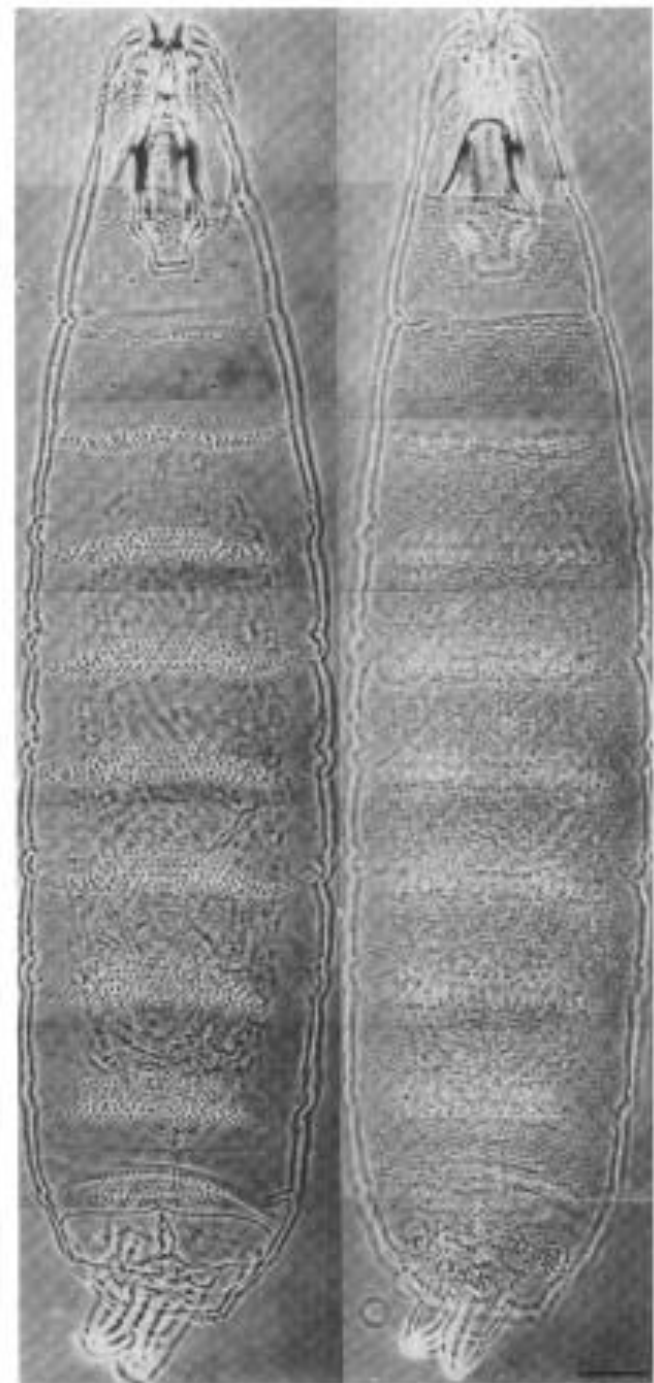
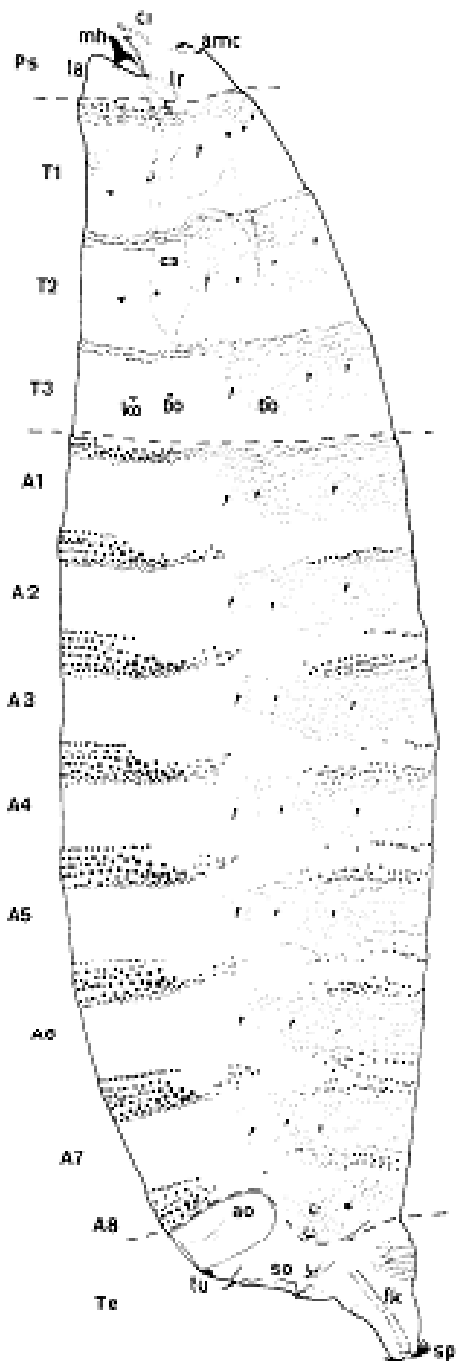
# Saturation Mutagenesis



# Saturation Mutagenesis

## Results of mutagenesis screens

<b>Total lines established and tested</b>	<b>26978</b>
<b>Lethal mutations</b>	<b>18136</b>
<b>Mutations causing embryonic lethality</b>	<b>4332</b>
<b>Mutations causing embryonic phenotypes</b>	<b>580</b>
<b>Complementation Groups (Genes)</b>	<b>139</b>



Lohs-Schardin et al. *Devl. Biol.* 1979



# Defining Segments in Drosophila

Anterior



Posterior

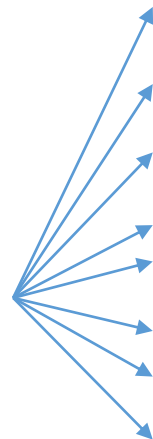
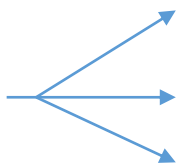
Head



Thorax

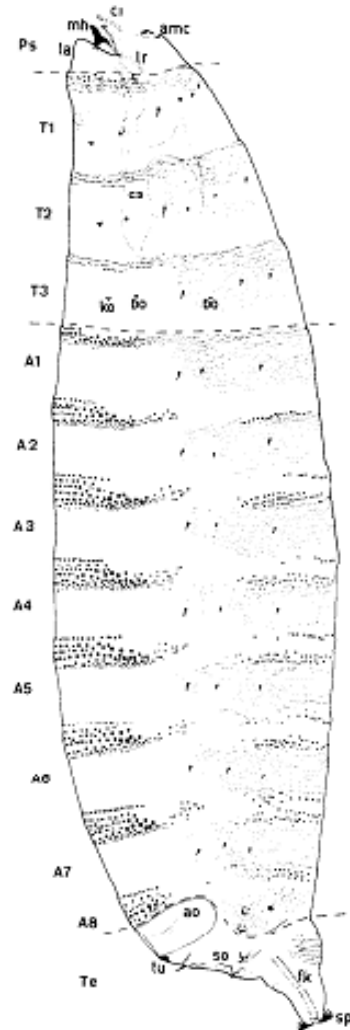


Abdomen



12 total segments

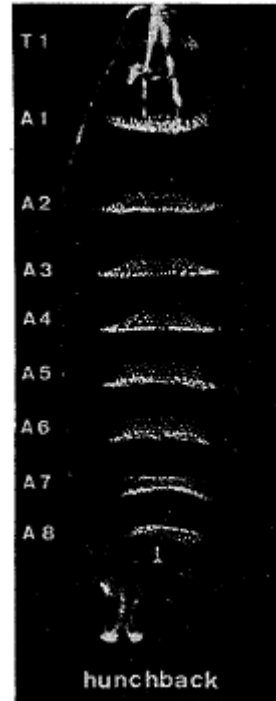
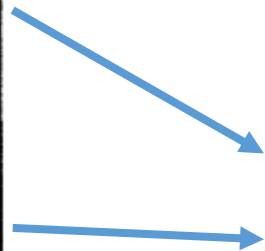
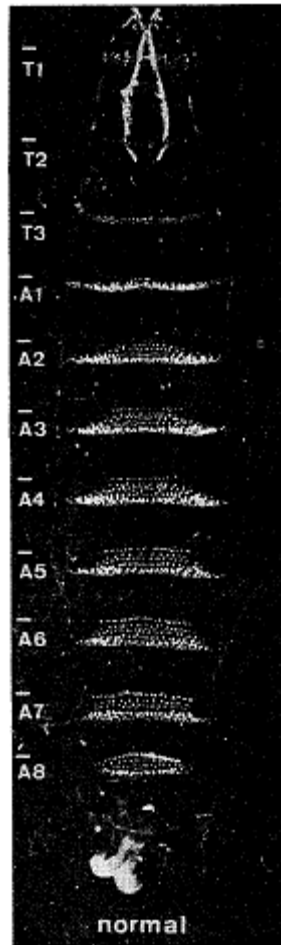
Polarity



# Increasing complexity beyond A→P: Gap Genes

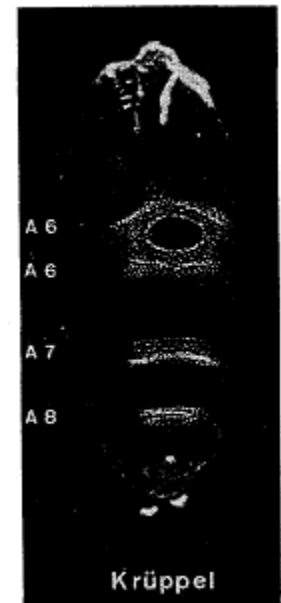
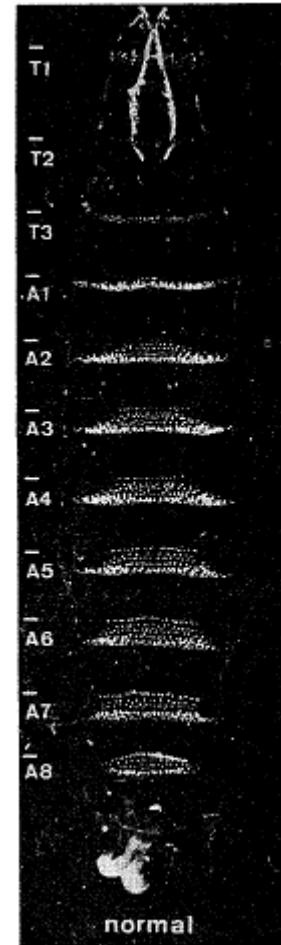
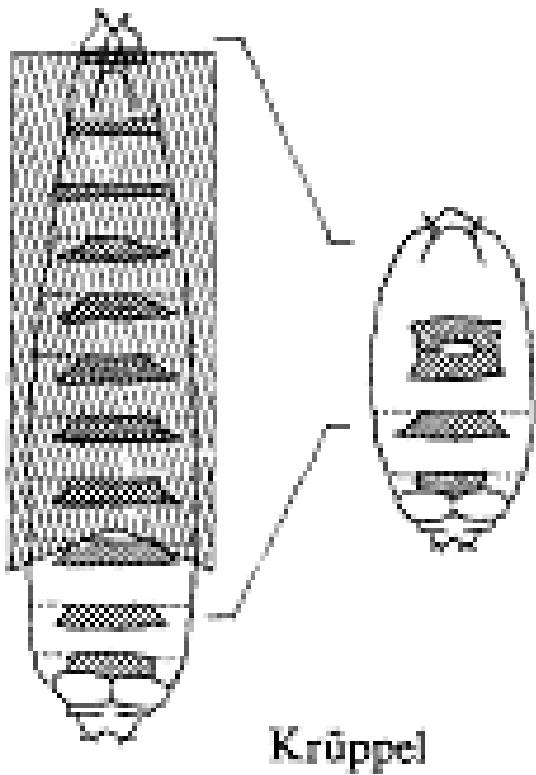
- Loss of function of gap genes results in deletions of entire, adjacent segments
- Krüppel (Kr) results in lack of thorax and anterior abdomen
- Knirps (kni) results in the loss of the anterior abdomen
- Hunchback results in the loss of meso- and metathoracic segments

# Hunchback: Thoracic identity



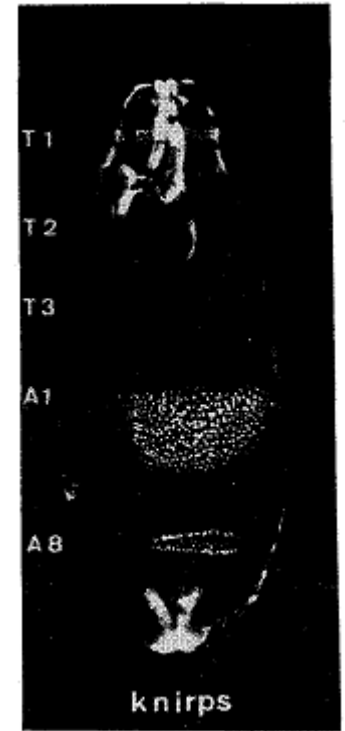
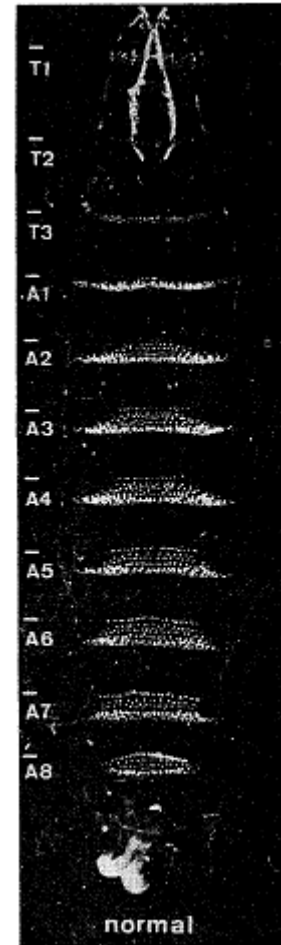
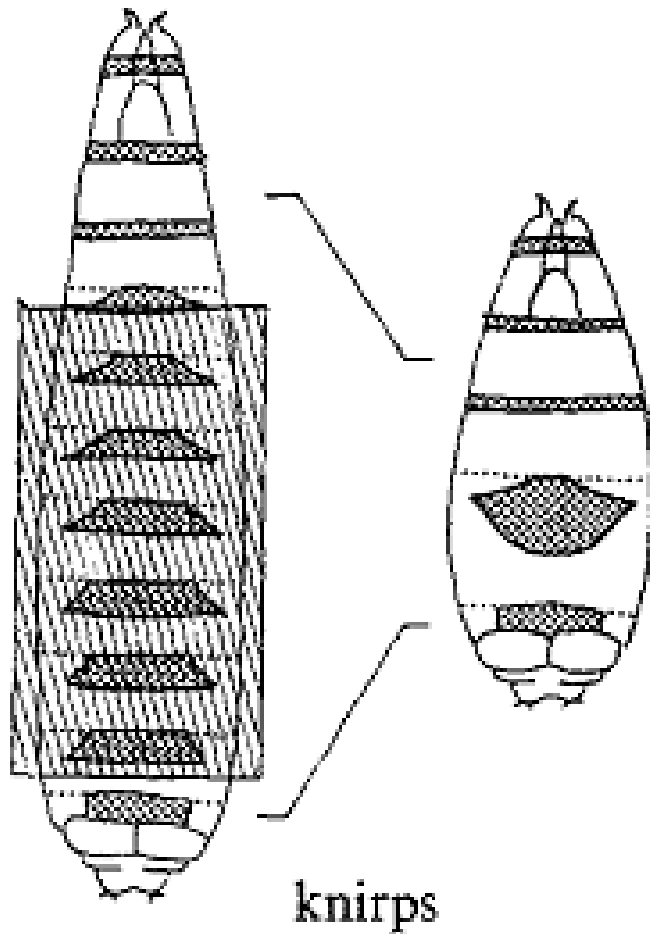
Note normal development of the abdominal sections

# Krüppel: Thoracic and anterior abdominal identity



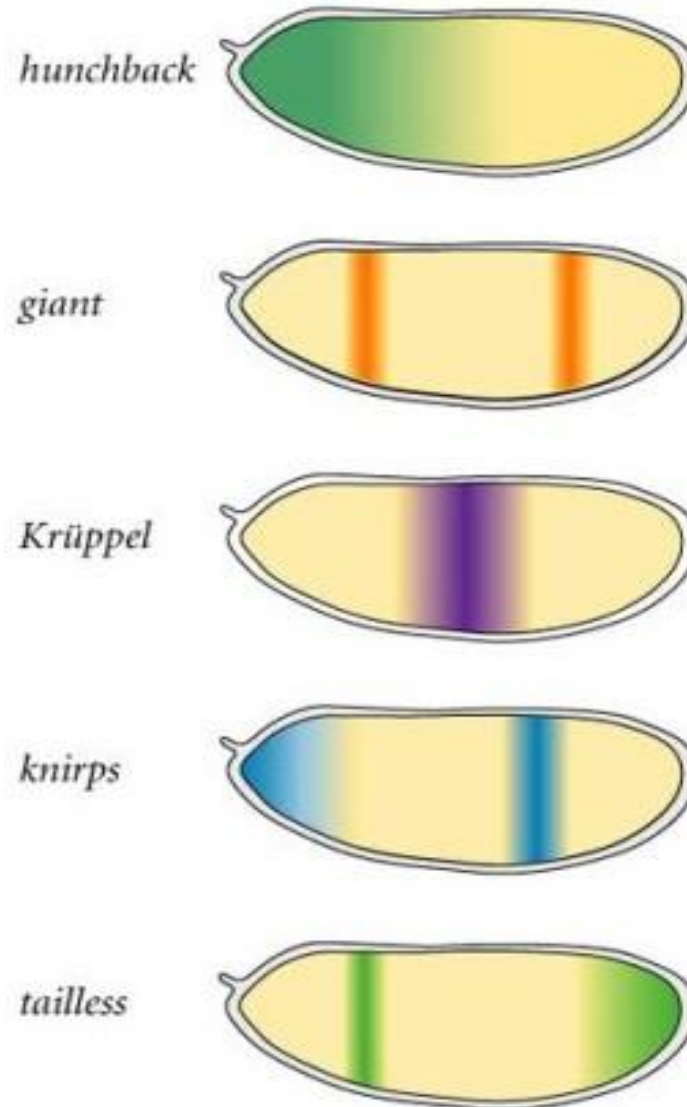
Arrows indicate a reversal in polarity

# Knirps: Anterior abdomen determination

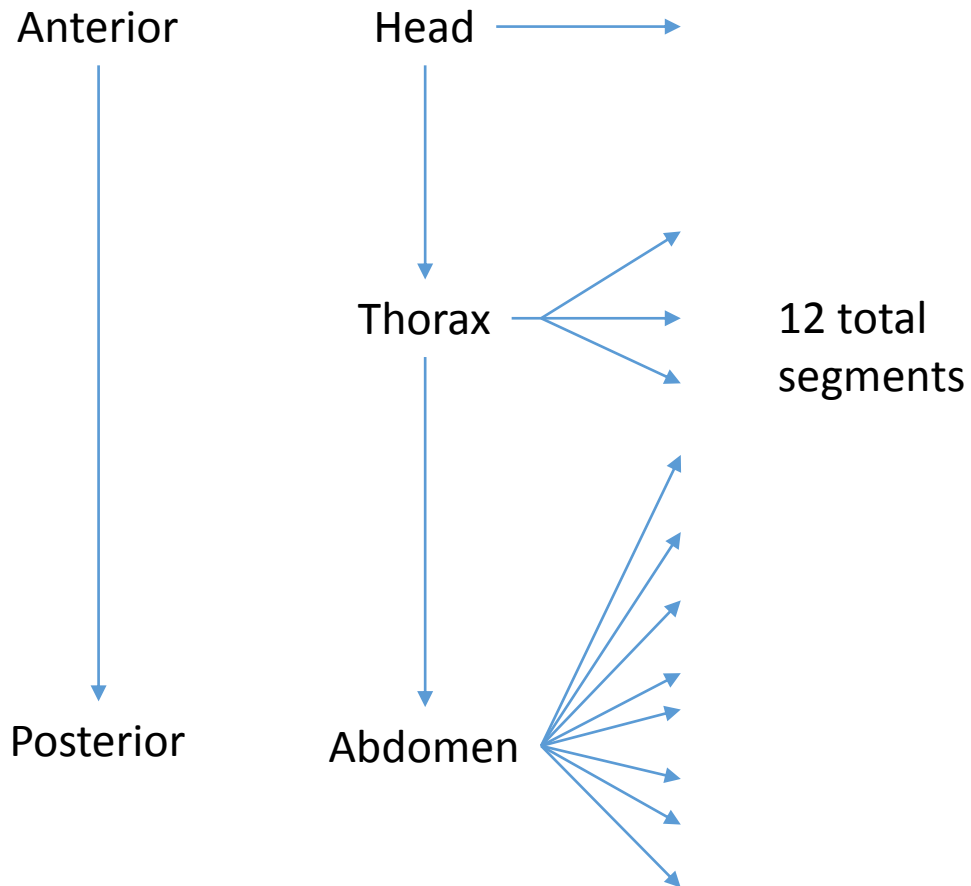


# What does the expression of gap genes look like in the developing embryo?

- Hunchback defines thorax
- Kruppel defines thorax and anterior abdomen
- Knirps defines anterior abdomen



# Defining Segments in Drosophila

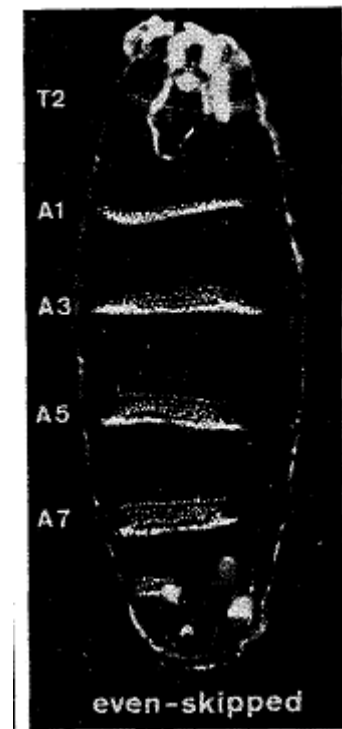
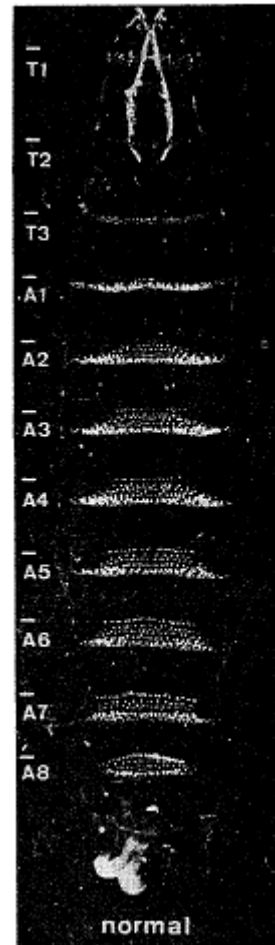
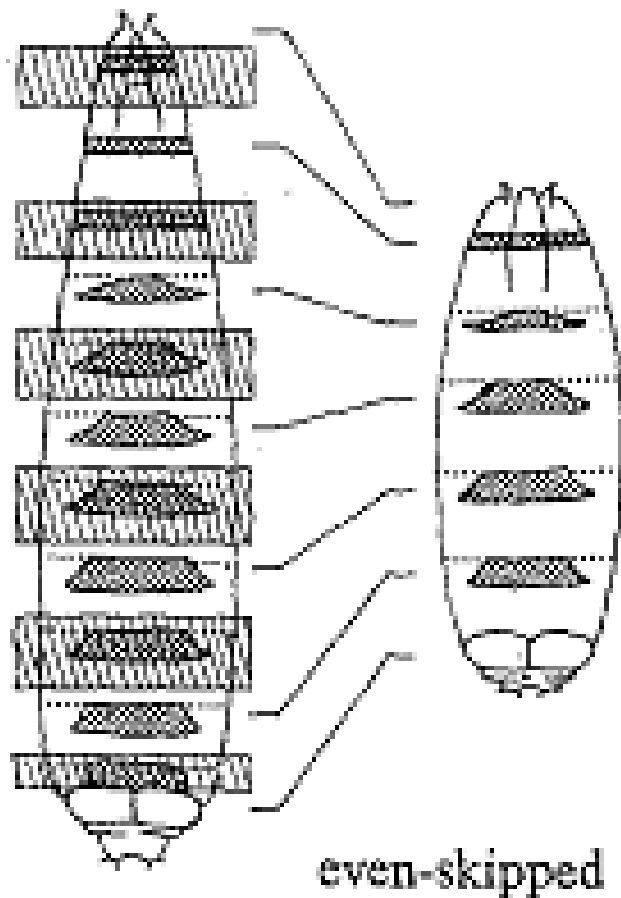


# Increasing complexity to 12 segments: Pair-rule genes

- Engrailed was provided by Thomas Kornberg at UCSF
- Even-skipped
- Odd-skipped
- Paired
- Runt
- Barrel

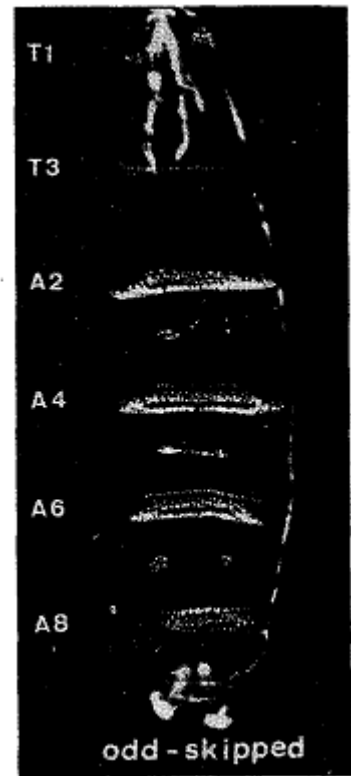
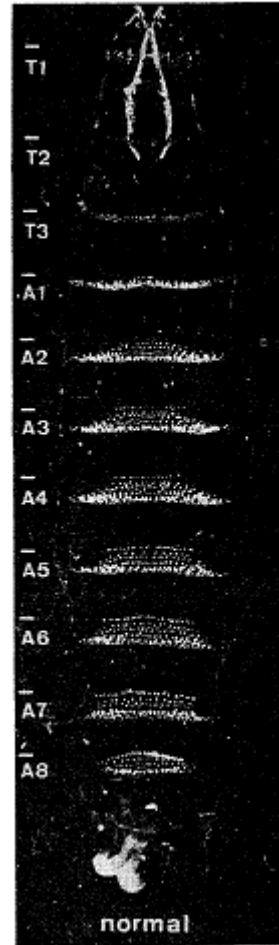
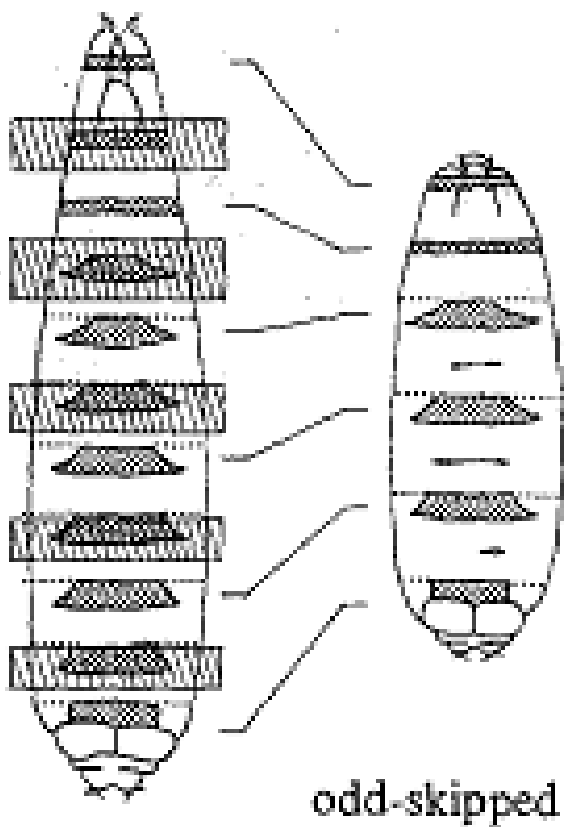


# Even-Skipped: Defining the T1, T3, A2, A4, A6, A8

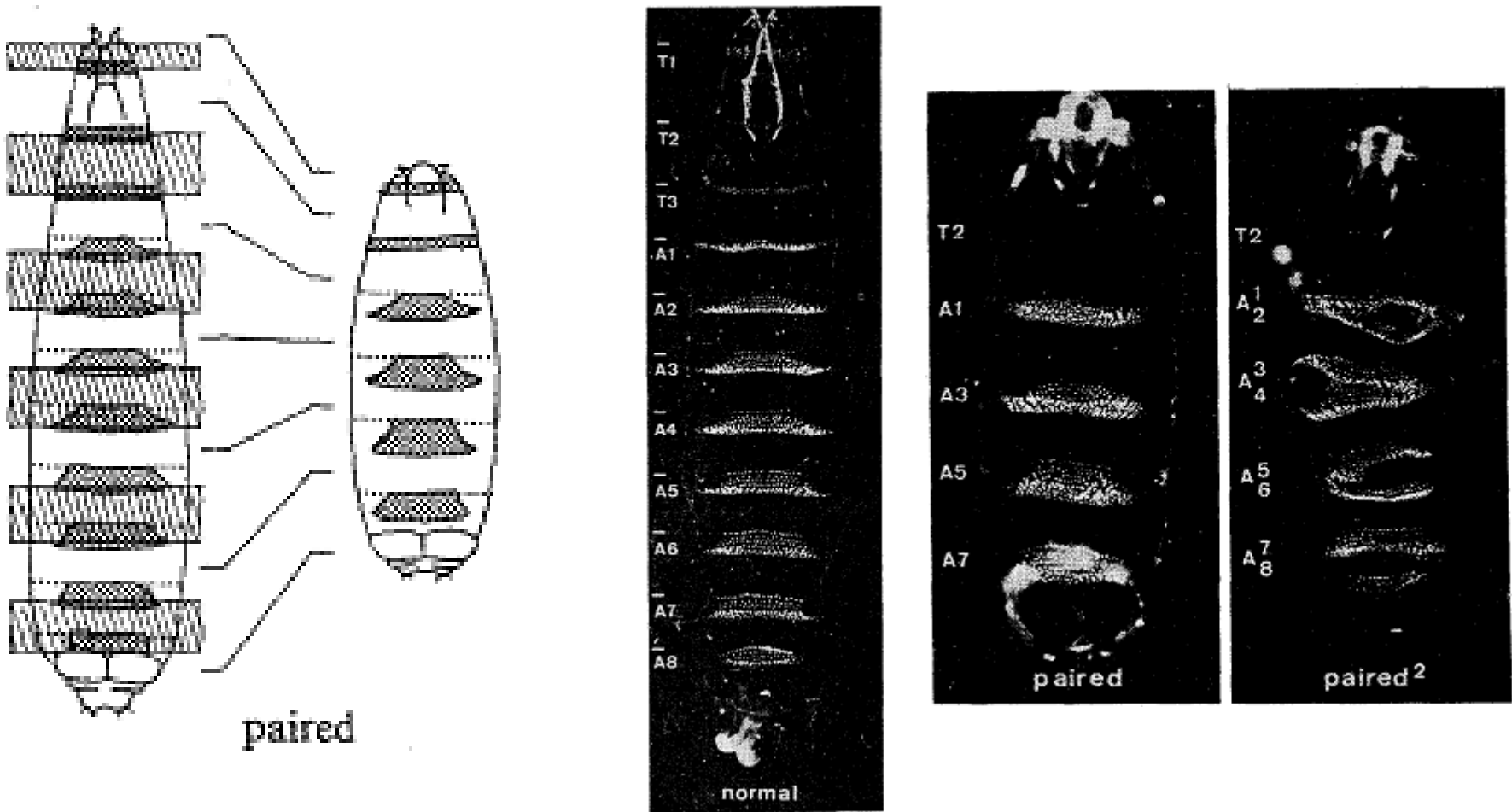


Defines the denticle band and naked cuticle of even numbered segments

# Odd-skipped: the determination of the rest of the segments

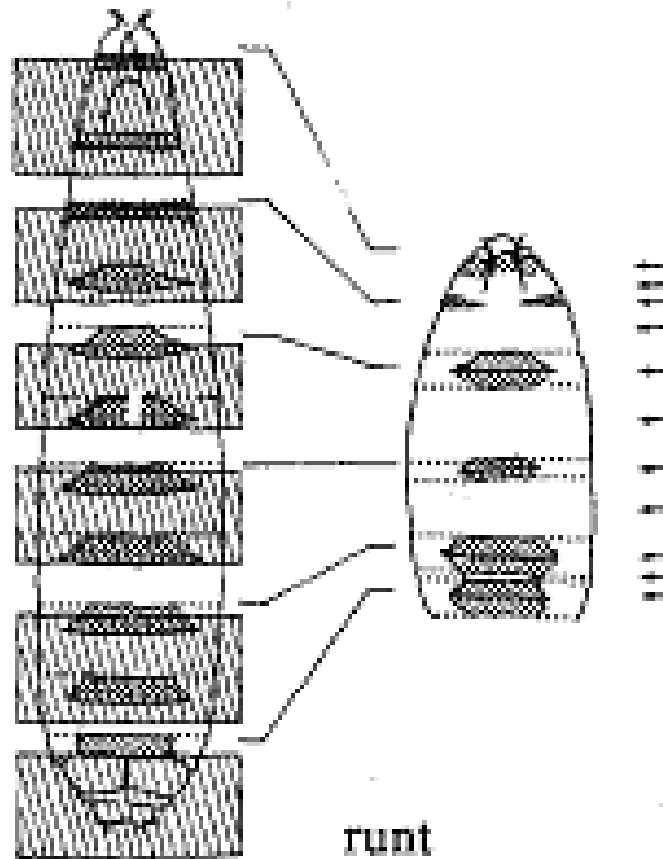


# Connecting the spaces between segments: Paired and runt

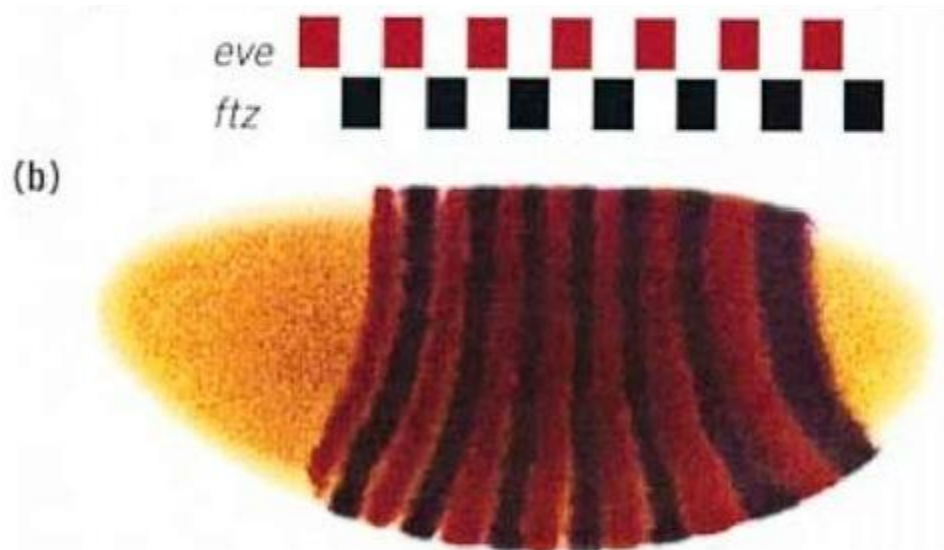


Overlaps in determination of segments: Segments of the fly are not isolated units

# Connecting the spaces between segments: Paired and runt



What does the expression of pair-rule genes look like?



# Defining Segments in Drosophila

Anterior

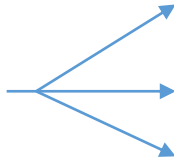


Posterior

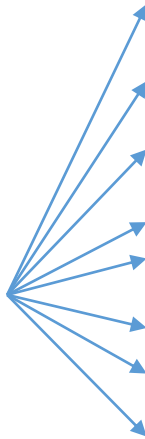
Head



Thorax

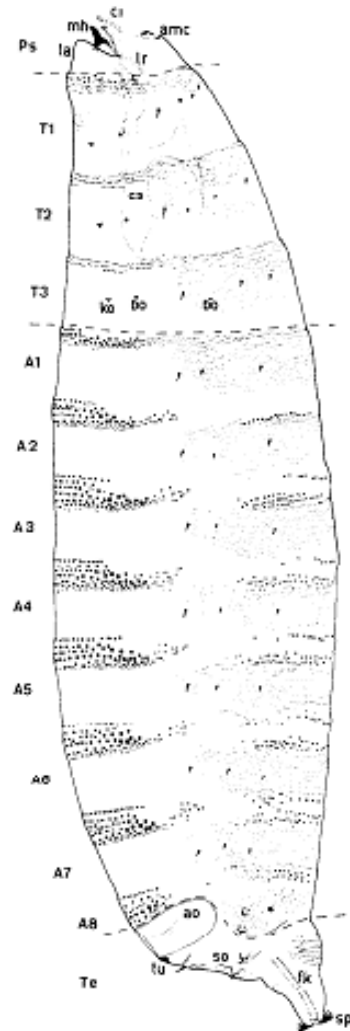


Abdomen



12 total segments

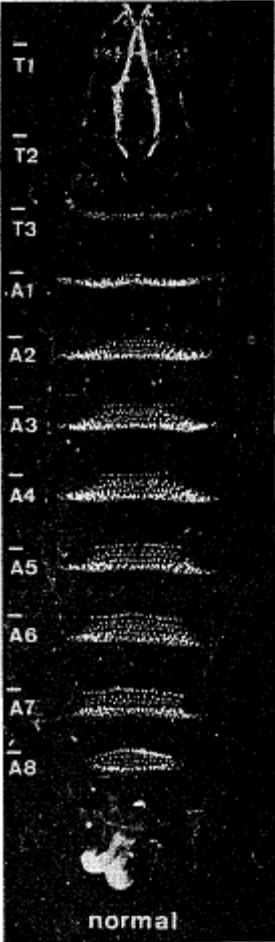
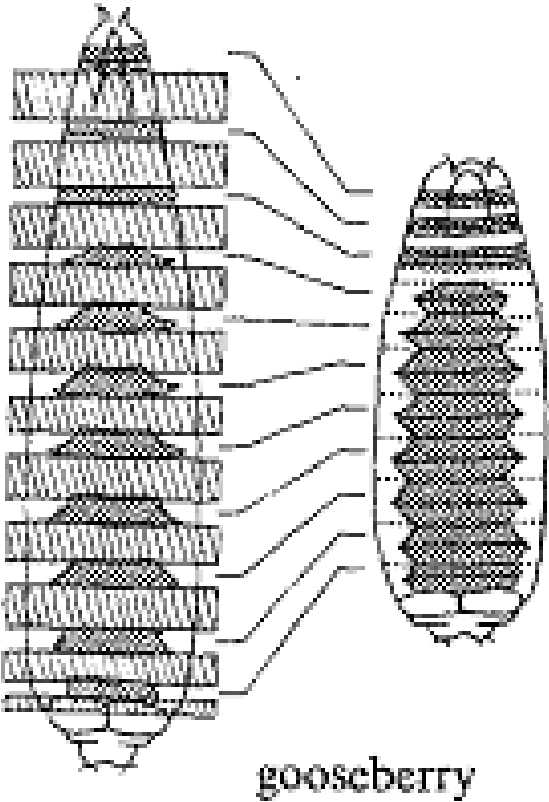
Polarity



# Defining segment polarity

- Gooseberry
- Hedgehog
- Patch
- Wingless was provided by Gary Struhl at Columbia University

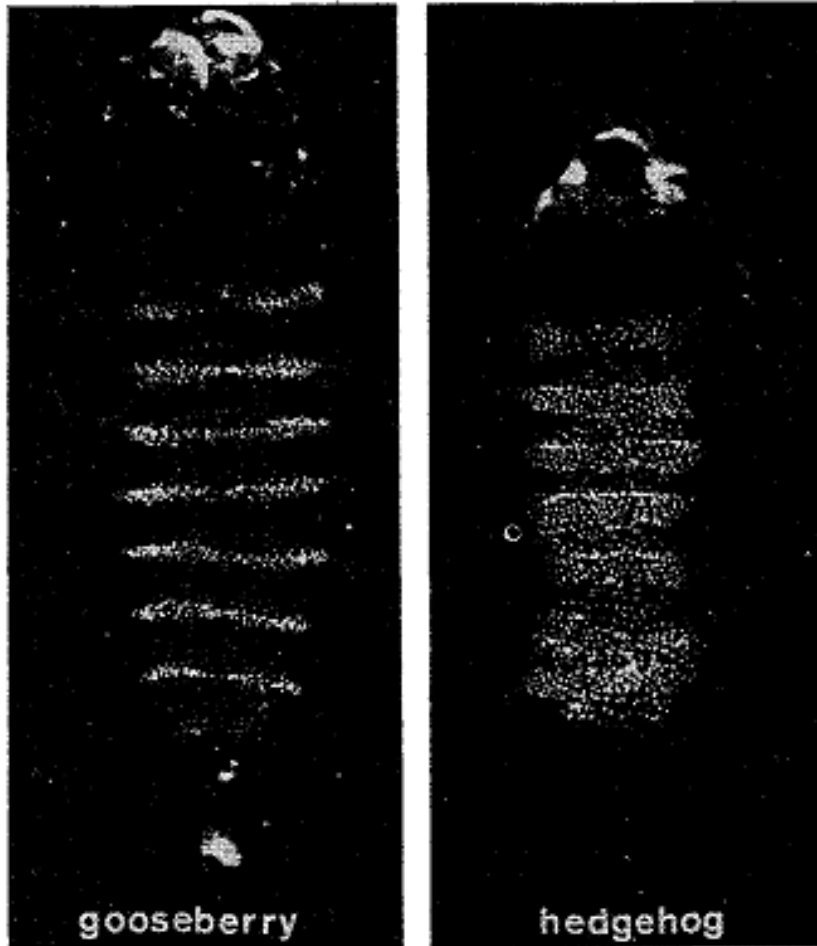
# Segment Polarity Genes: Gooseberry



Segment number is retained, but there is a loss of naked cuticle and a duplication of denticle band

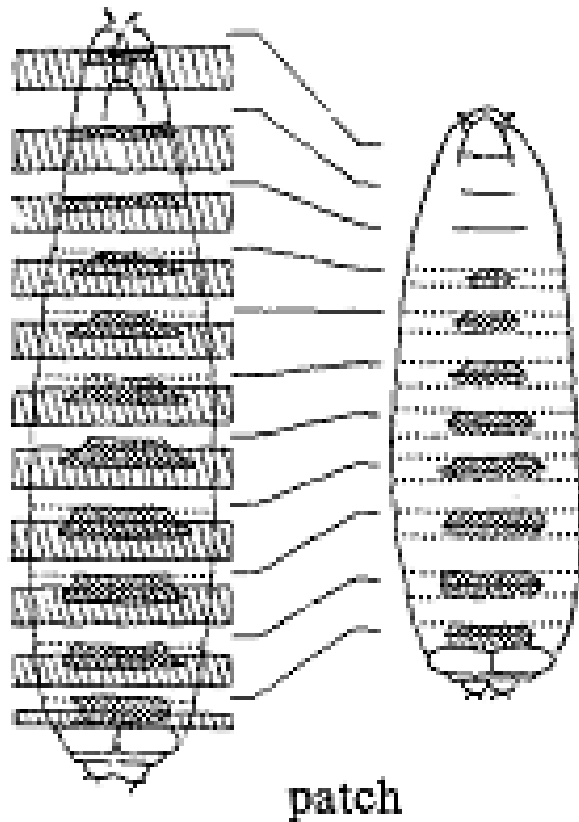


# Hedgehog: very similar to gooseberry

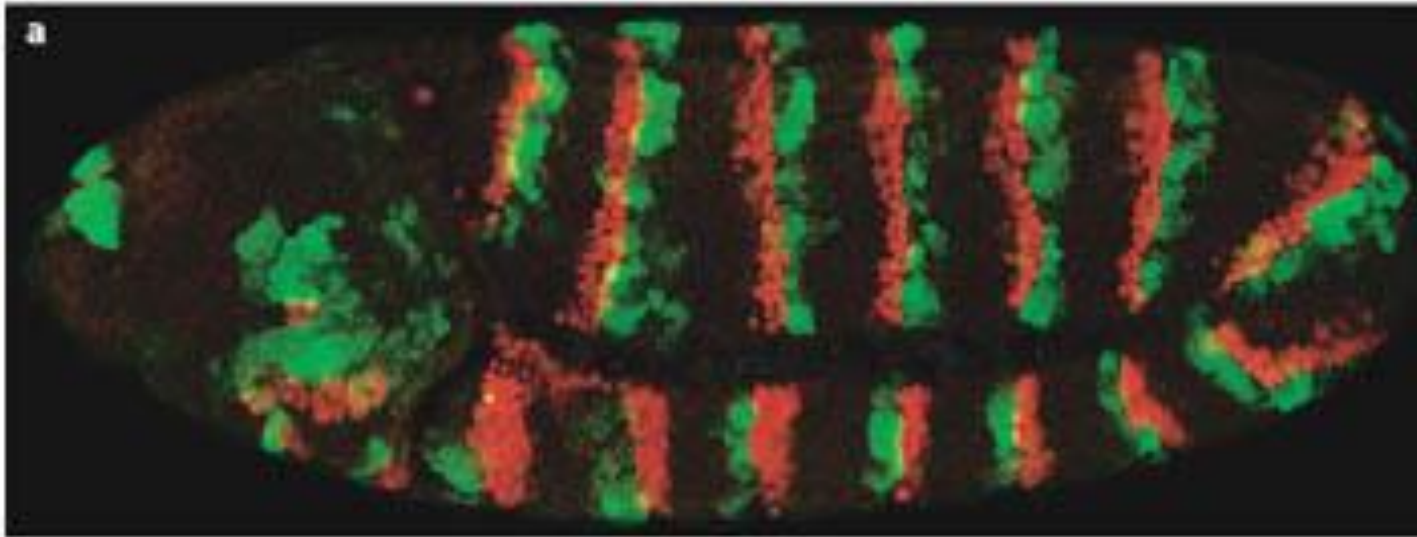


Almost a complete loss of  
segment identity

# Patch: duplication of number of segments

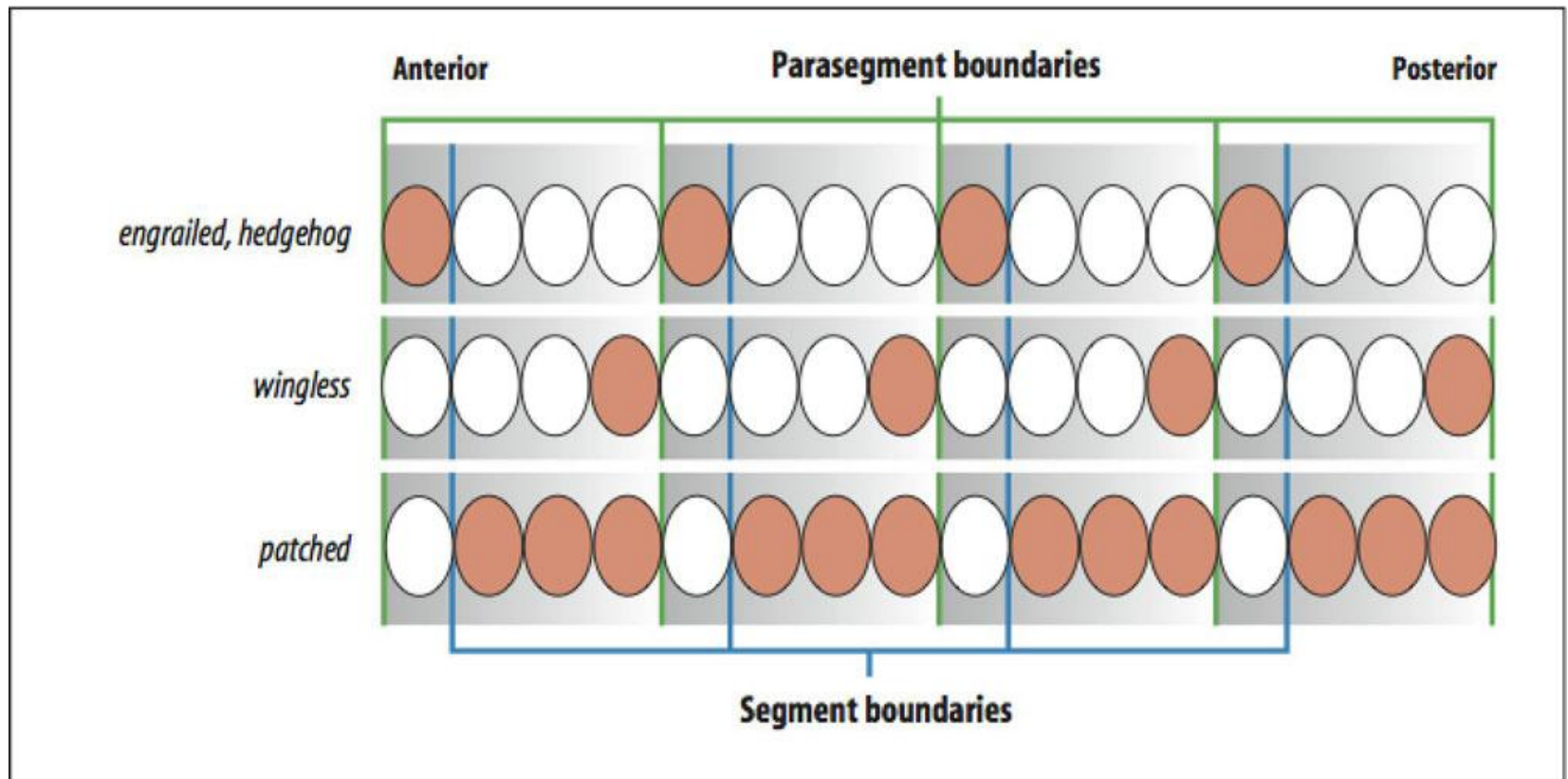


What is the pattern of segment polarity genes?



Wingless (green) and Engrailed (red)

# Segment polarity genes



In Summary, this is a lot of work for one table

**Table 1** Loci affecting segmentation in *Drosophila*

Class	Locus	Map position*	No. of alleles†	Ref.
Segment-polarity	<i>cubitus interruptus</i> <sup>D</sup> ( <i>ct</i> <sup>D</sup> )	4-0	(2)	20
	<i>wingless</i> ( <i>wg</i> )	2-30	6	9
	<i>gooseberry</i> ( <i>gsb</i> )	2-104	1	This work
	<i>hedgehog</i> ( <i>hh</i> )	3-90	2	This work
	<i>fused</i> ( <i>fu</i> )‡	1-59.5	(9)	8, 20
	<i>patch</i> ( <i>pat</i> )	2-55	8	This work
Pair-rule	<i>paired</i> ( <i>prd</i> )	2-45	3	This work
	<i>even-skipped</i> ( <i>eve</i> )	2-55	2	This work
	<i>odd-skipped</i> ( <i>odd</i> )	2-8	2	This work
	<i>barrel</i> ( <i>brr</i> )	3-27	2	This work
	<i>runt</i> ( <i>run</i> )	1-65	1	This work
	<i>engrailed</i> ( <i>en</i> )	2-62	6	11, 20
Gap	<i>Krüppel</i> ( <i>Kr</i> )	2-107.6	6	12, 20
	<i>knirps</i> ( <i>kni</i> )	3-47	5	This work
	<i>hunchback</i> ( <i>hb</i> )	3-48	1	This work

# Drosophila embryogenesis

