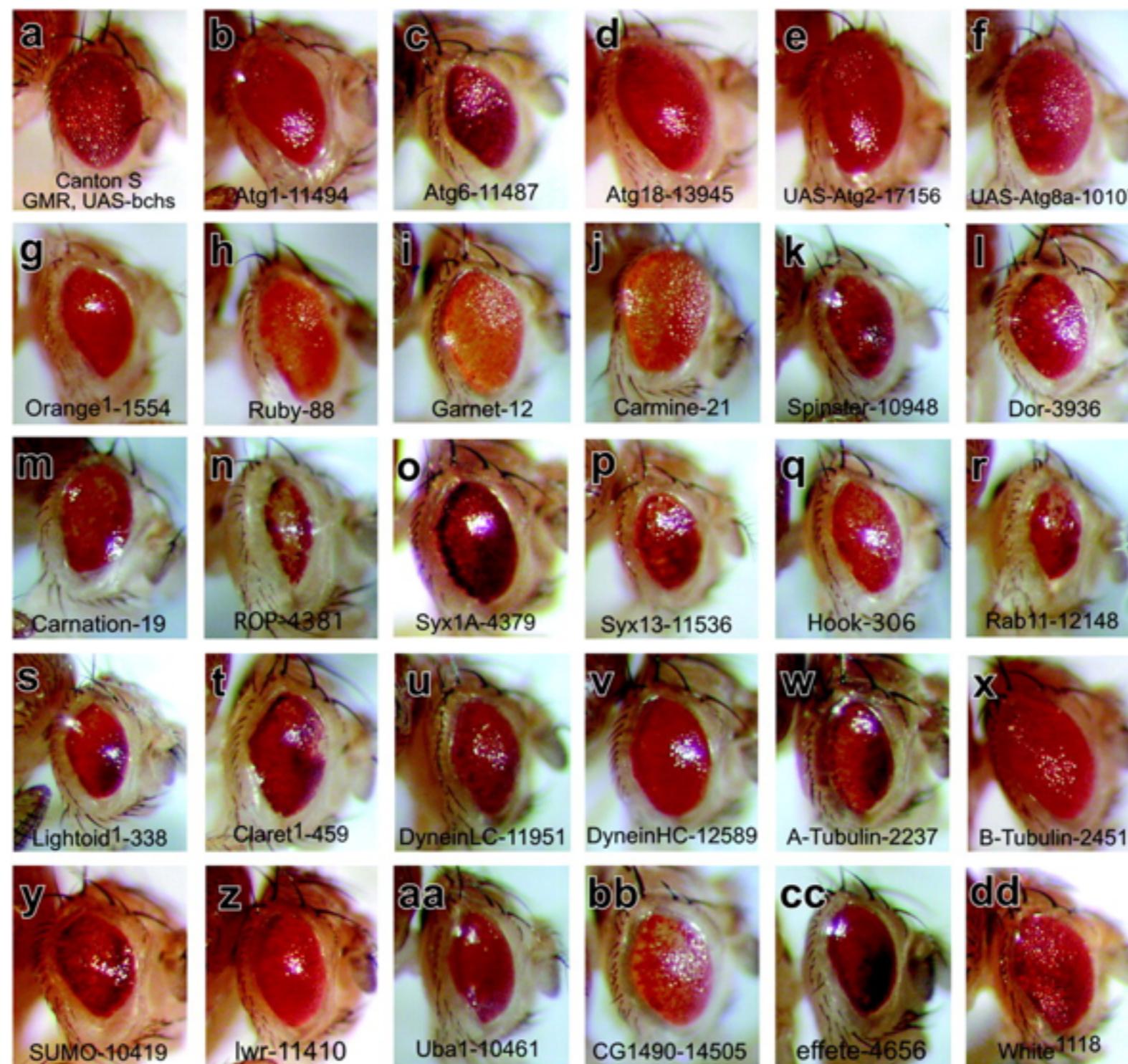
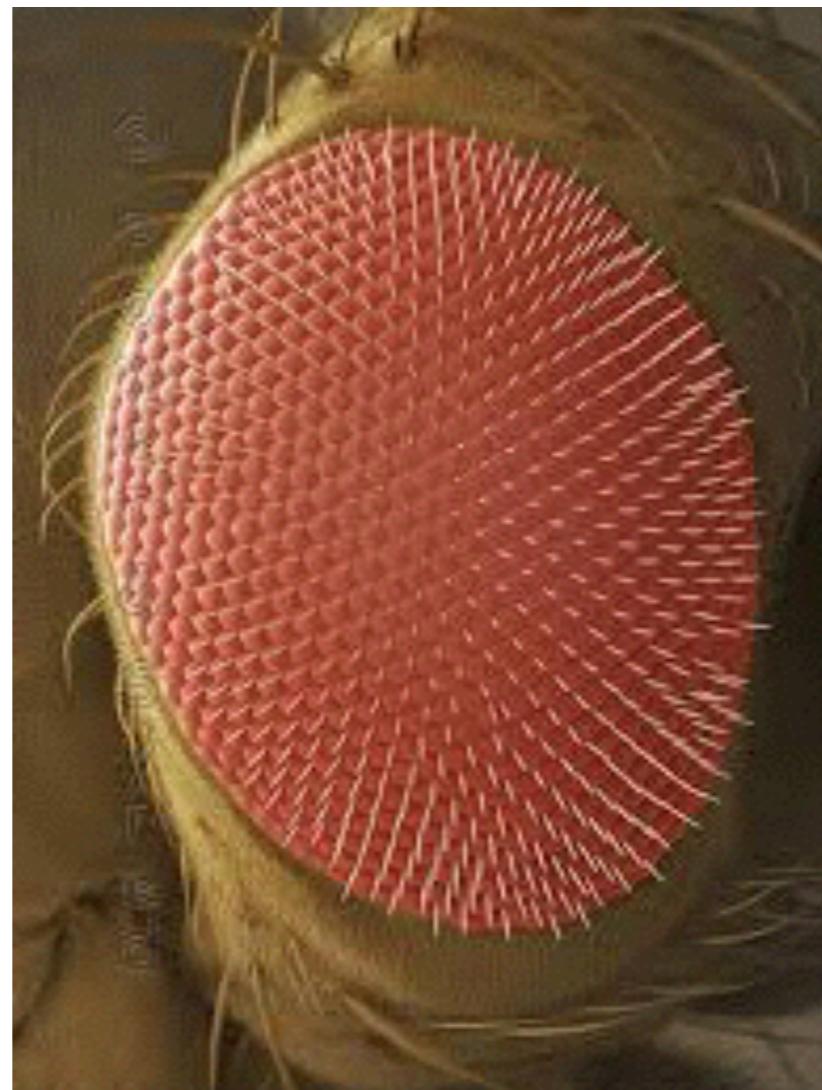


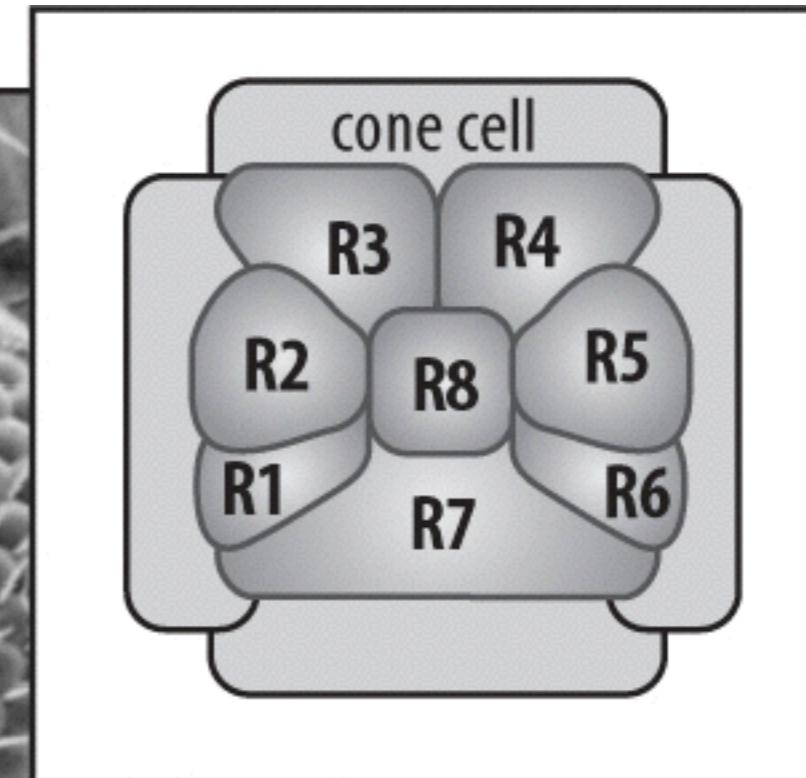
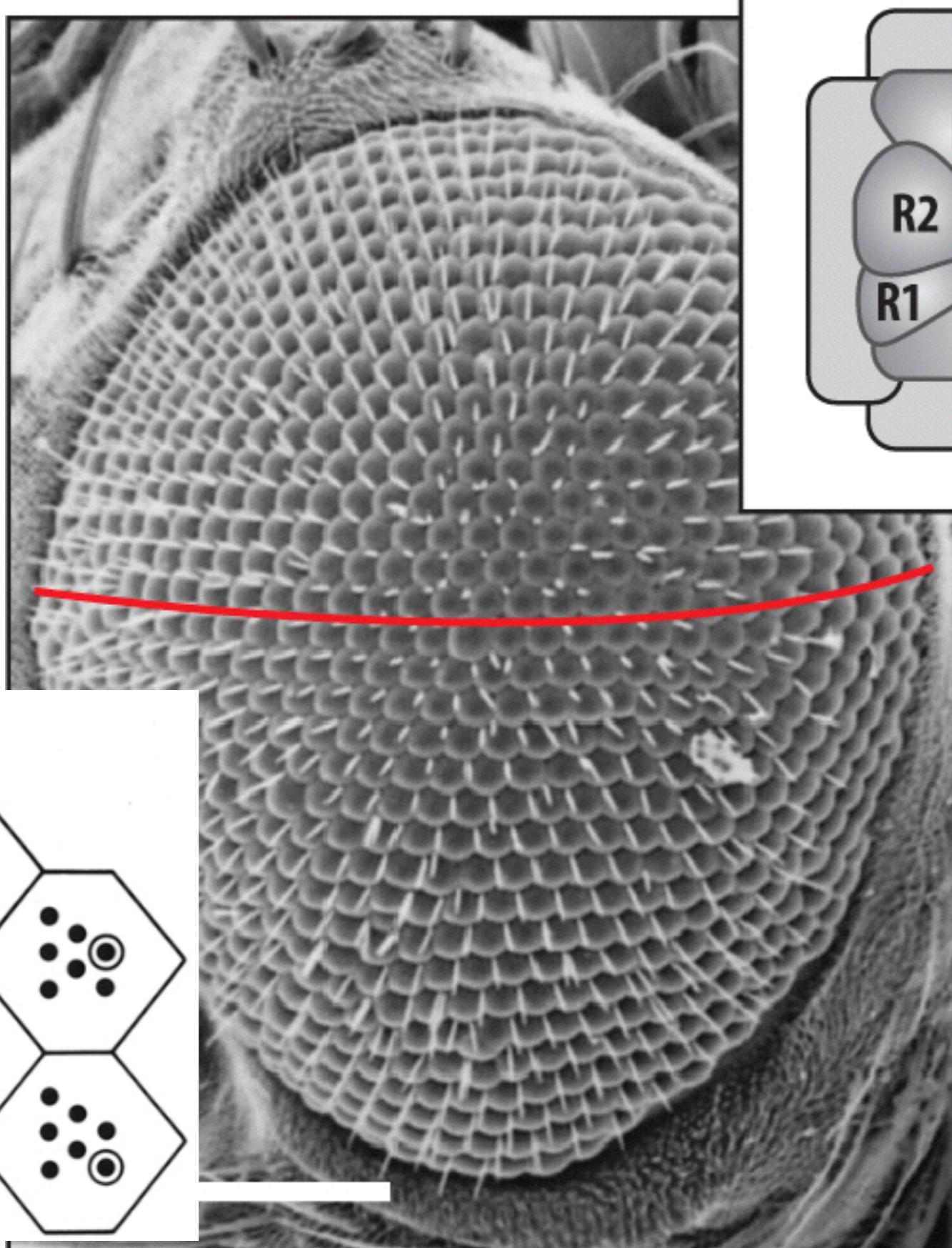
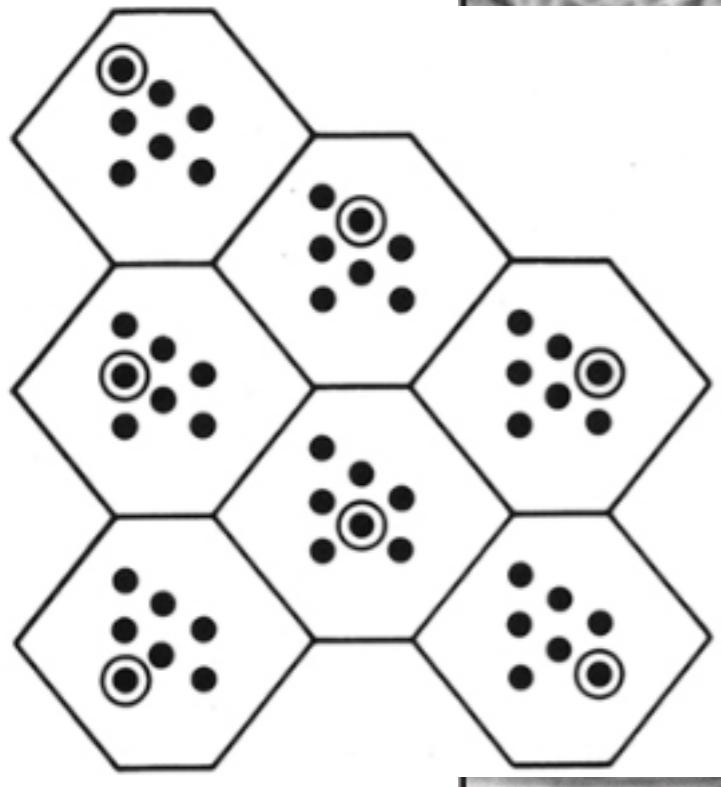
# Bio393: Genetic Analysis

## Developmental genetics II





The *Drosophila* eye



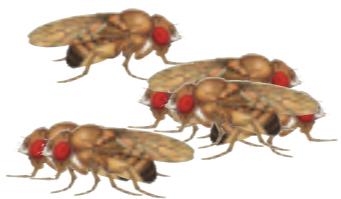


# Seymour Benzer

# A simple behavioral selection



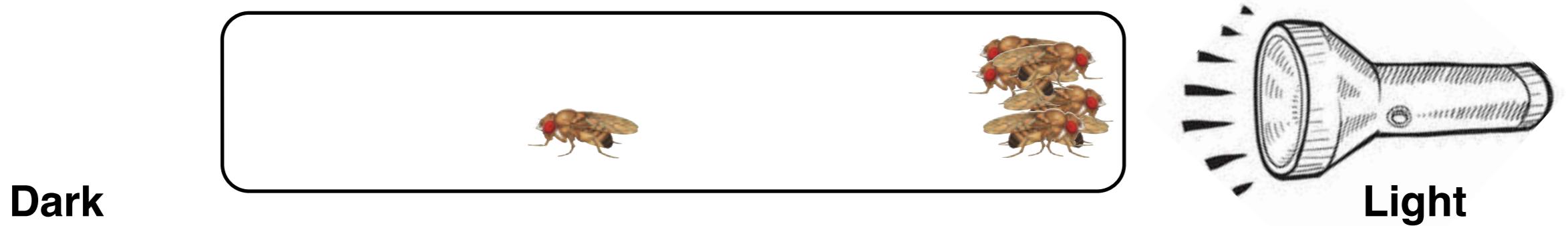
# A simple behavioral selection



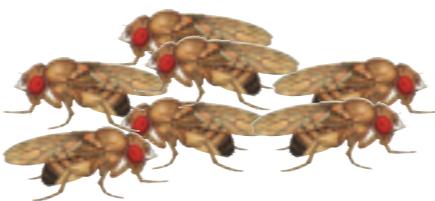
# A simple behavioral selection



# A simple behavioral selection



# A simple behavioral selection



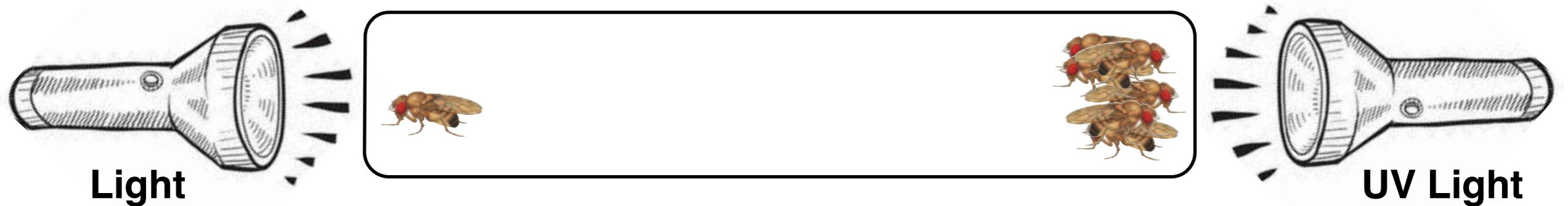
# A simple behavioral selection



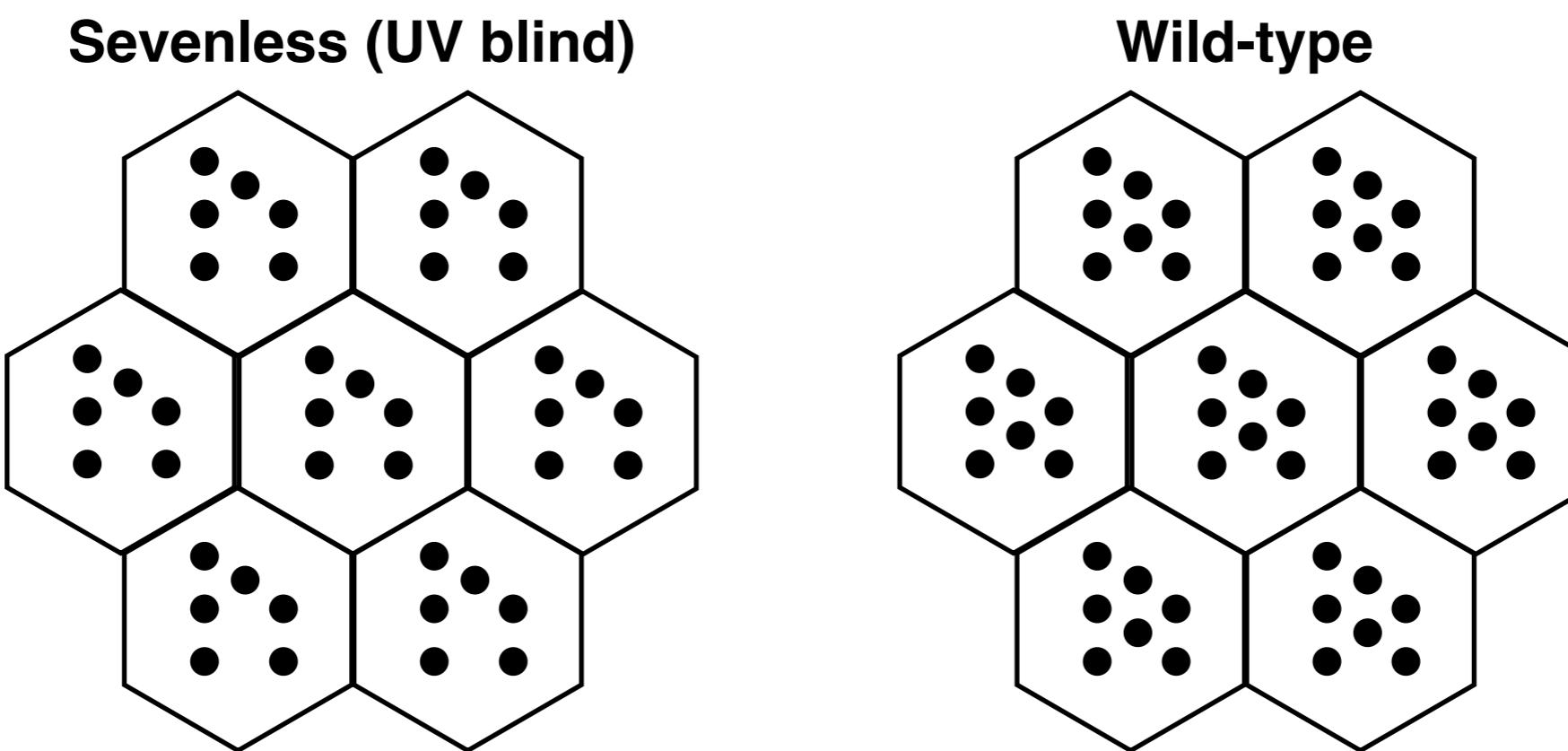
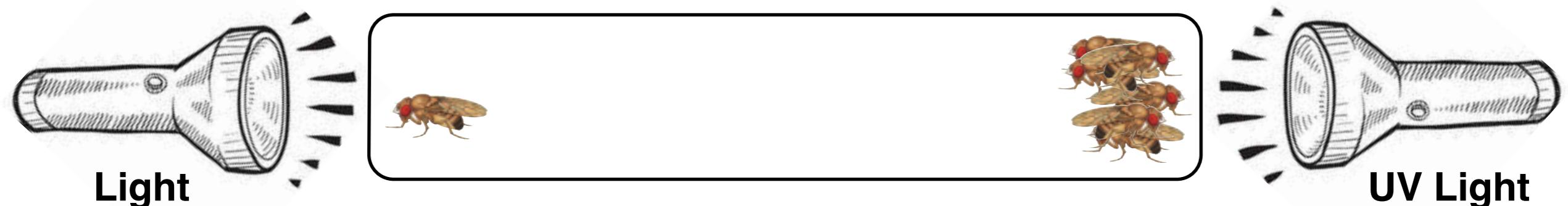
# A simple behavioral selection



# A simple behavioral selection



# A simple behavioral selection

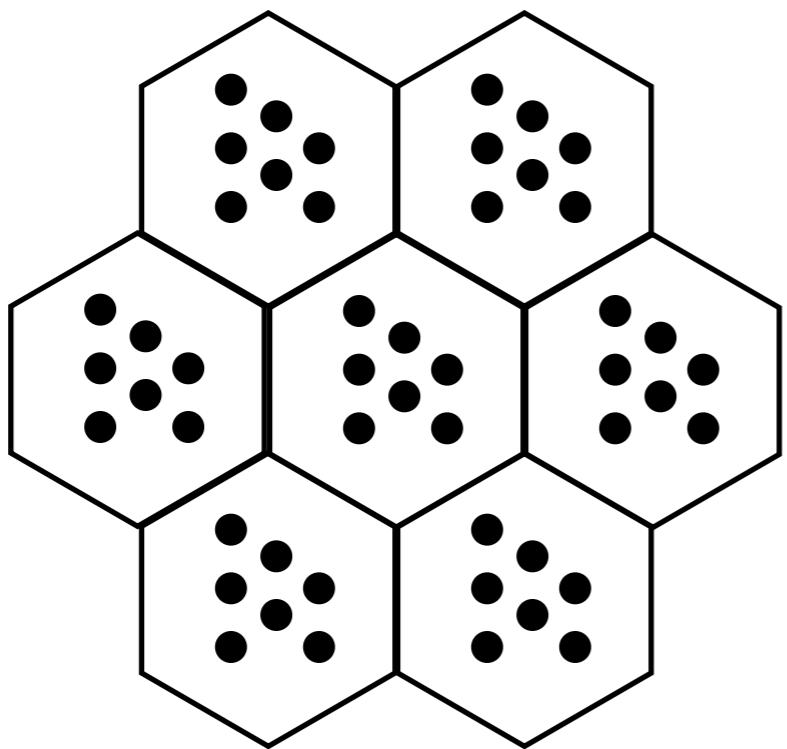




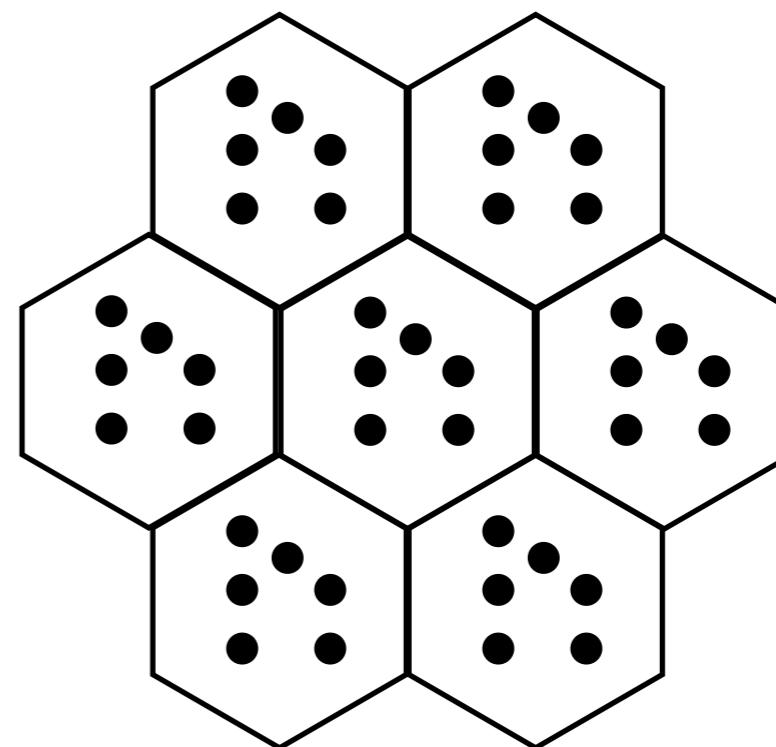
**Gerry Rubin**

# Other UV blind mutants

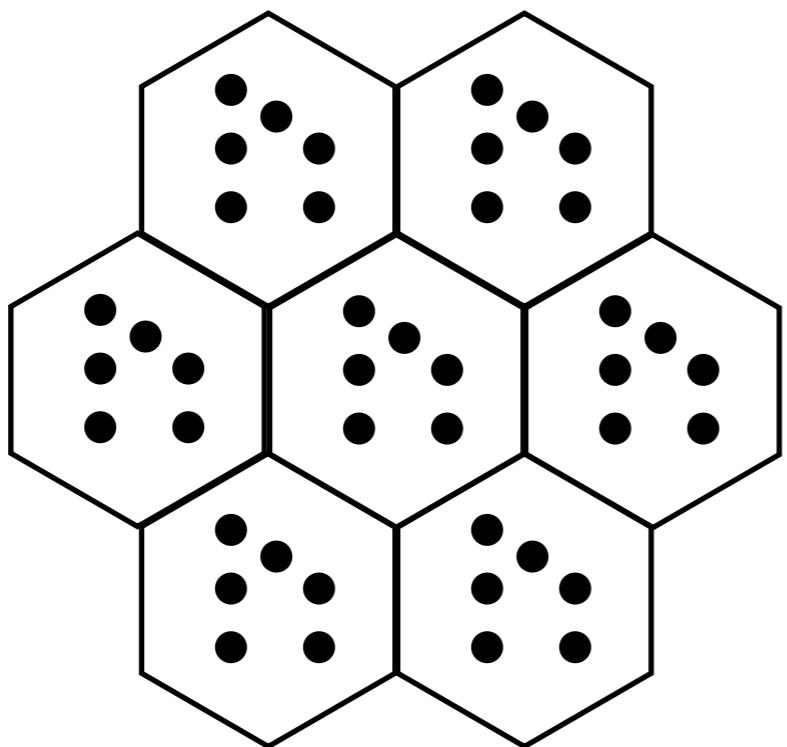
**Wild-type**



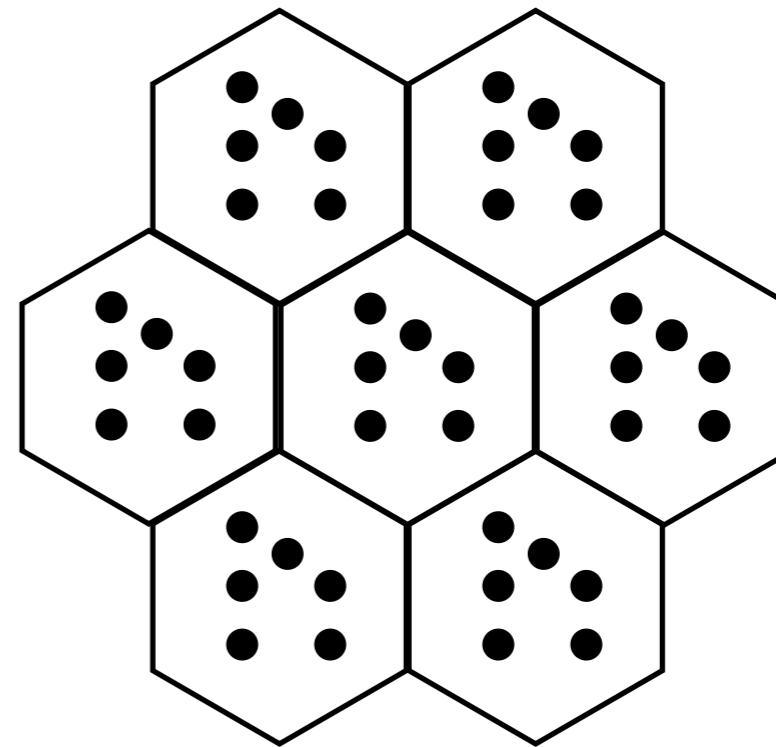
**Sevenless (UV blind)**



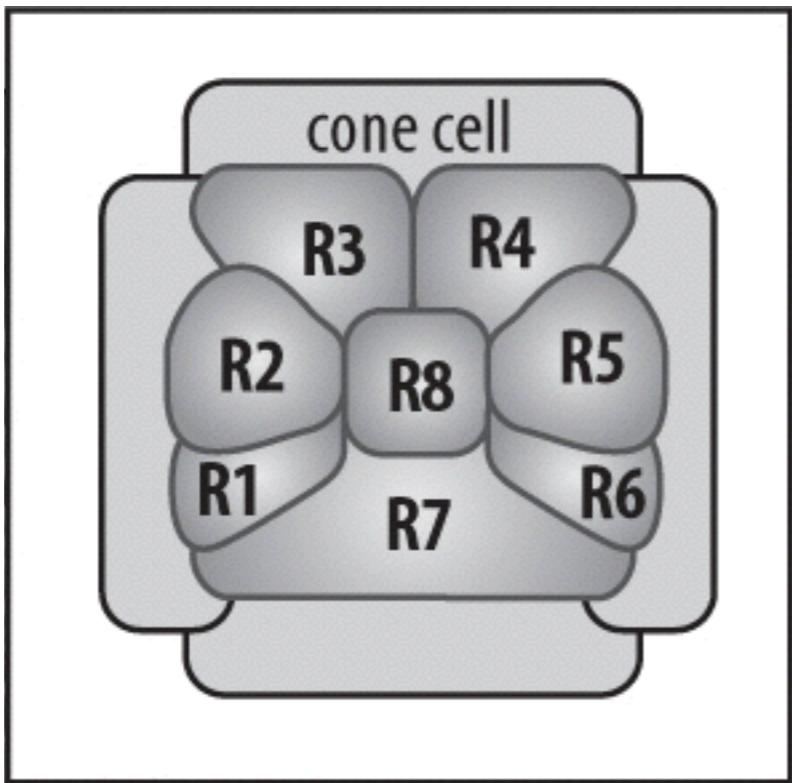
**Bride of sevenless (UV blind)**



**Seven-in-absentia (UV blind)**



# Development of an ommatidium

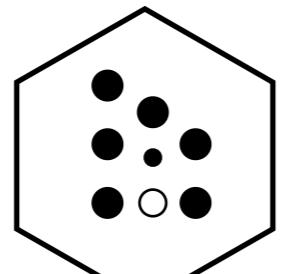


R8 born first

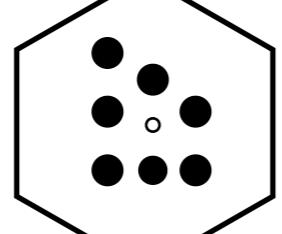
R1-R6 born after

R7 last to be born

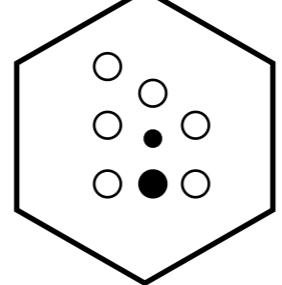
# ***boss* and *sev* are required in different R cells for R7 fate**



R7 cell mutant

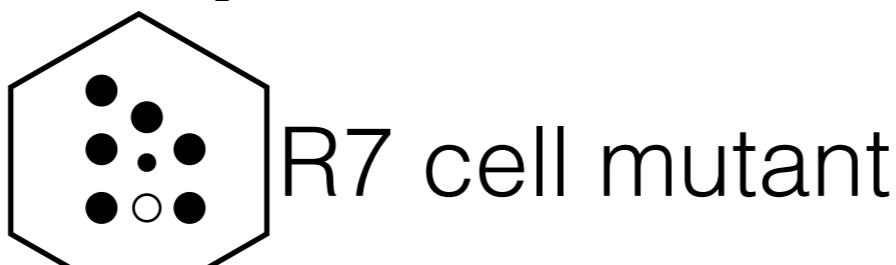


R8 cell mutant

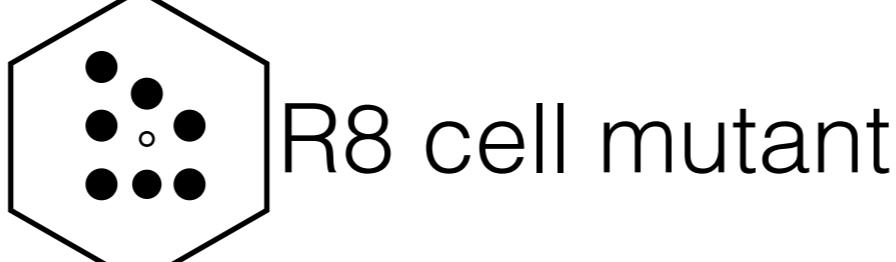


R1-R6 cells mutant

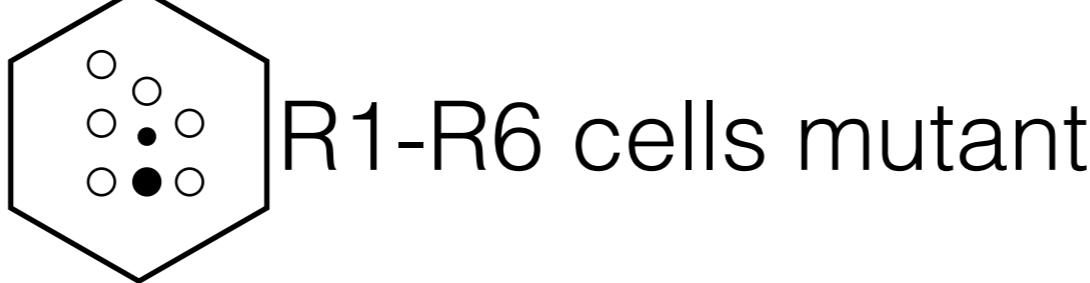
# ***boss* and *sev* are required in different R cells for R7 fate**



R7 cell mutant

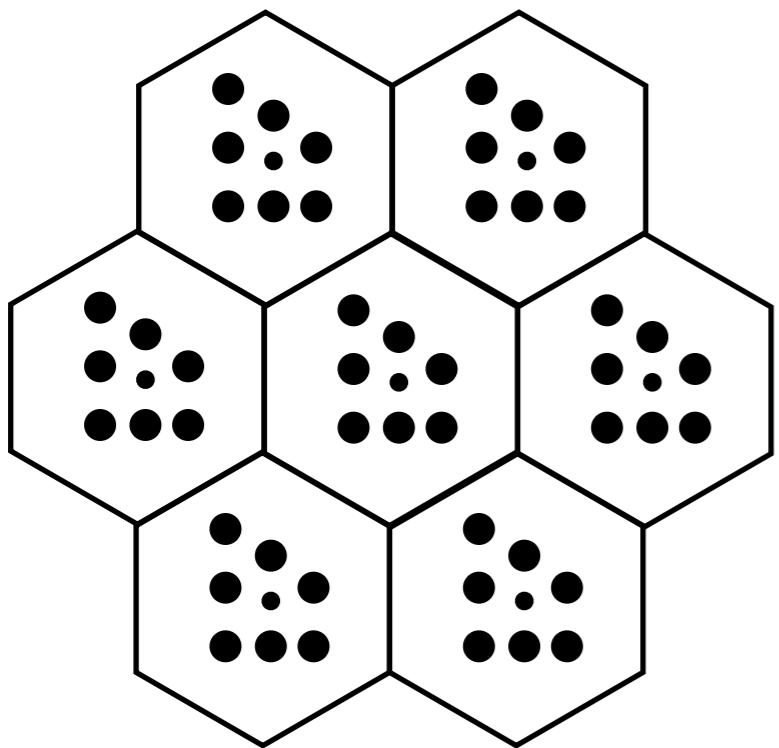


R8 cell mutant

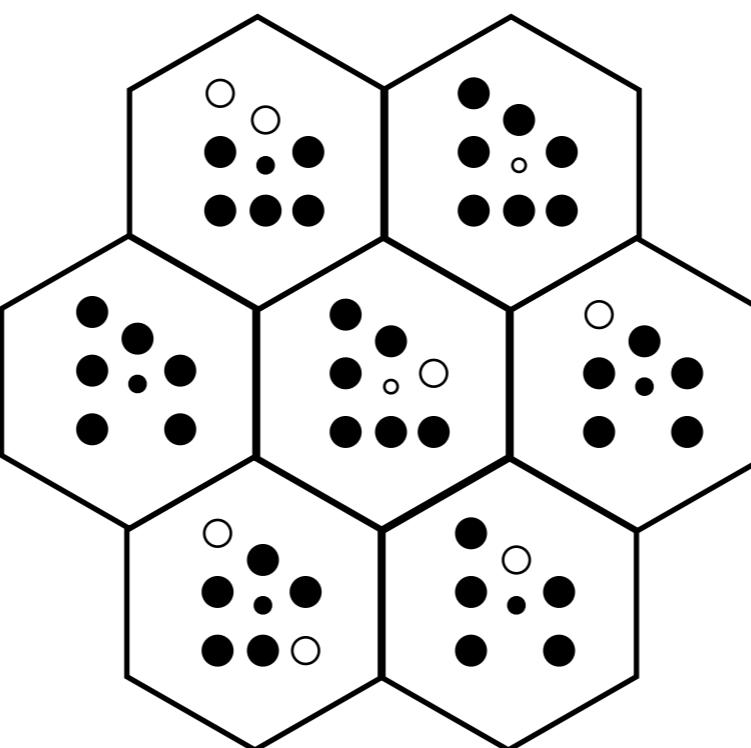


R1-R6 cells mutant

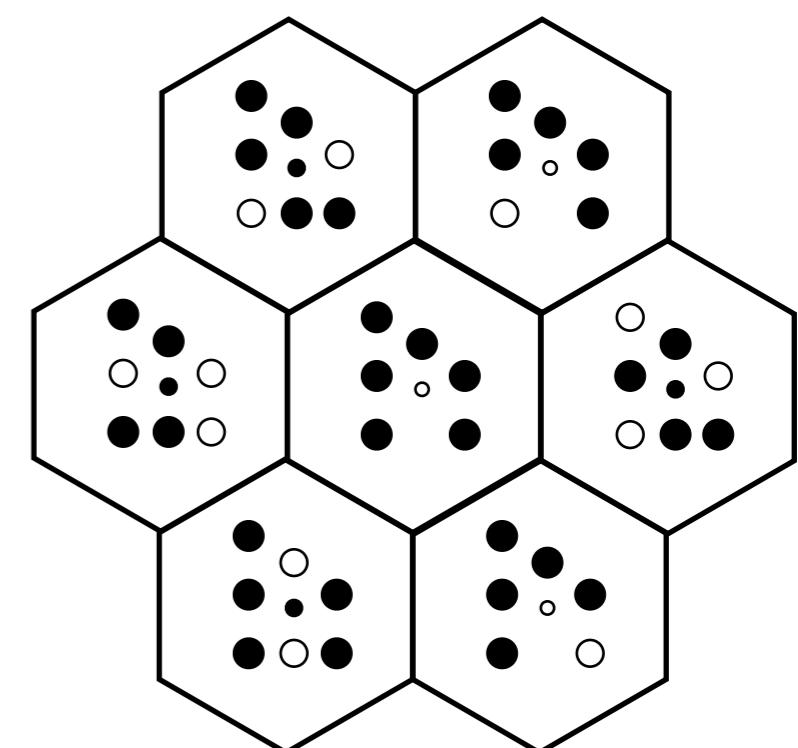
Wild-type



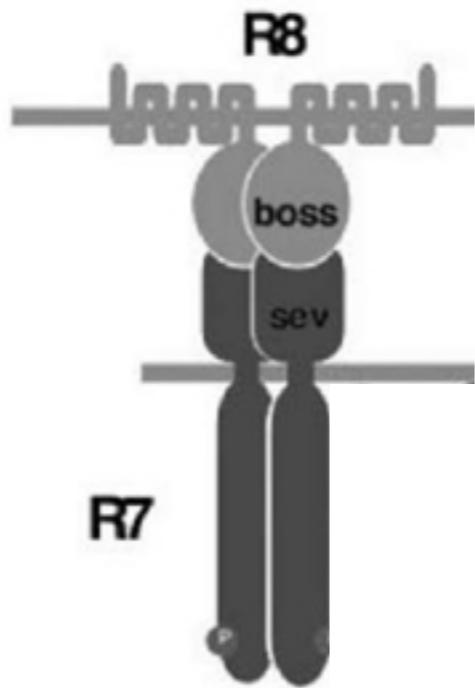
*sev* mutant



*boss* mutant

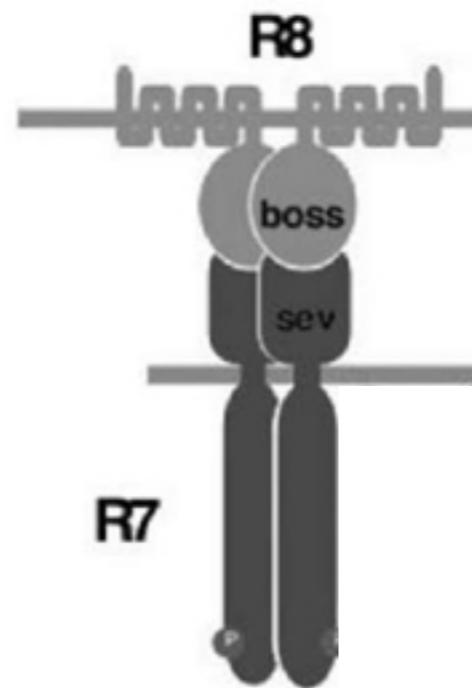
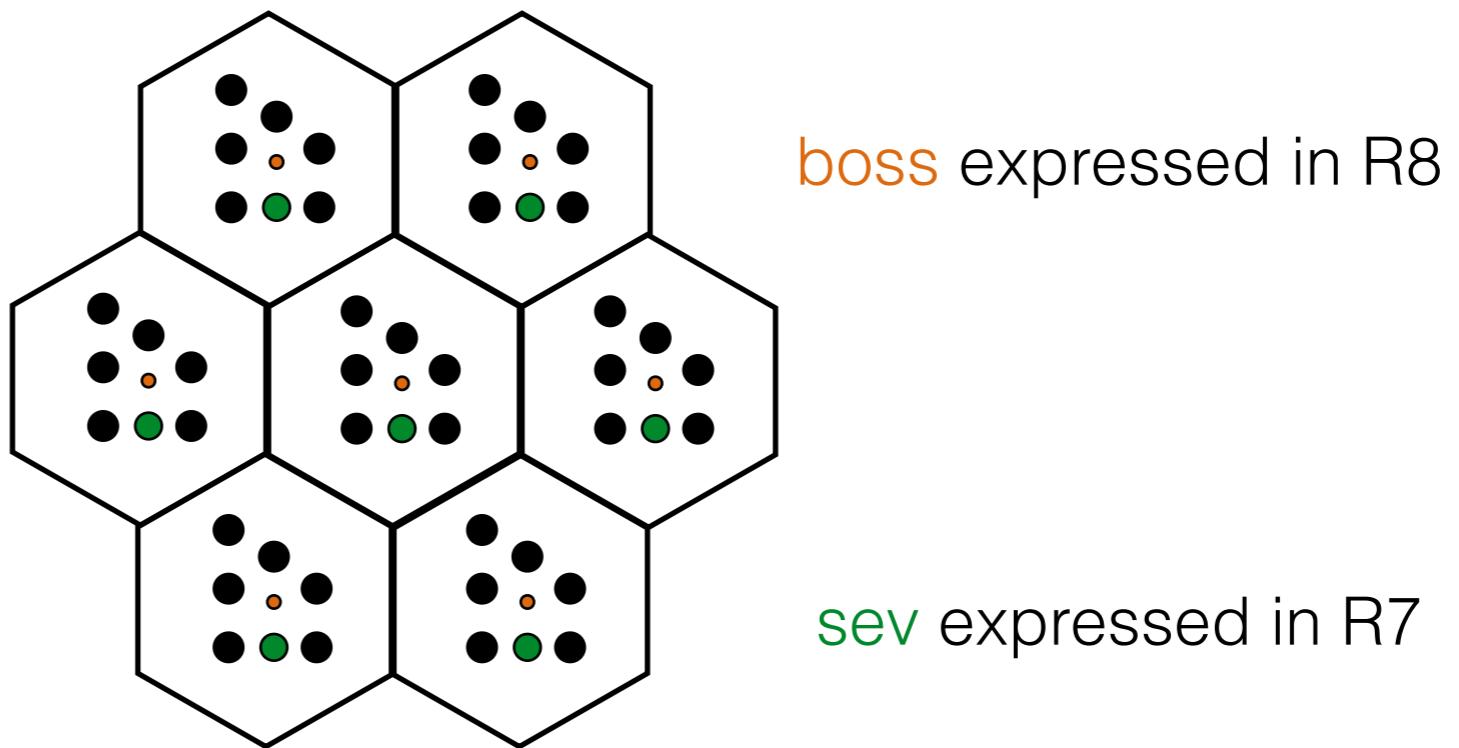


*boss* encodes  
a membrane-bound protein

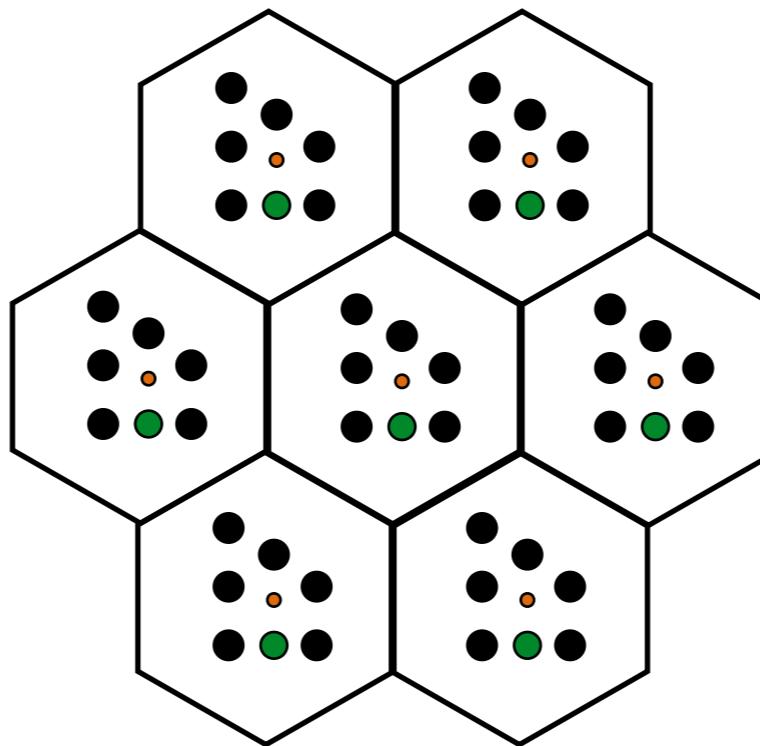


*sev* encodes  
a membrane receptor tyrosine kinase

# Expression of *sev* and *boss*

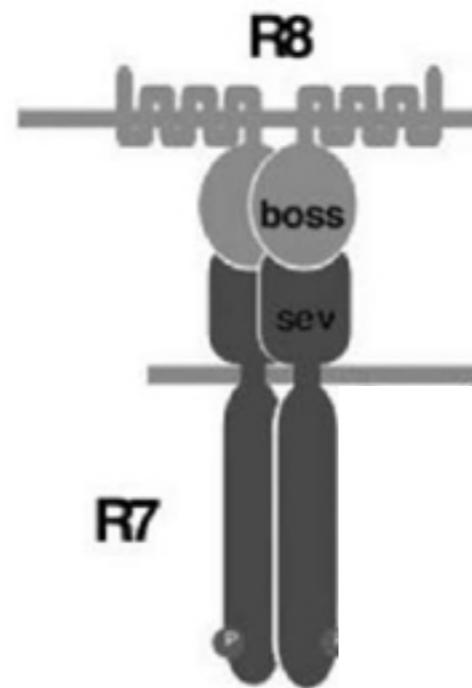


# Expression of *sev* and *boss*



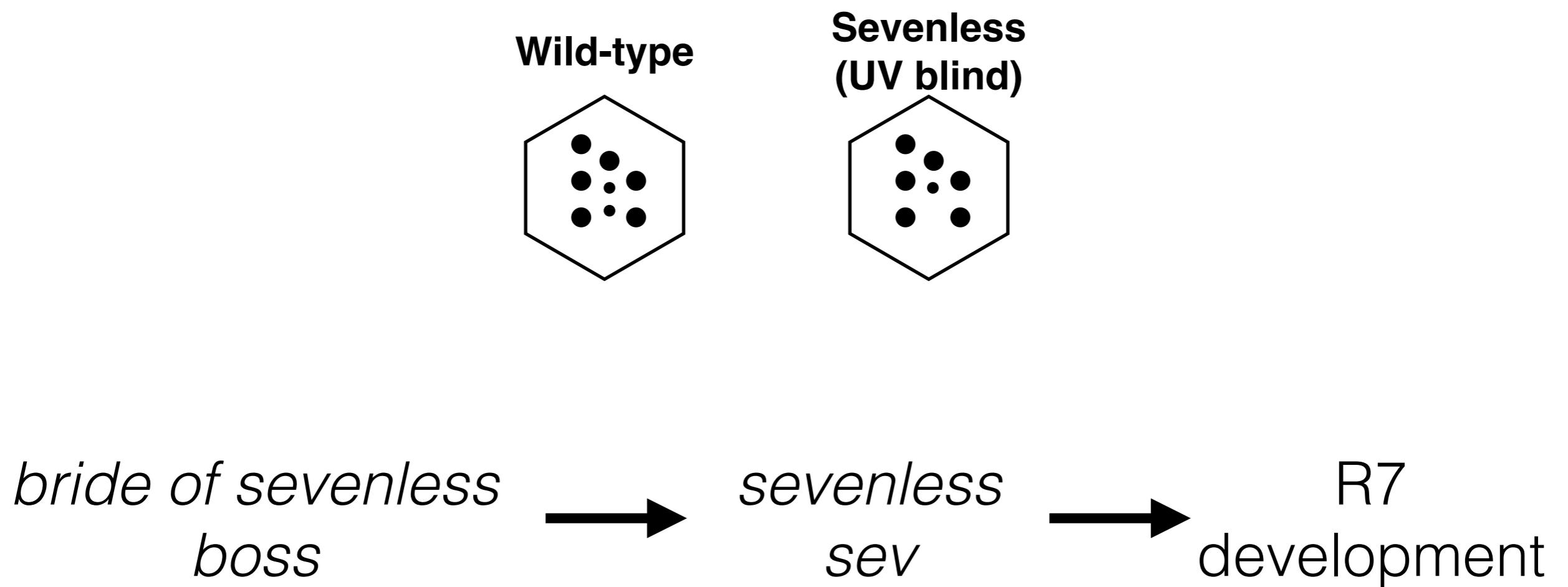
boss expressed in R8

sev expressed in R7



boss internalized into R7

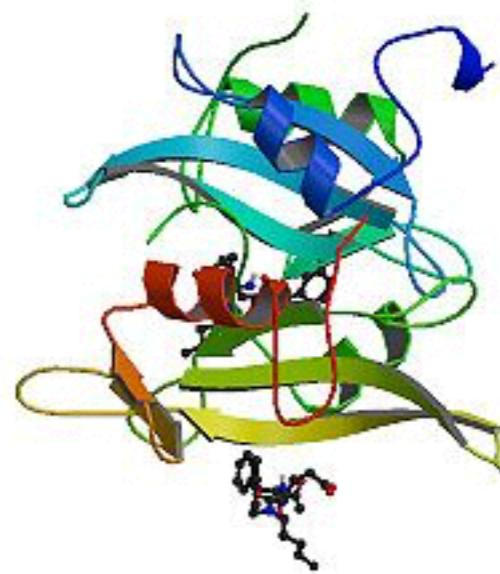
# UV blind mutants led to elements of signaling pathway



# Virus gene mutant from chicken to *Drosophila*



Peyton Rous discovered the first oncogenic virus in chicken



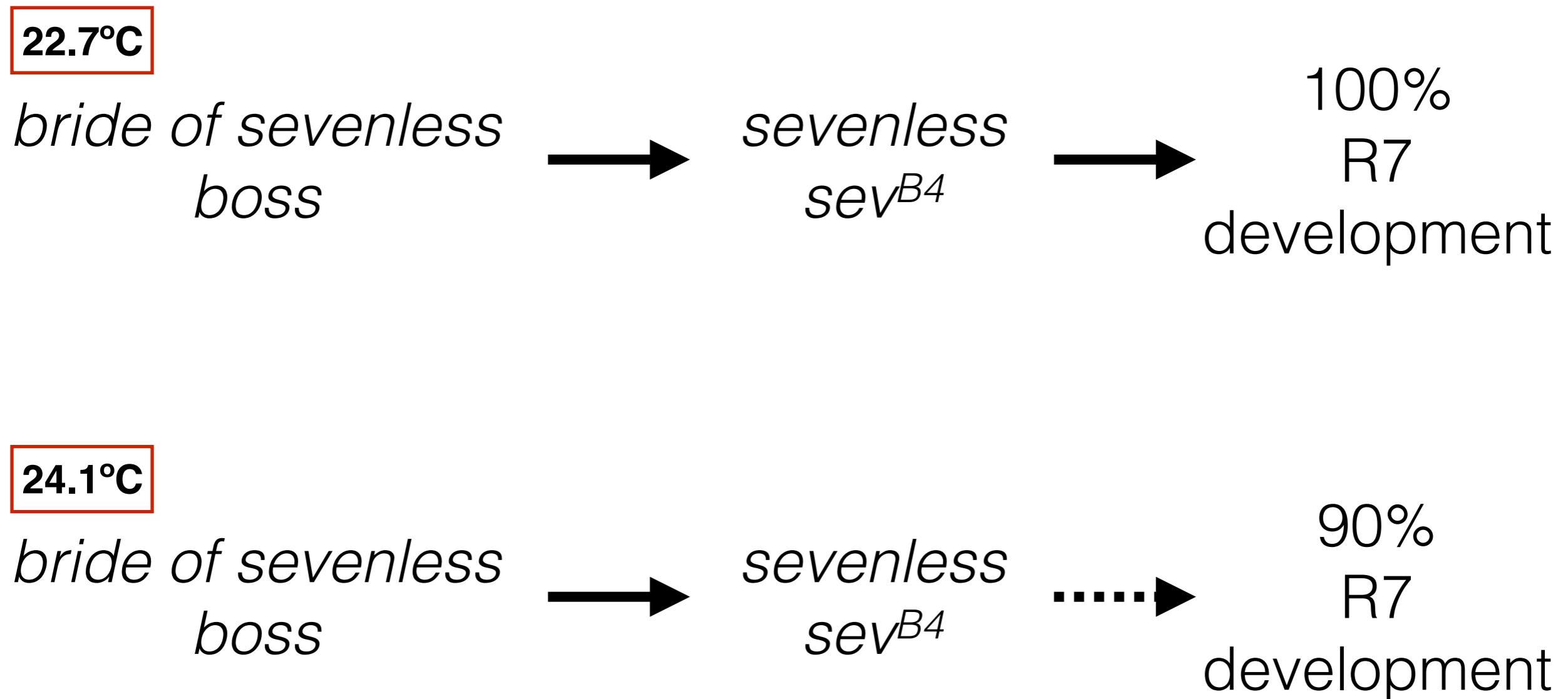
The virus expressed v-src (a tyrosine kinase) to control cell cycle

Mutagenesis of v-src led to temperature-sensitive alleles

# A sensitized enhancer screen for the *sevenless* pathway



# A sensitized enhancer screen for the *sevenless* pathway



# Strains used for the sensitized screen

$sev^{d2}; TM3\ ry / CxD$

$sev^{d2}$  = complete loss of  $sev$

$TM3$  = third chromosome balancer

$ry$  = allele conferring recessive rosy eye phenotype

$CxD$  = third chromosome balancer

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$P[ry^+ sev^{B4}]$

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$ry$  = allele conferring recessive rosy eye phenotype

$CxD$  = third chromosome balancer

$P[ry^+ sev^{B4}]$

$sev^{B4}$  = temperature-sensitive  $sev$  hypomorph

# Screen for dominant enhancers of sensitized phenotype

$sev^{d2}; TM3\ Sb\ ry\ P[ry^+ sev^{B4}]/\text{CxD}$

# Screen for dominant enhancers of sensitized phenotype

$sev^{d2}; \text{TM3 } Sb \ ry \ P[ry^+ sev^{B4}]/\text{CxD}$

**22.7°C**

*bride of sevenless  
boss*



*sevenless  
sev<sup>B4</sup>*



100%  
R7  
development

**24.1°C**

*bride of sevenless  
boss*



*sevenless  
sev<sup>B4</sup>*



10%  
R7  
development

# Screen for dominant enhancers of sensitized phenotype

$sev^{d2}; \text{TM3 } Sb \ ry \ P[ry^+ sev^{B4}]/\text{CxD}$

**22.7°C**

*bride of sevenless  
boss*



*sevenless  
sev<sup>B4</sup>*



100%  
R7  
development

**24.1°C**

*bride of sevenless  
boss*



*sevenless  
sev<sup>B4</sup>*



10%  
R7  
development

**22.7°C**

*bride of sevenless  
boss*



*sevenless  
sev<sup>B4</sup>*

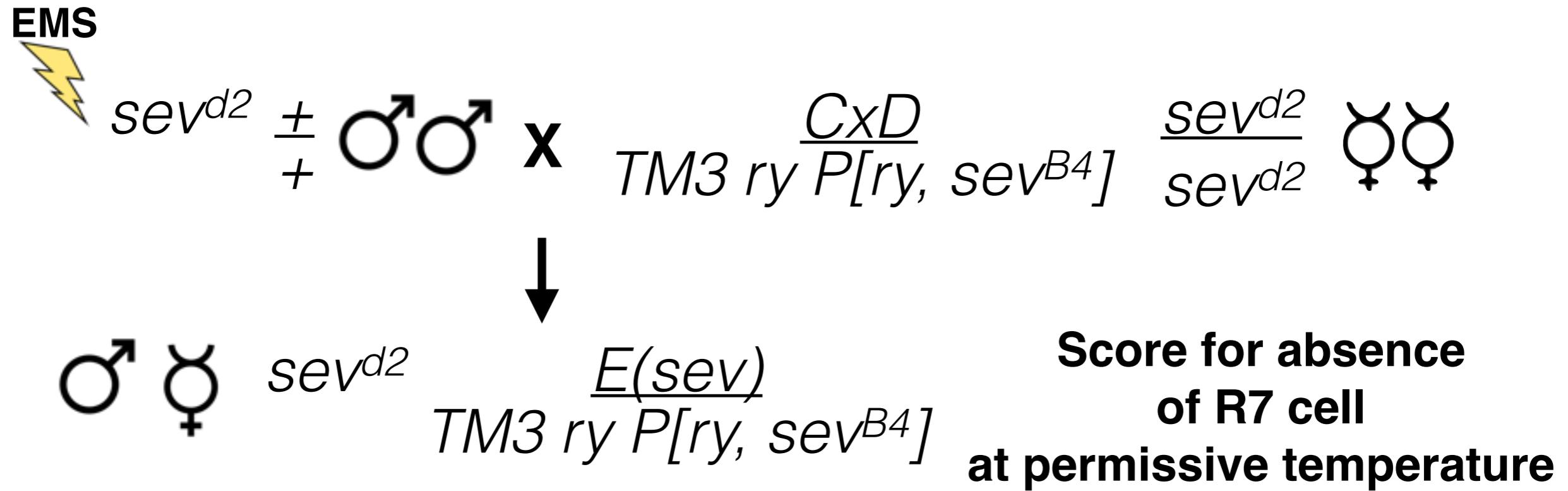


$E(sev)$



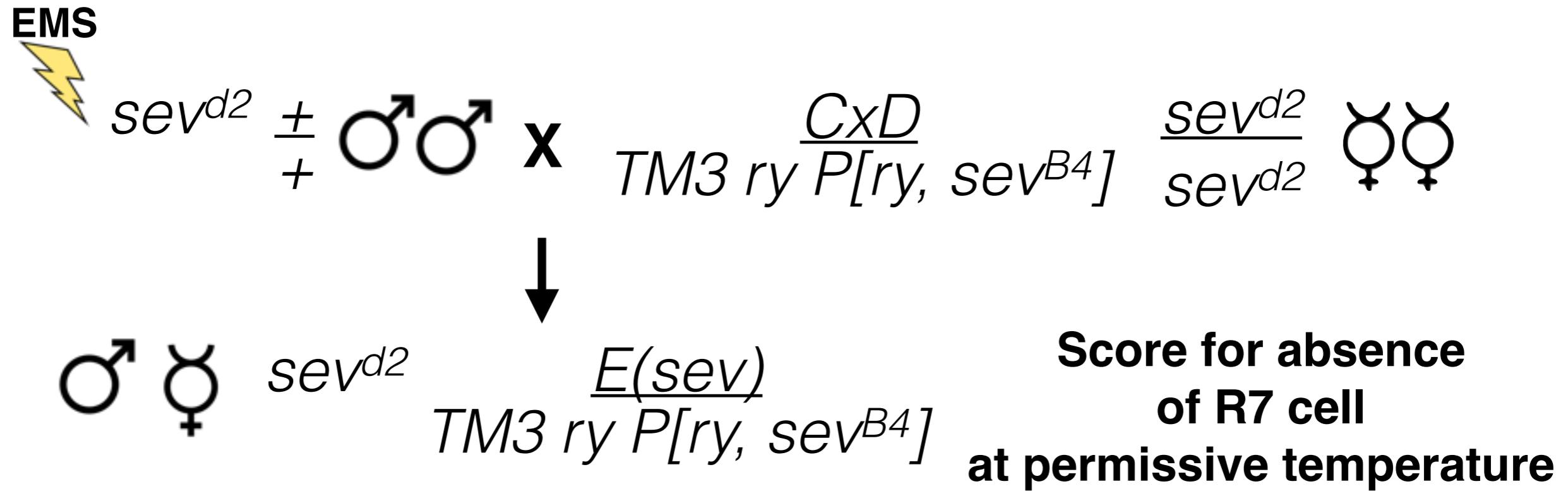
~10%  
R7  
development

# Screen for dominant enhancers of sensitized mutant R7 phenotype



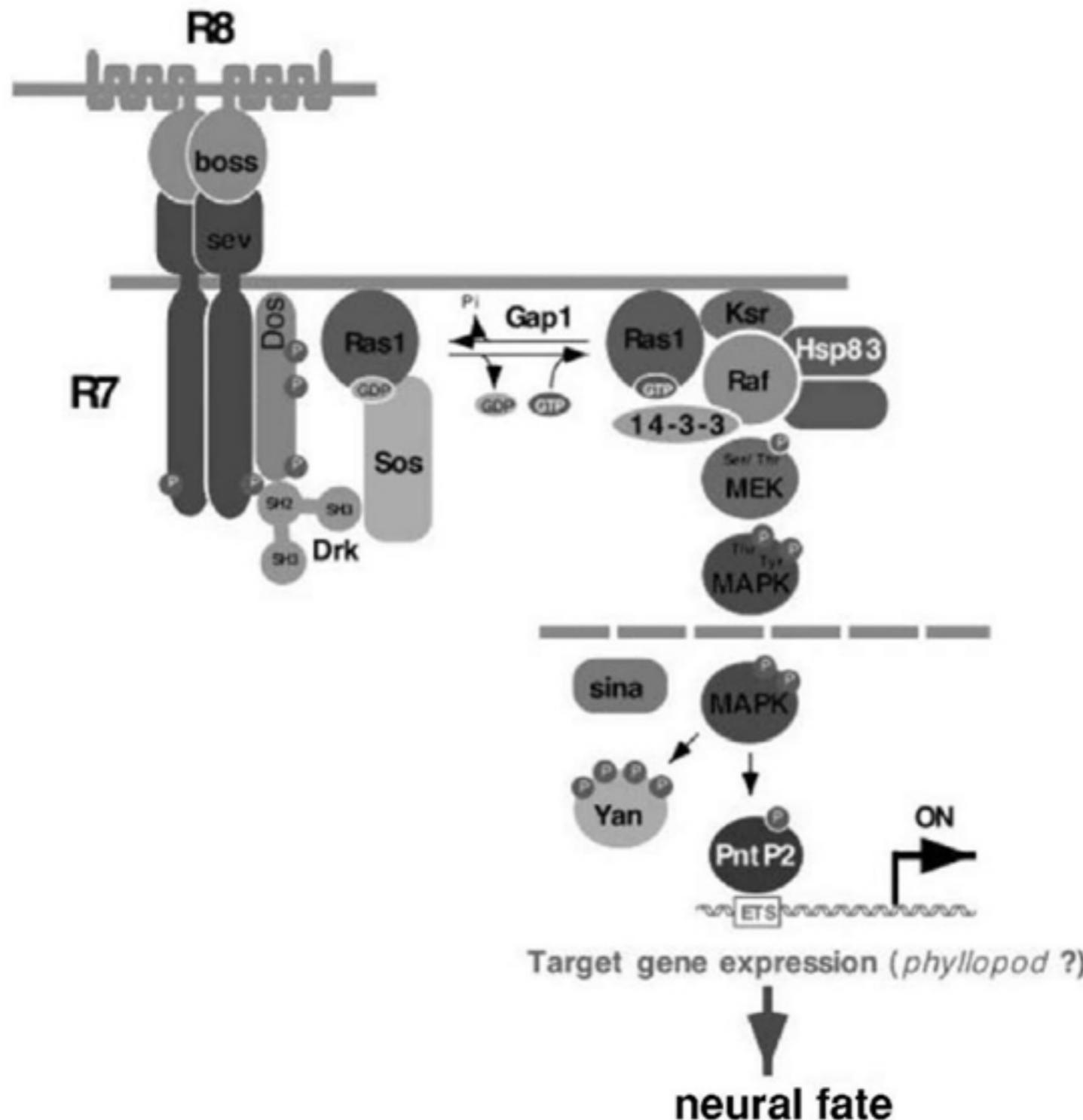
Assumptions: (1) Mutations in downstream genes required for viability and R7 fate  
(2) Most genes are not haploinsufficient

# Screen for dominant enhancers of sensitized mutant R7 phenotype

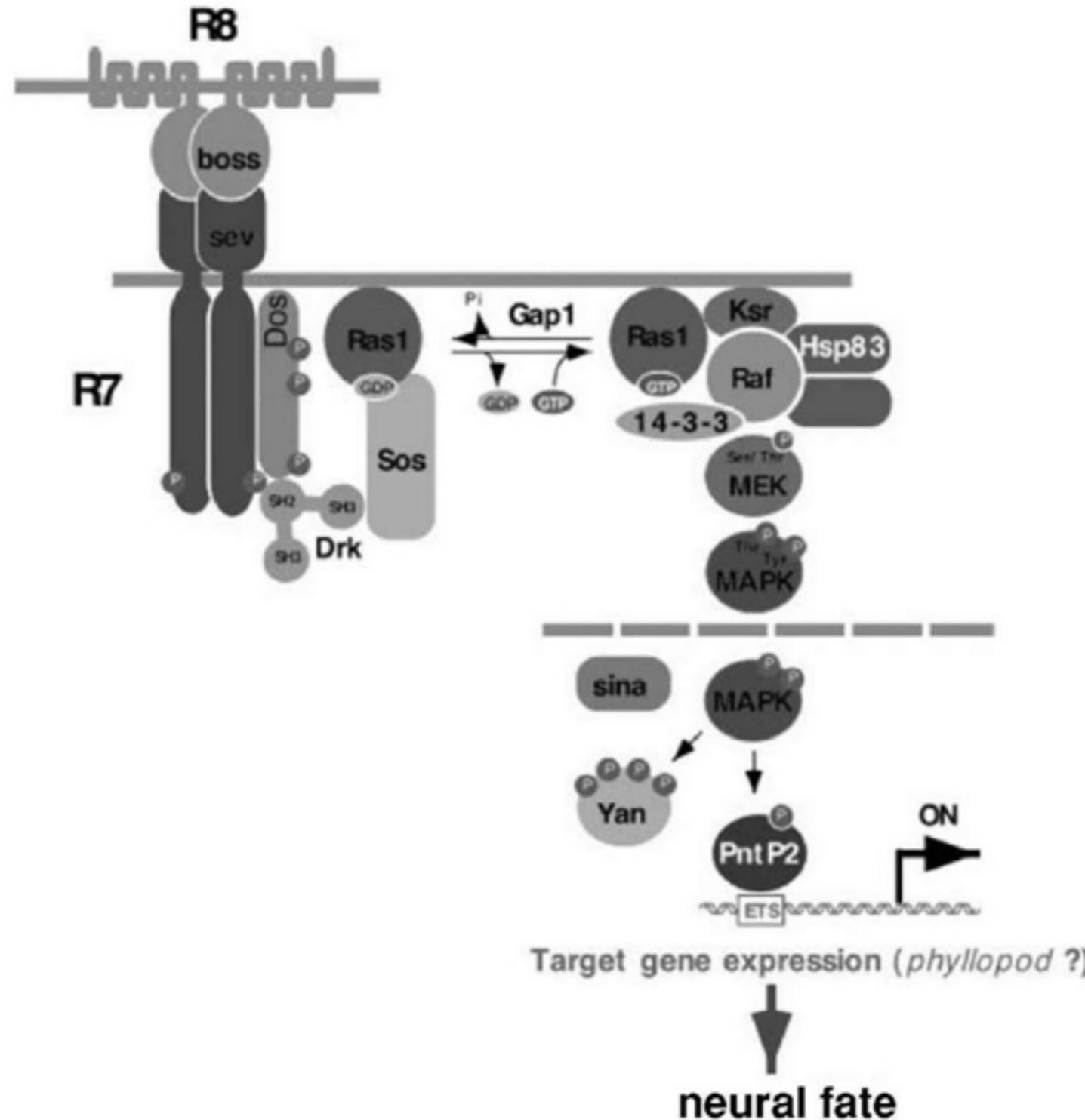


Screened 30,000 flies using pseudopupil technique  
Got 20  $E(sev)$  in seven complementation groups

# R7 fate is determined through a Ras pathway

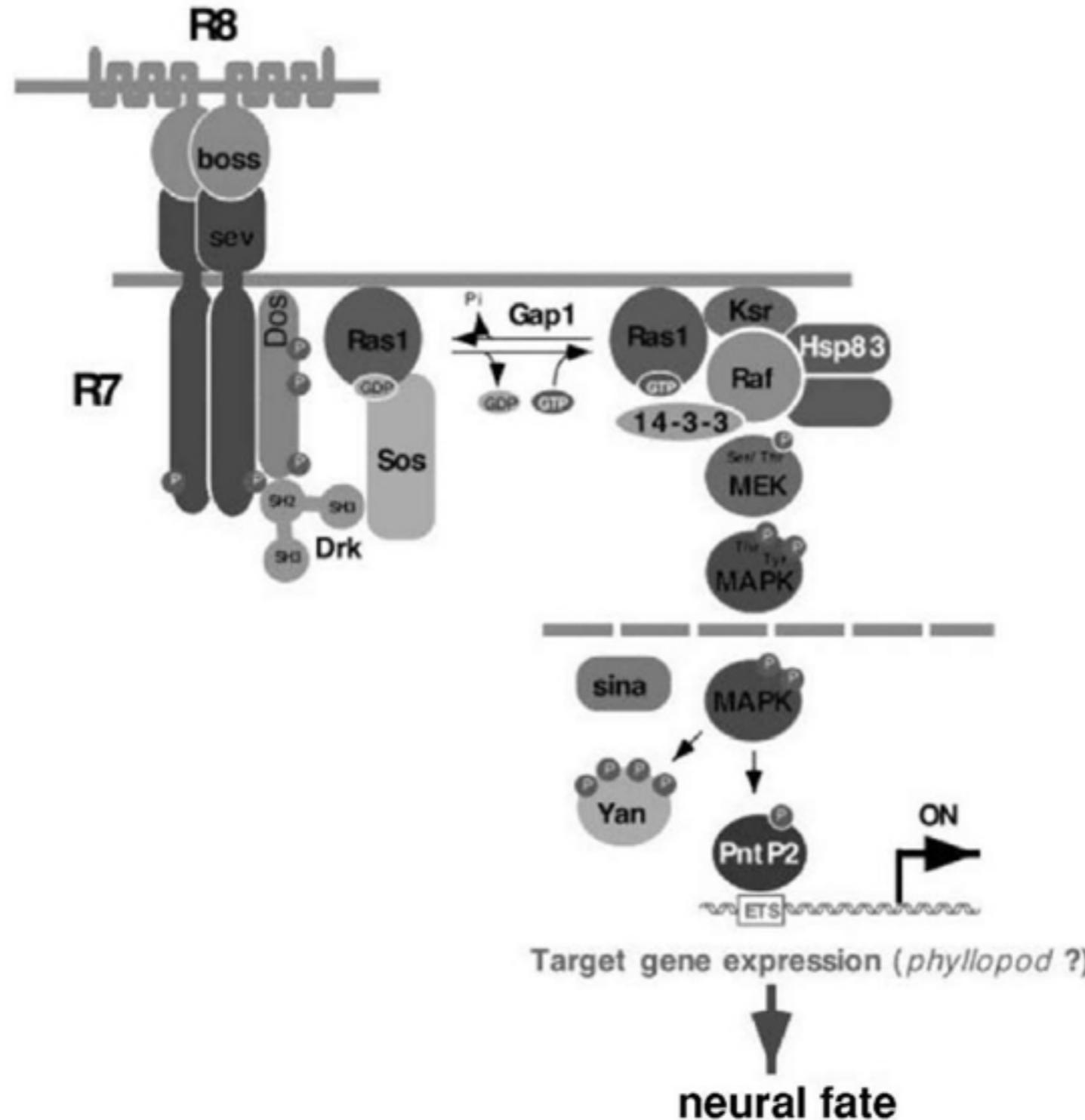


# R7 fate is determined through a Ras pathway



What cells require *E(sev)* for function?

# R7 fate is determined through a Ras pathway



What cells require *E(sev)* for function?

**Mitotic recombination**

# **Are genes required in ommatidia for cell viability?**

We want to make flies that lack the *E(sev)* gene in certain cells

# Are genes required in ommatidia for cell viability?

We want to make flies that lack the *E(sev)* gene in certain cells

1.   $\underline{E(sev)}^- ; \underline{w}$   
+  $w$

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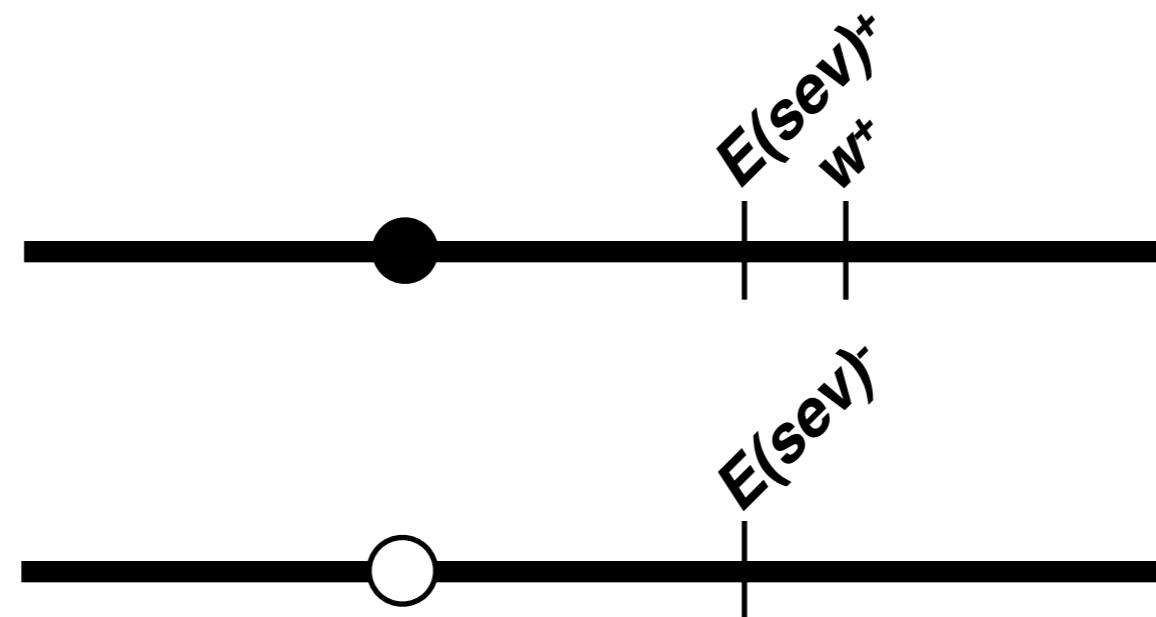
1.   $\underline{E(sev)}^- ; \underline{w}$   
+  $w$
2. Use a P element with  $w^+$  distal to the wild-type *E(sev)* gene

# Are genes required in ommatidia for cell viability?

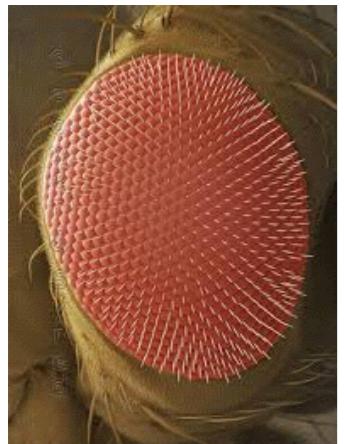
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+  
 $w$

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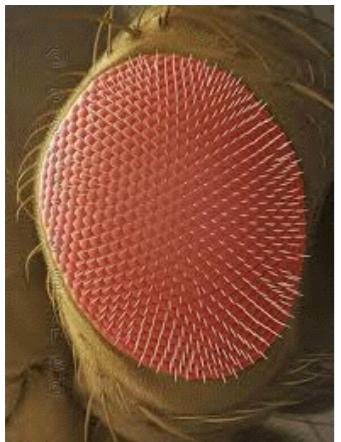


# Are genes required in ommatidia for cell viability?

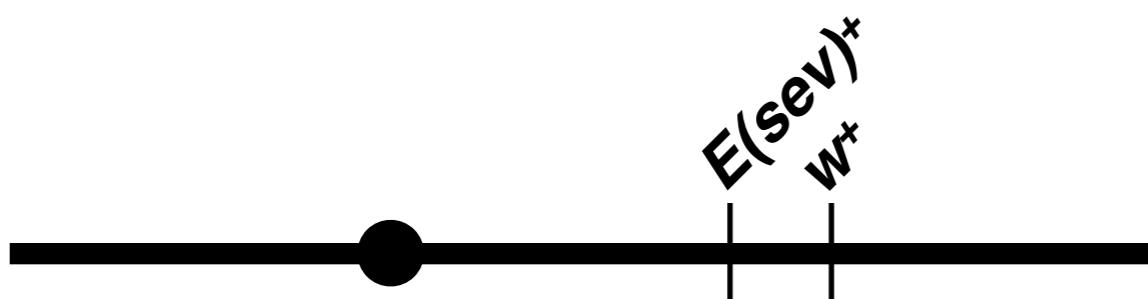


During mitosis for the cells that make up the eye, recombination can occur to repair double-strand breaks.

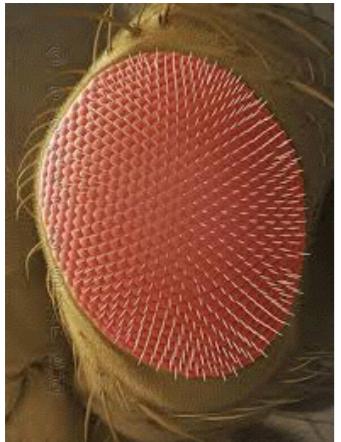
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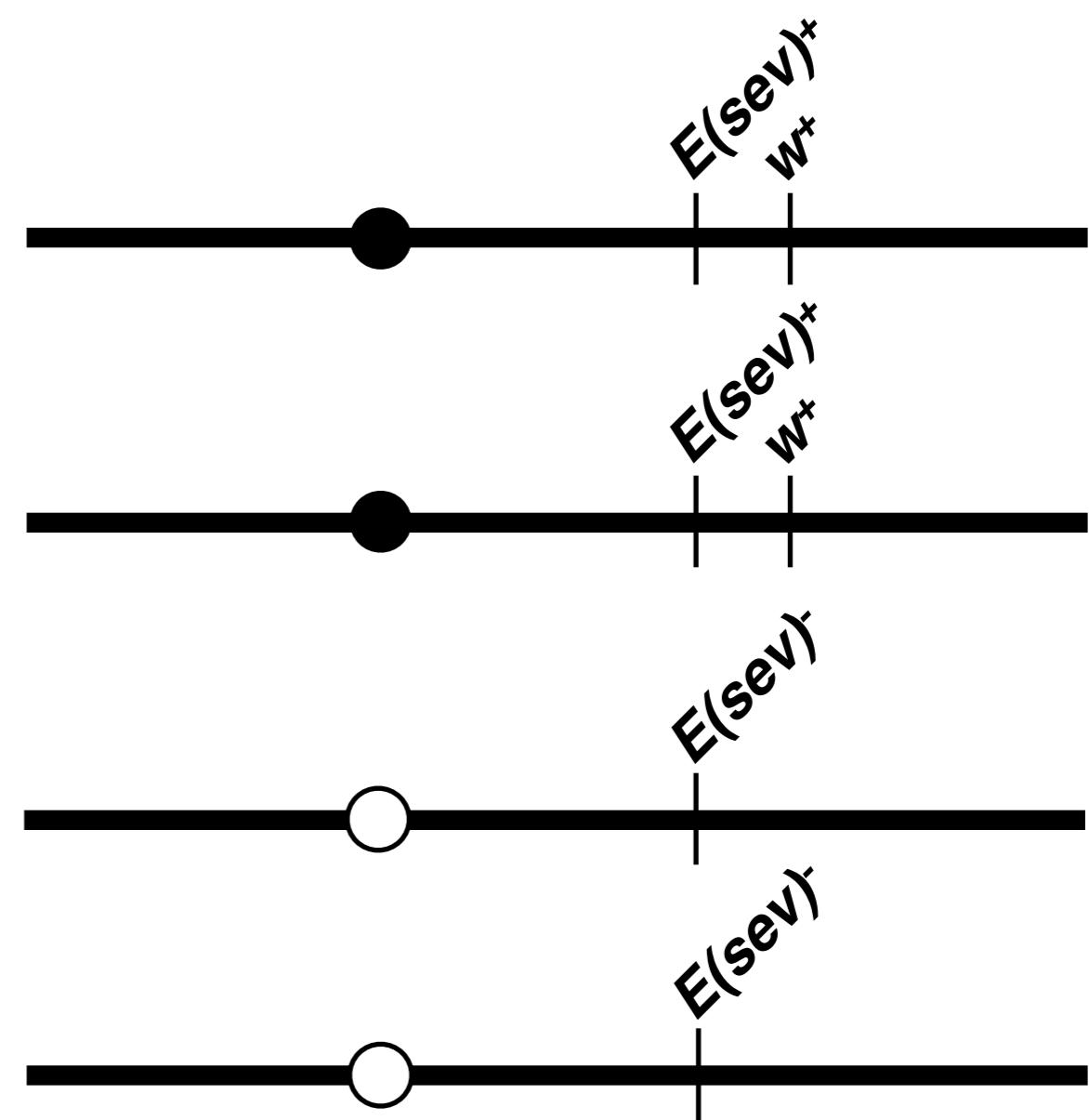
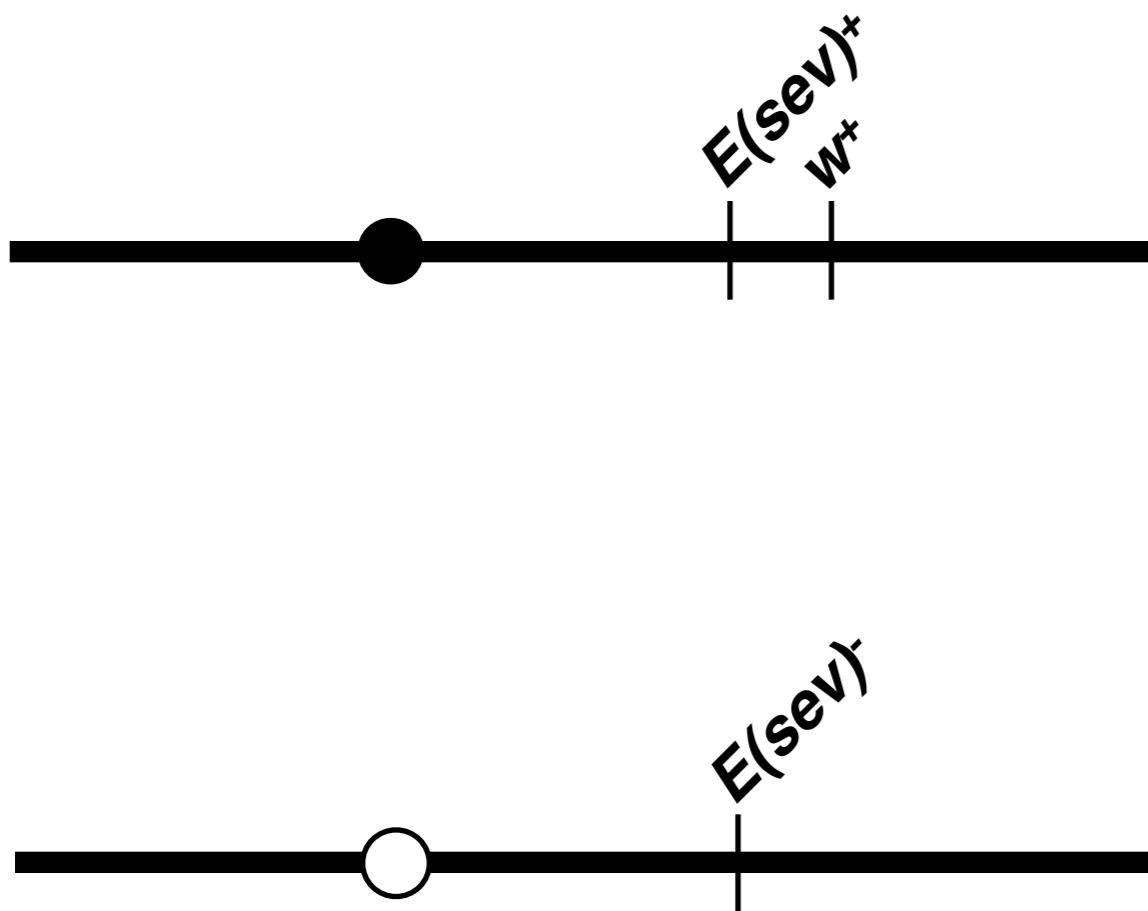
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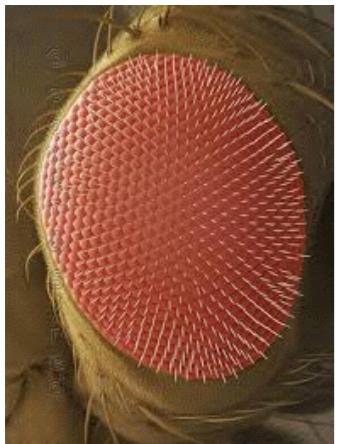
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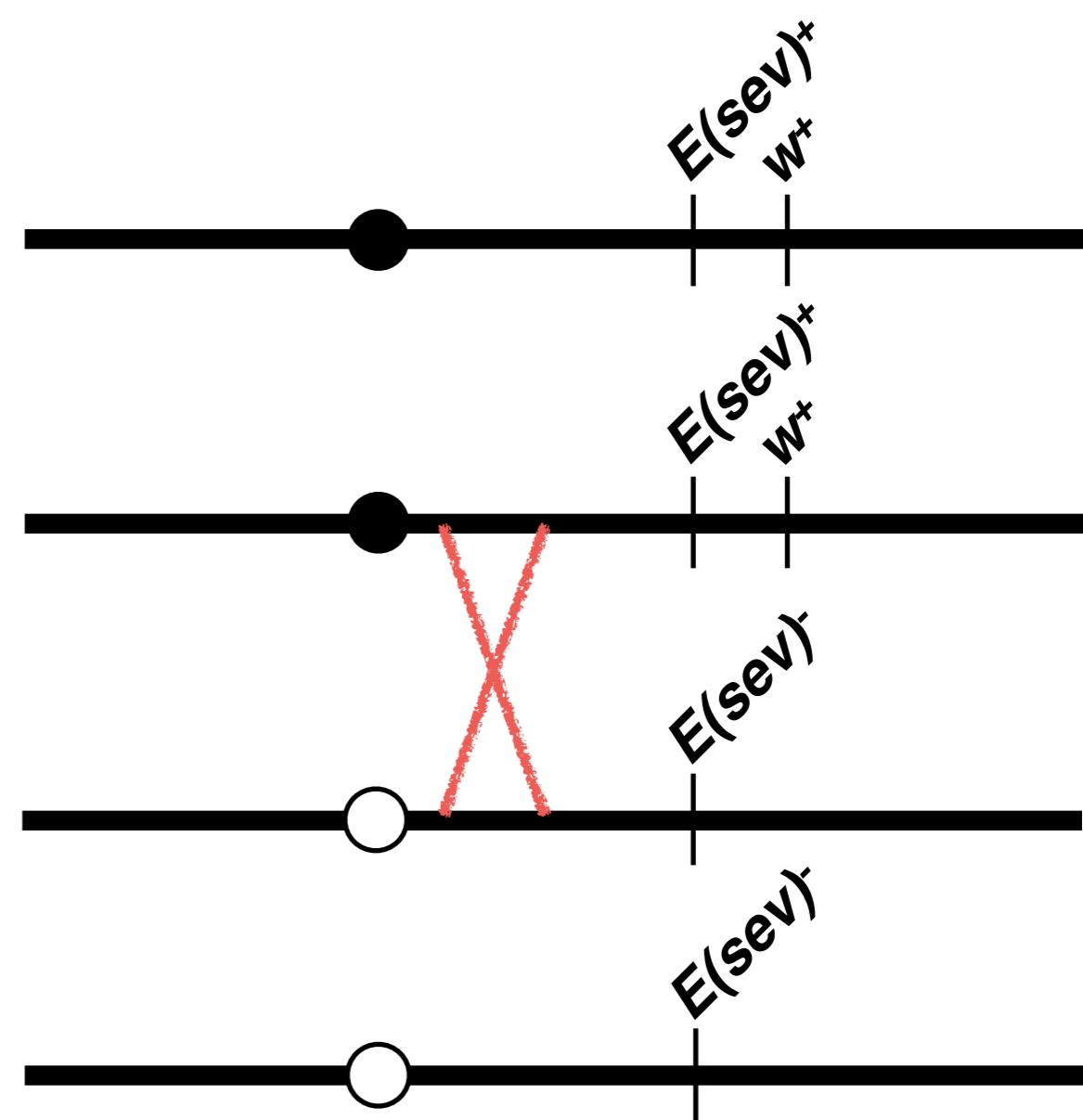
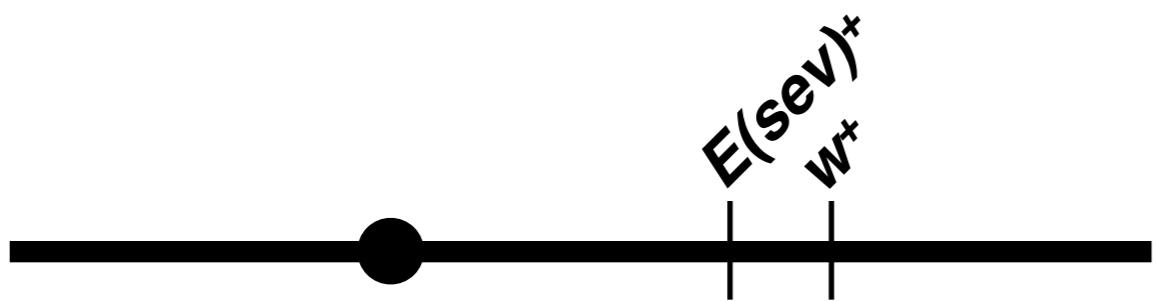
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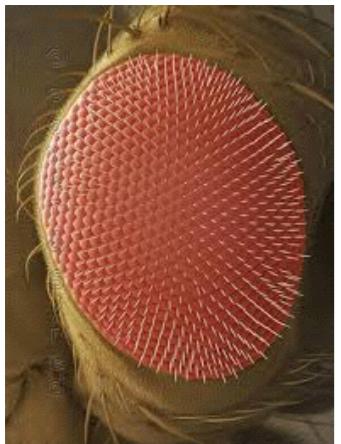
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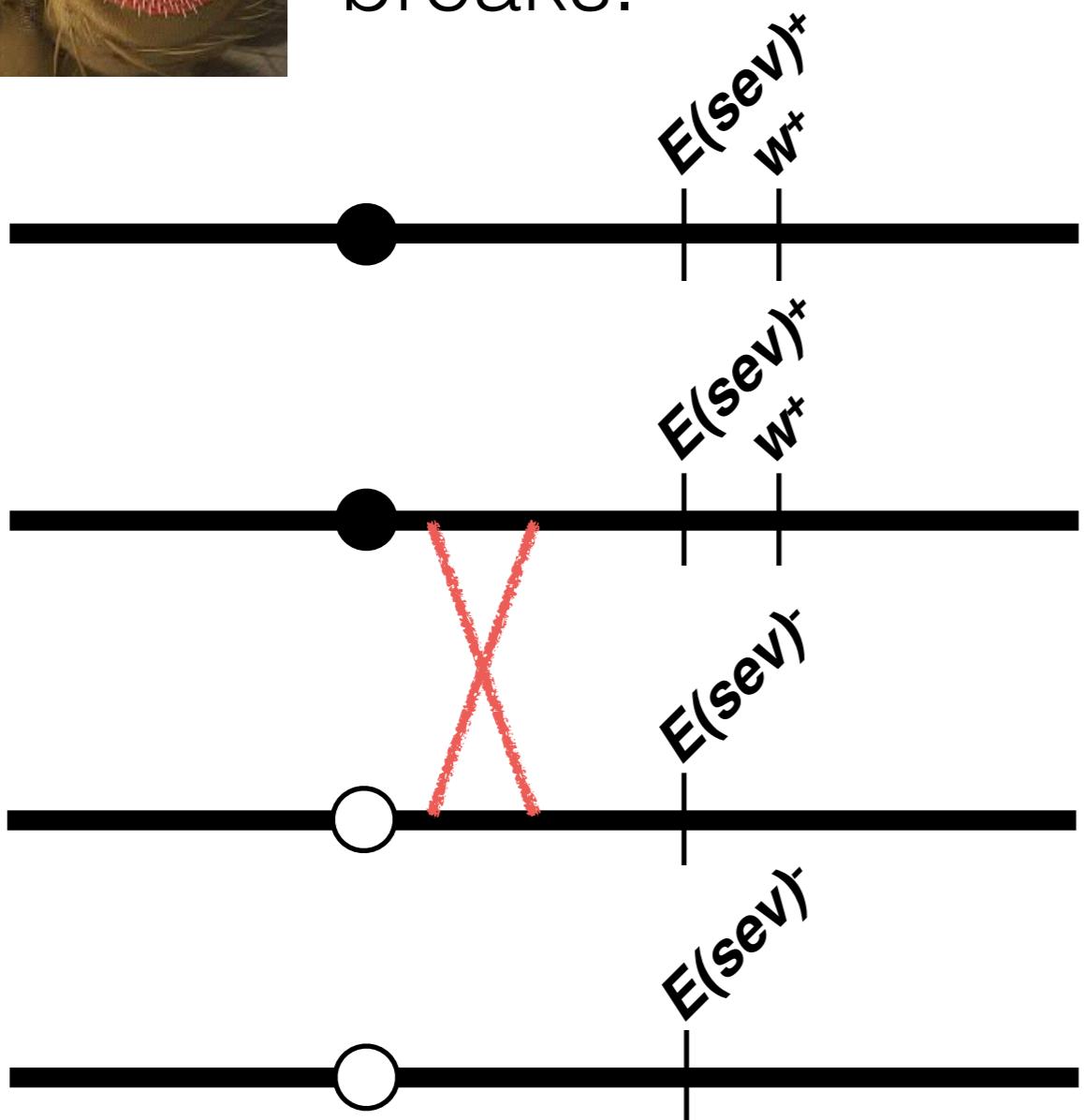
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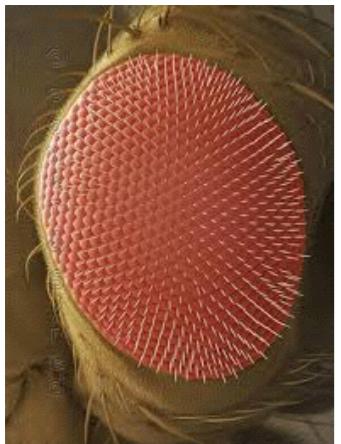
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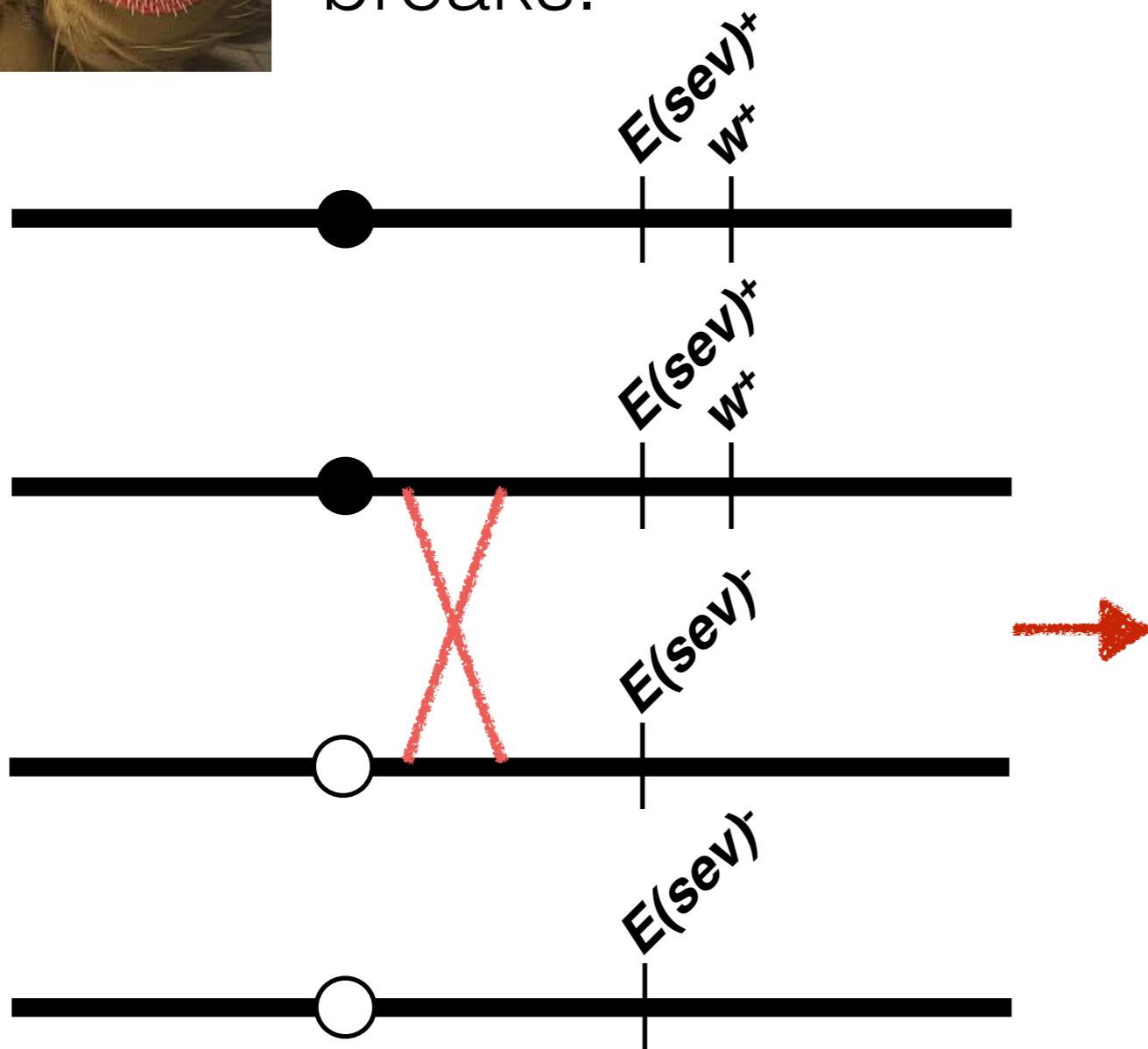
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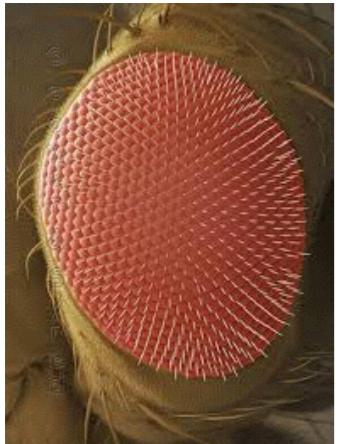
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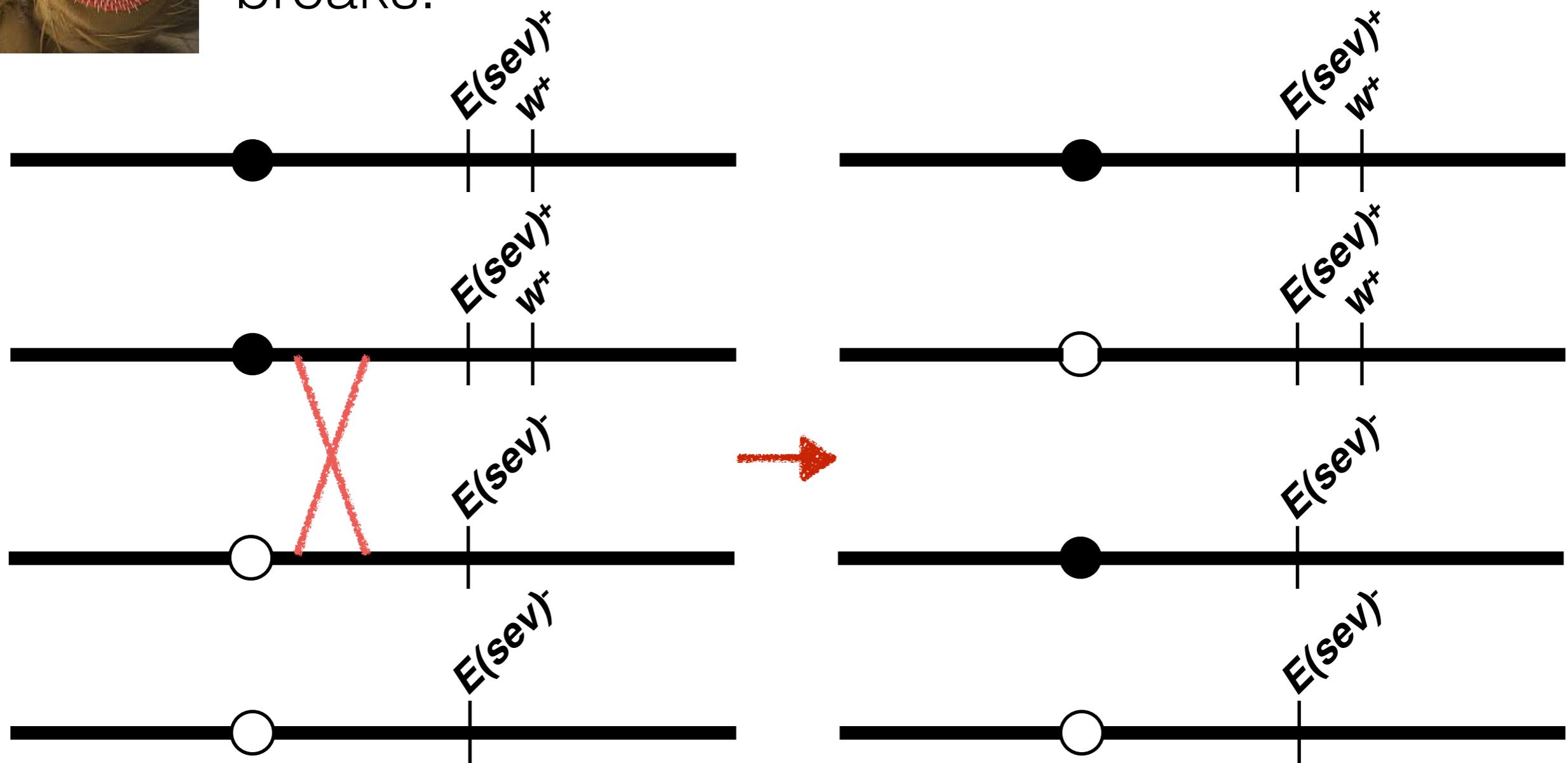
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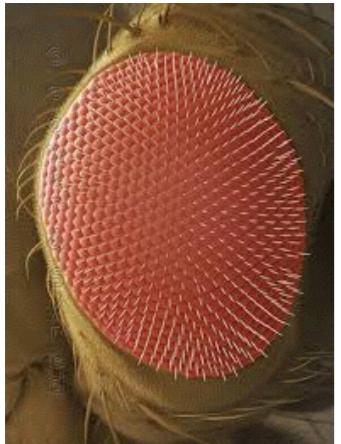
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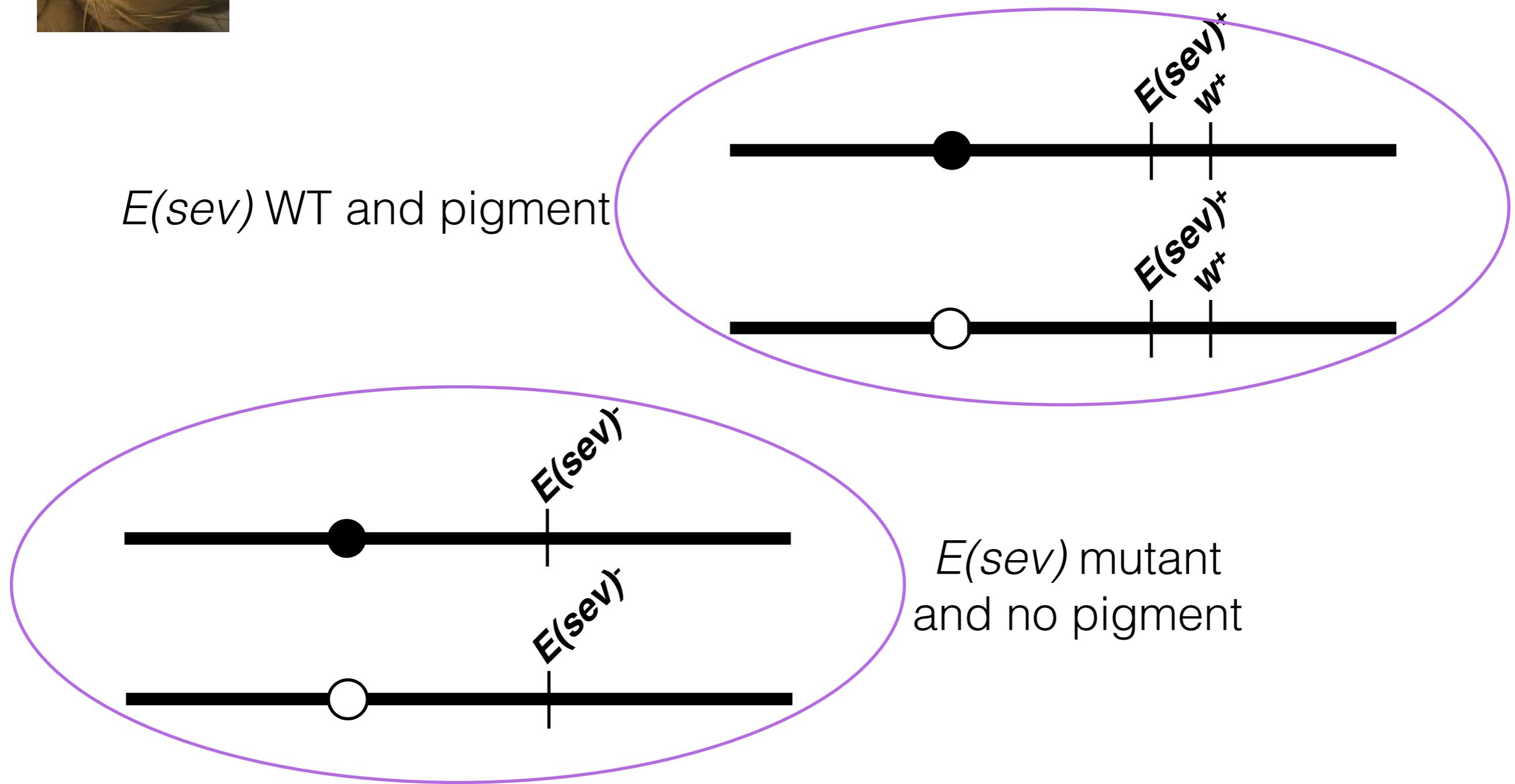
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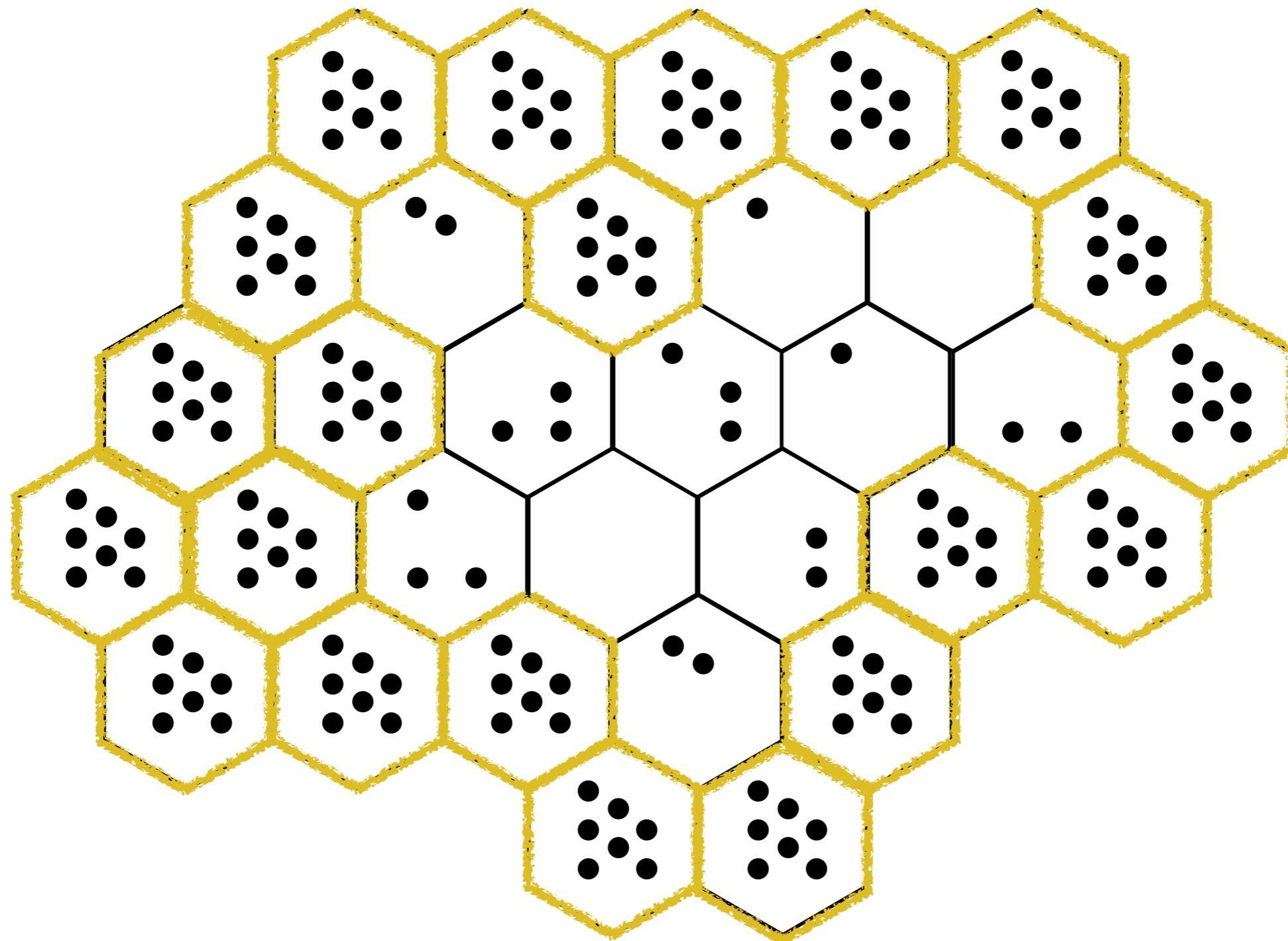
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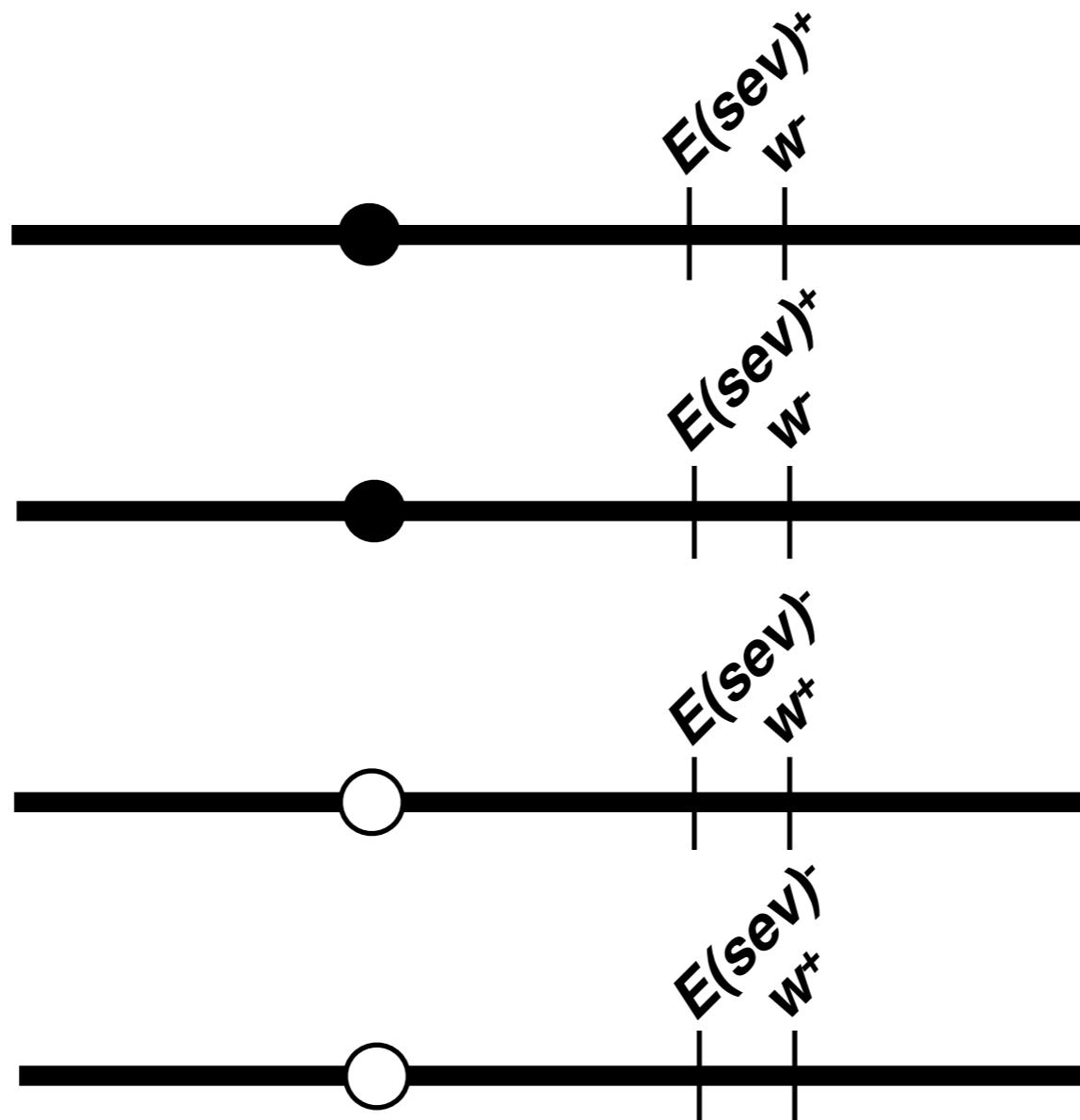
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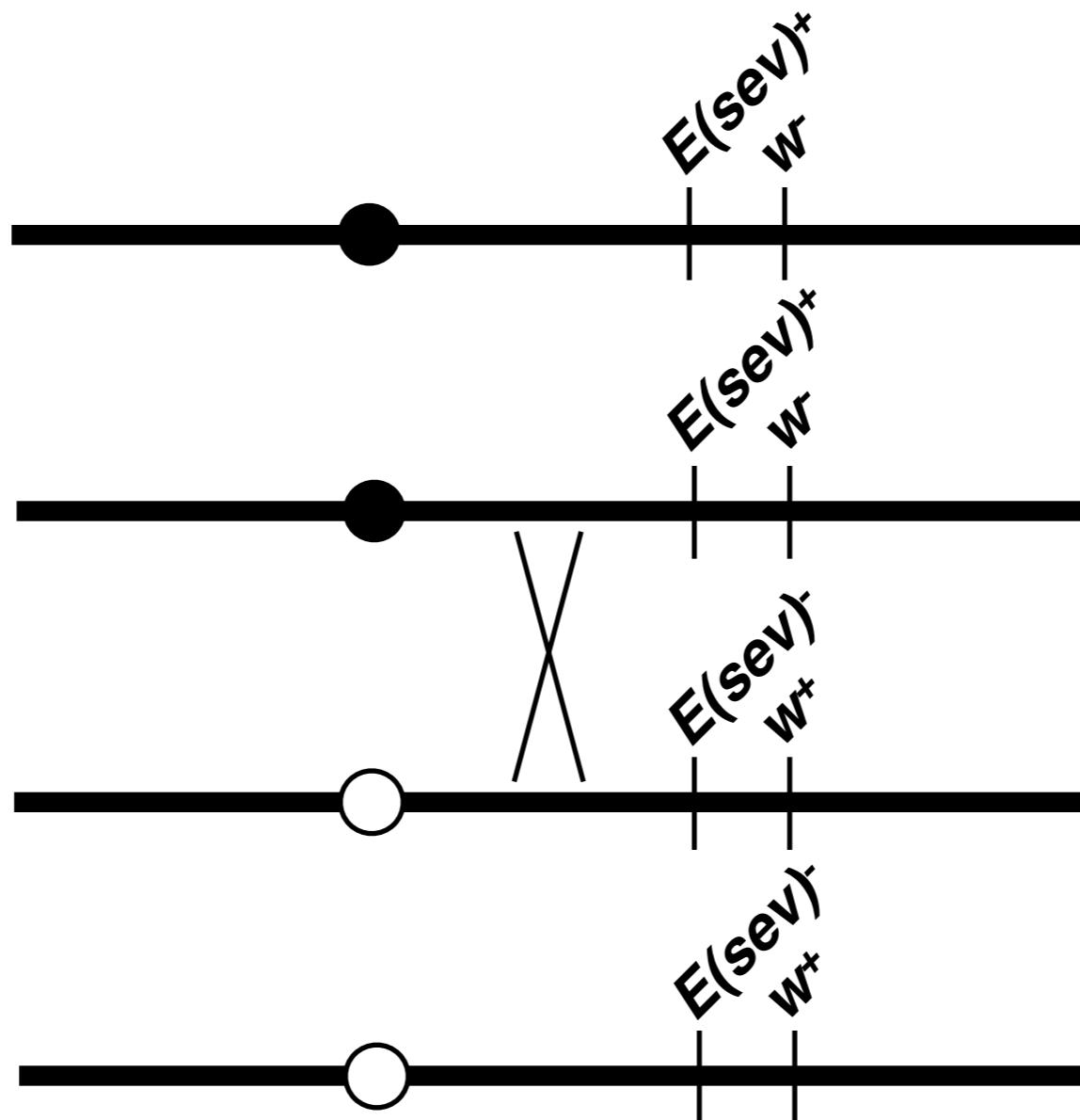
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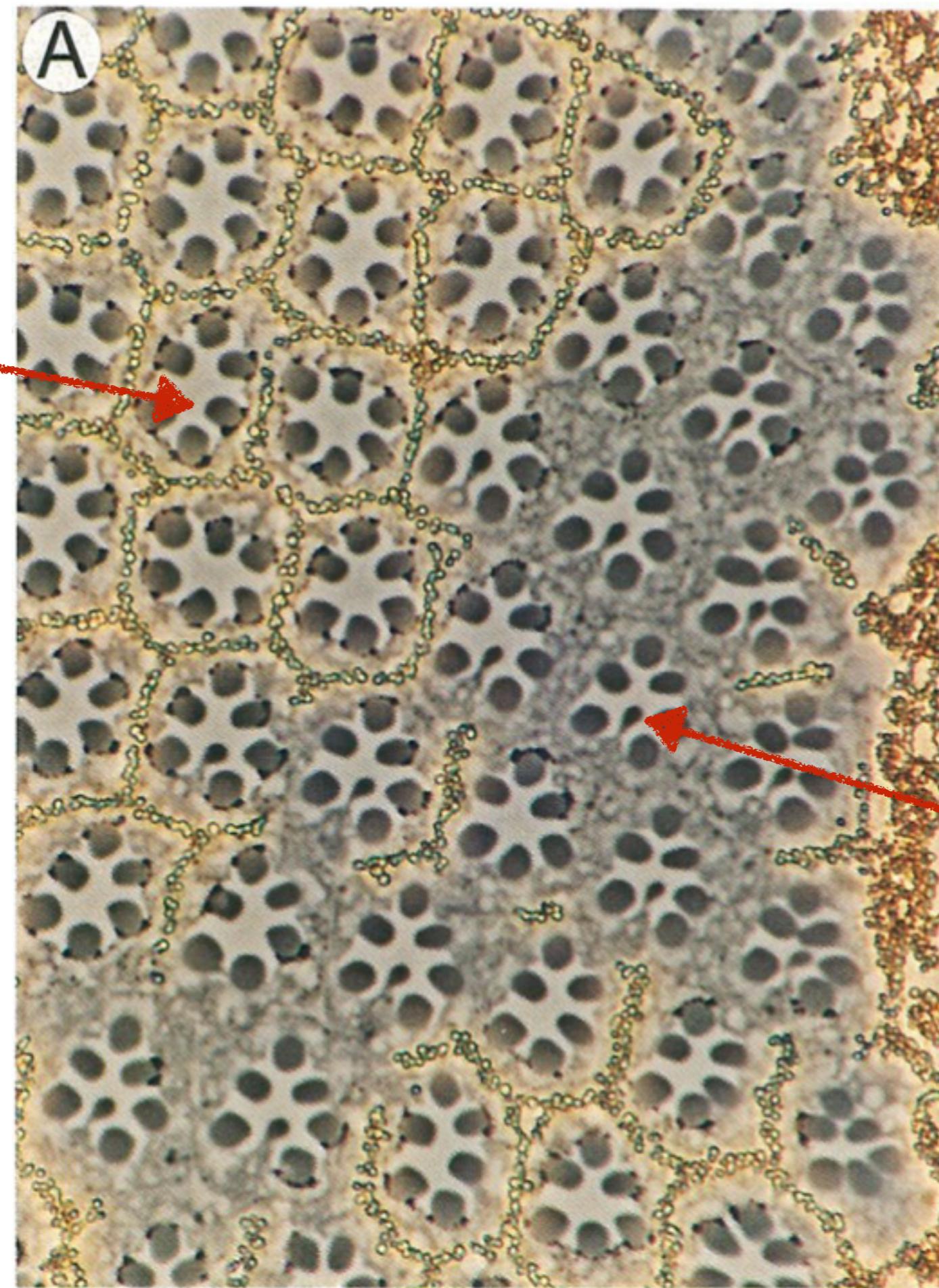
# Are genes required in the R7 cell for controlling R7 cell fate?



# Are genes required in the R7 cell for controlling R7 cell fate?



Pigment  
and  
*E(sev)*  
mutant



No pigment  
and  
wild-type  
*E(sev)*

# Screen for dominant enhancers of sensitized phenotype led to the Ras pathway controlling R7 fate

*bride of sevenless*  
*boss*



*sevenless*  
*sev*



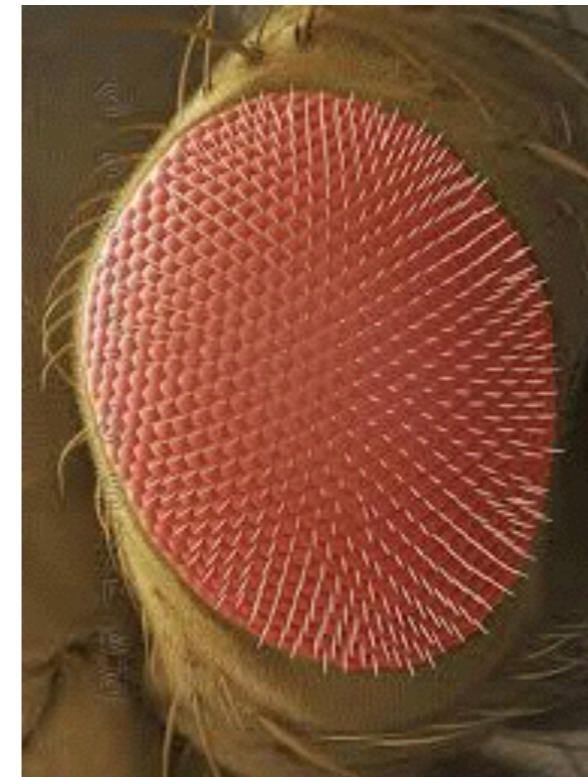
*son of sevenless*  
*sos*



*ras*



R7  
development

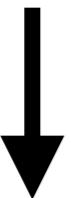


# Screen for dominant enhancers of sensitized phenotype led to the Ras pathway controlling R7 fate

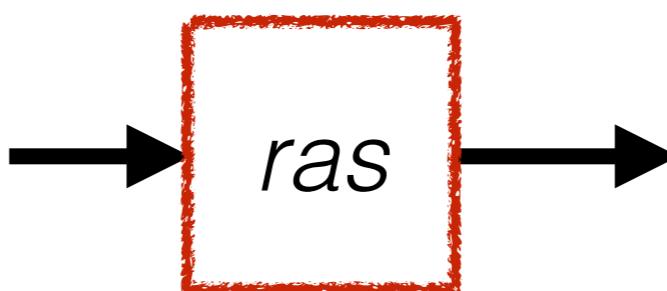
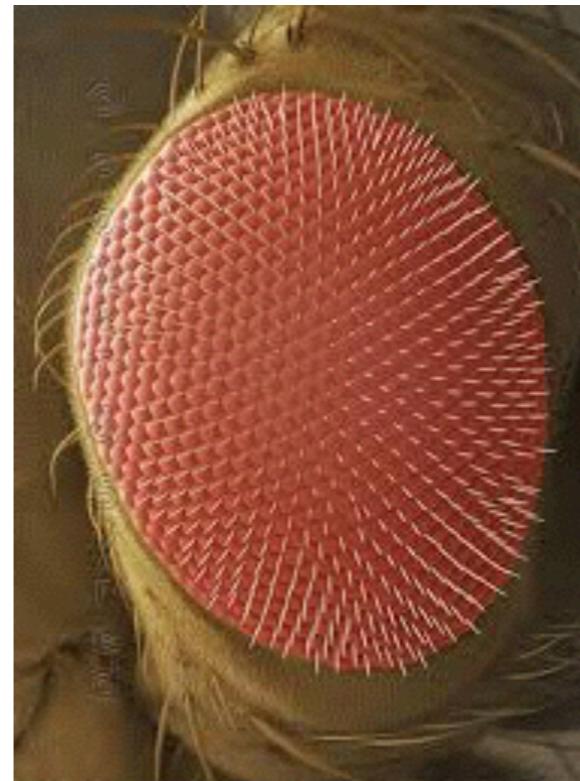
*bride of sevenless*  
*boss*



*sevenless*  
*sev*

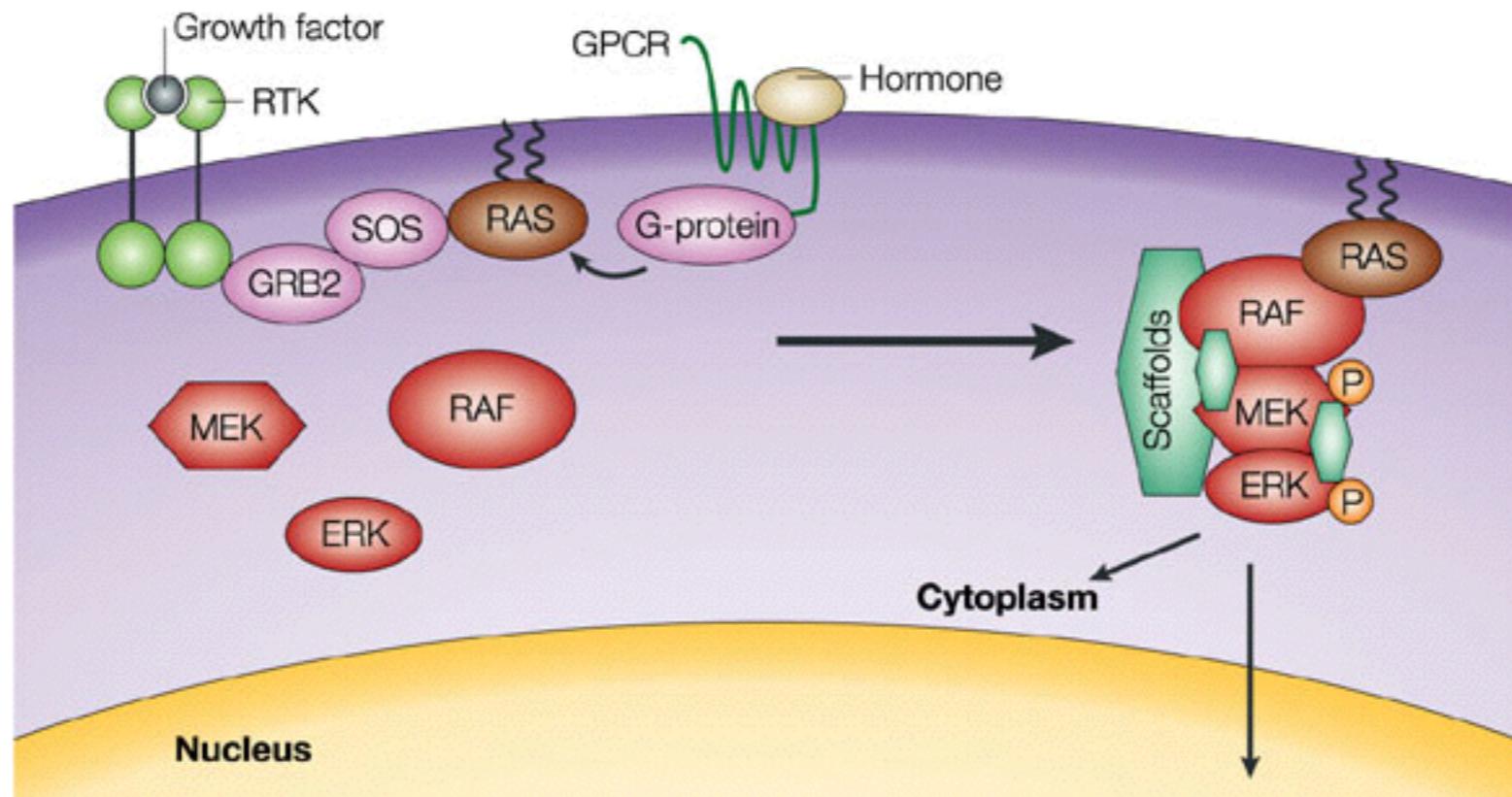


*son of sevenless*  
*sos*



R7  
development

# Two decades of research in *Drosophila* and *C. elegans* led to these pathways



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