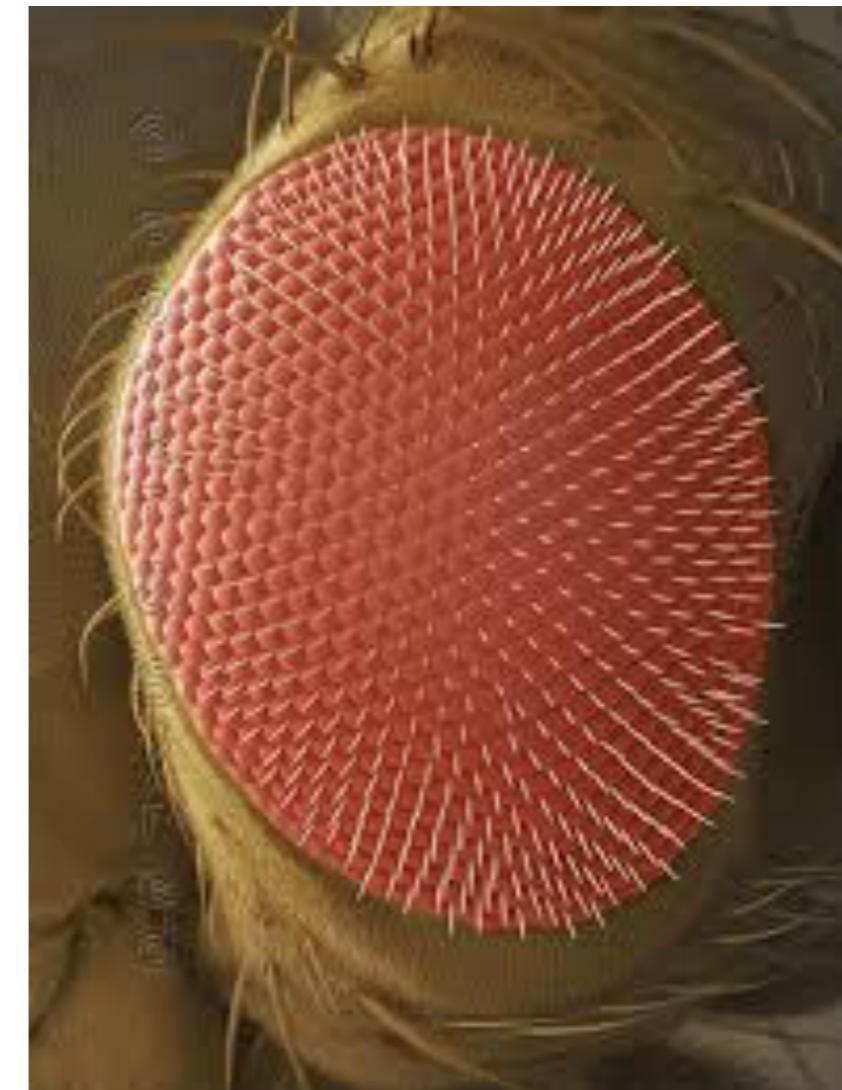


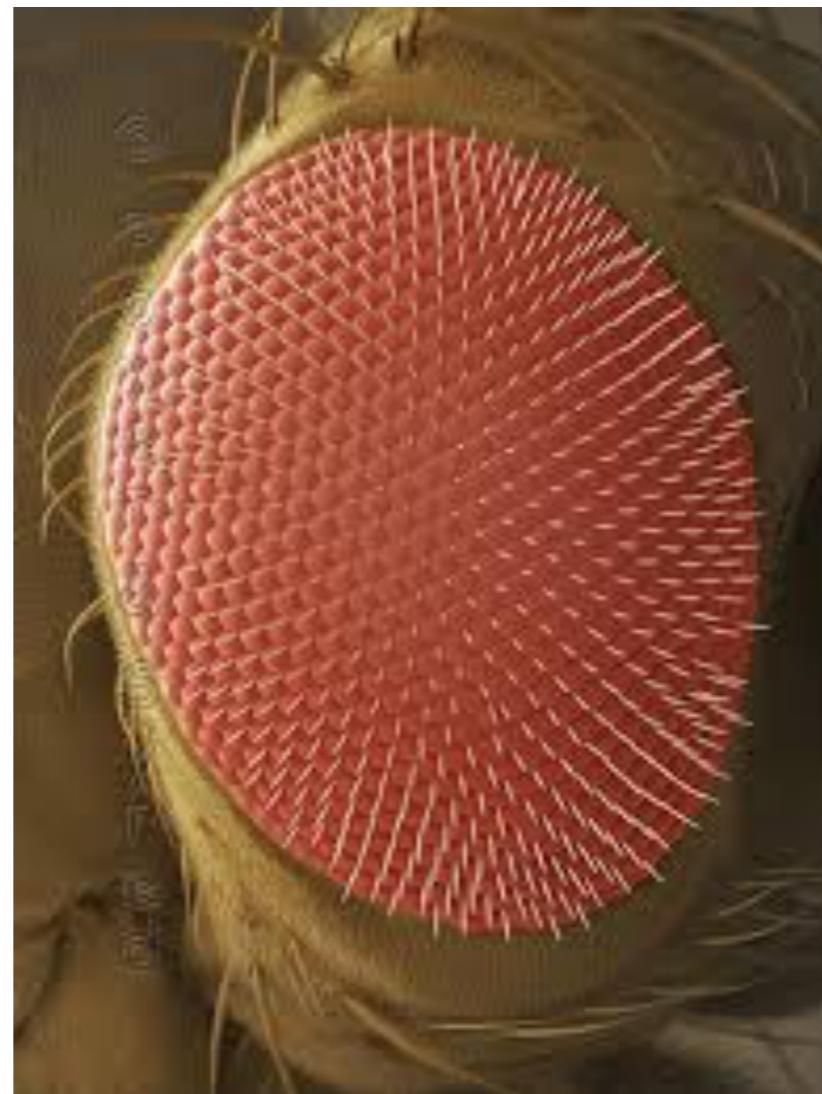
# Developmental genetics



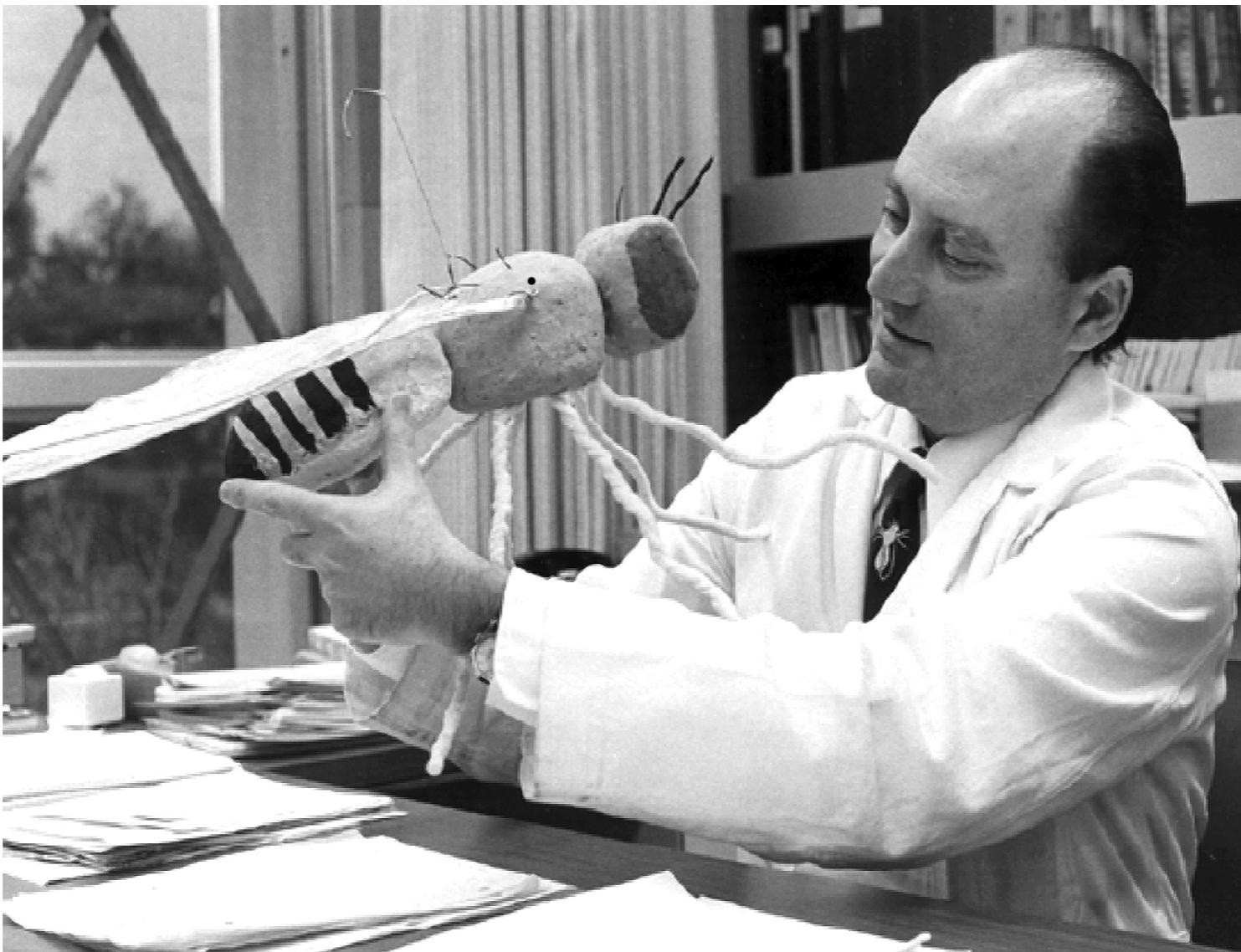
*C. elegans*



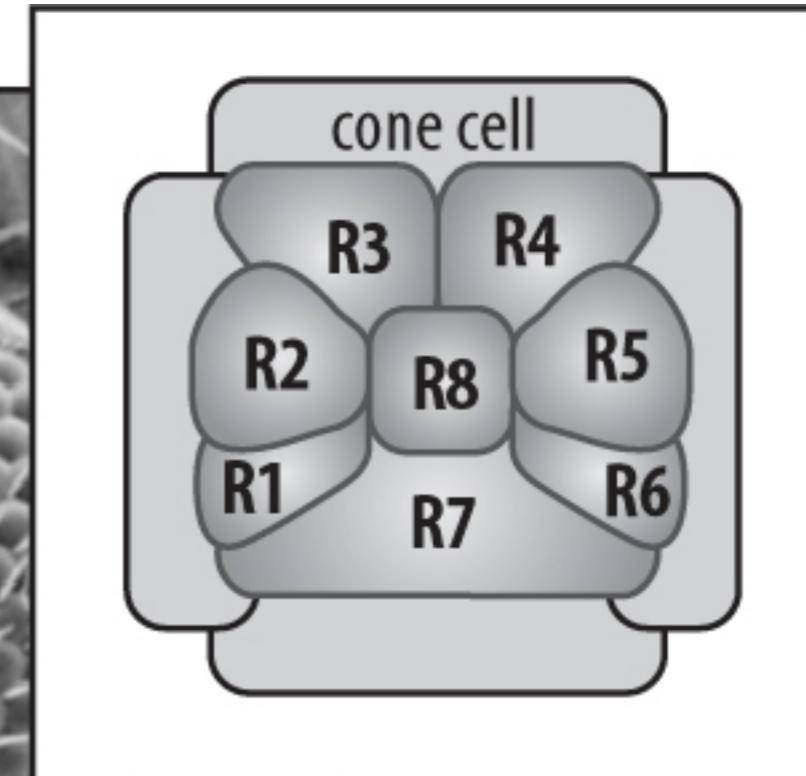
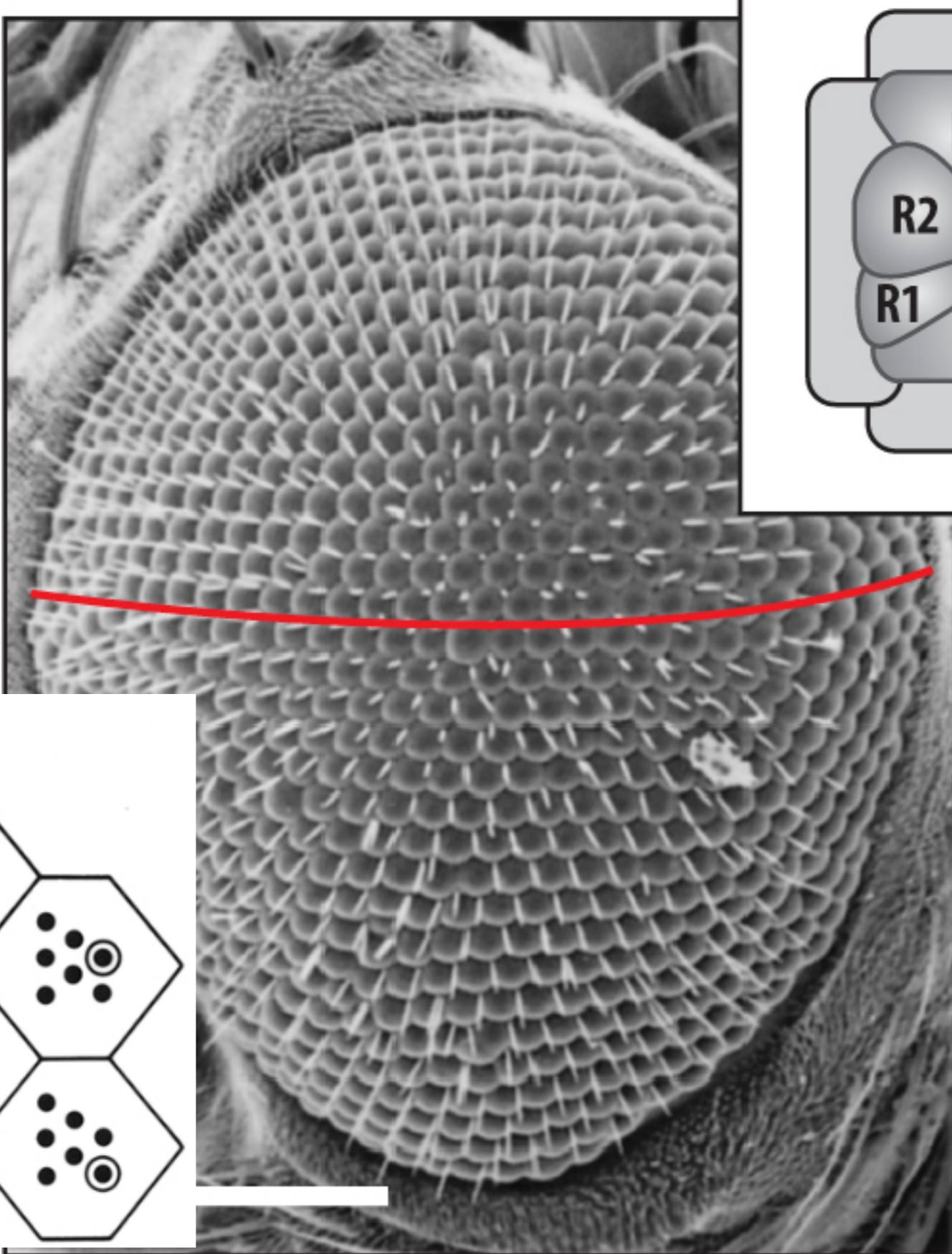
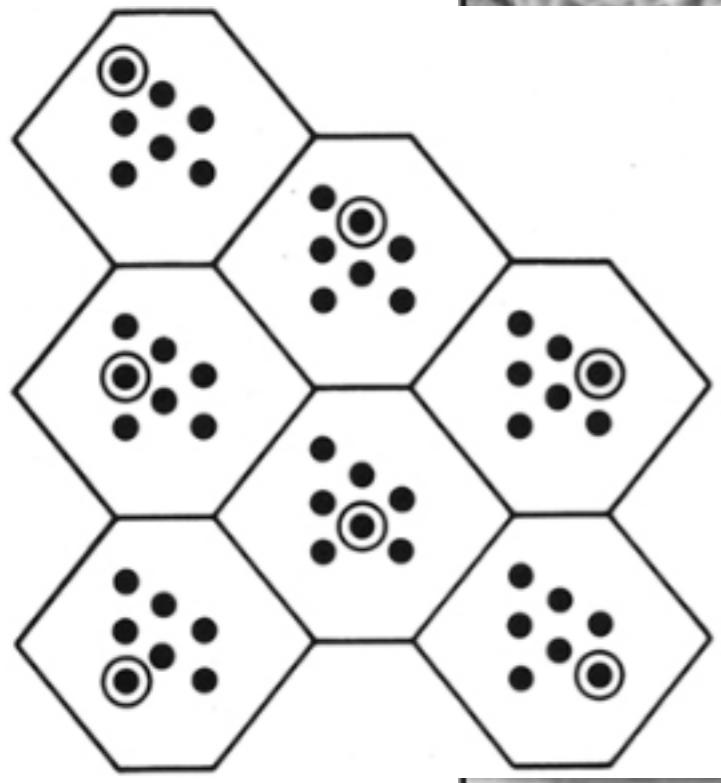
*D. melanogaster*



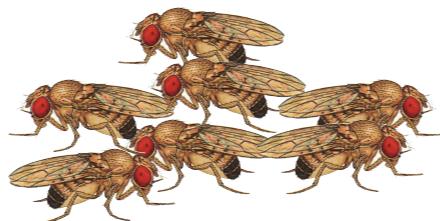
The *Drosophila* eye



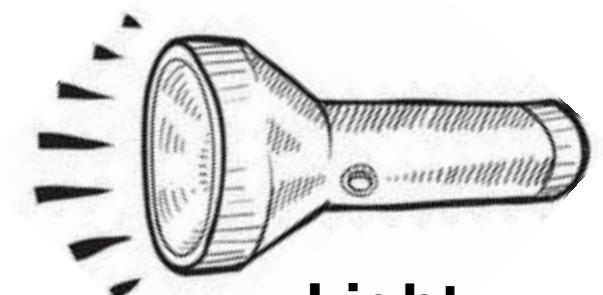
# Seymour Benzer



# A simple behavioral selection

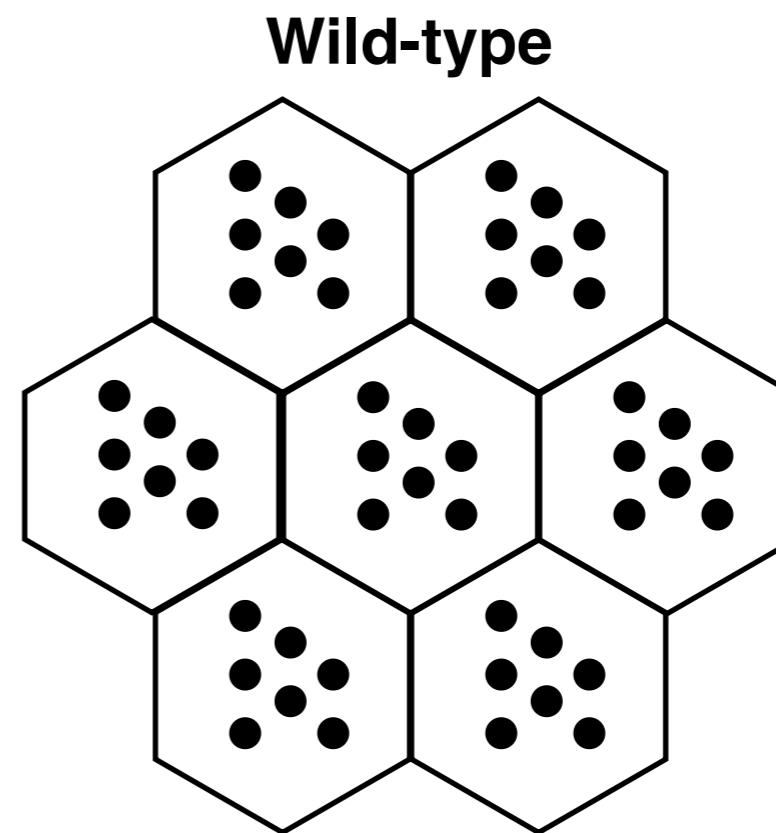
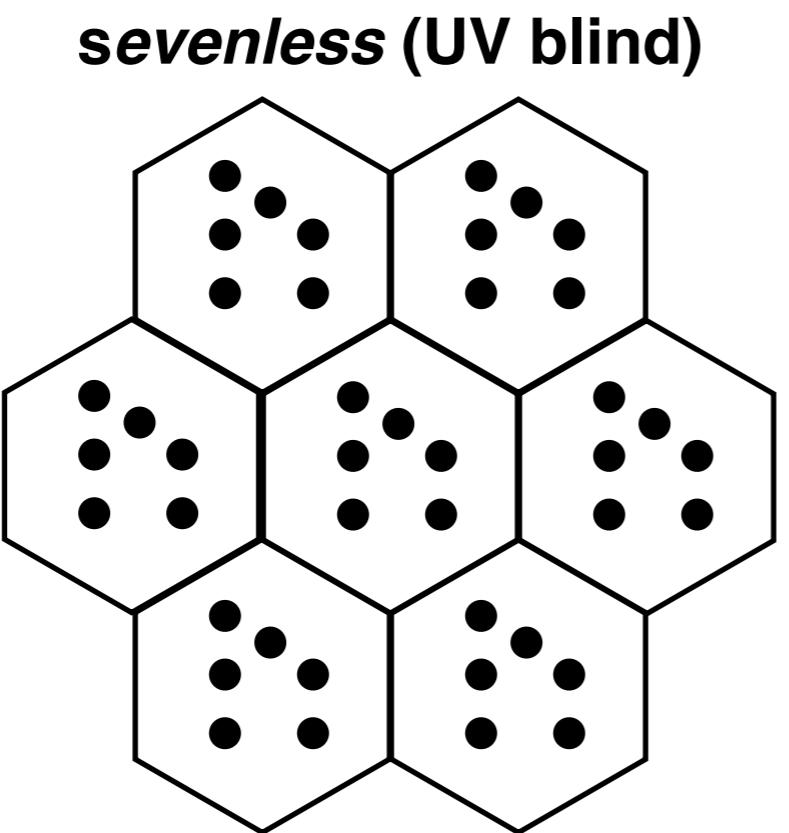
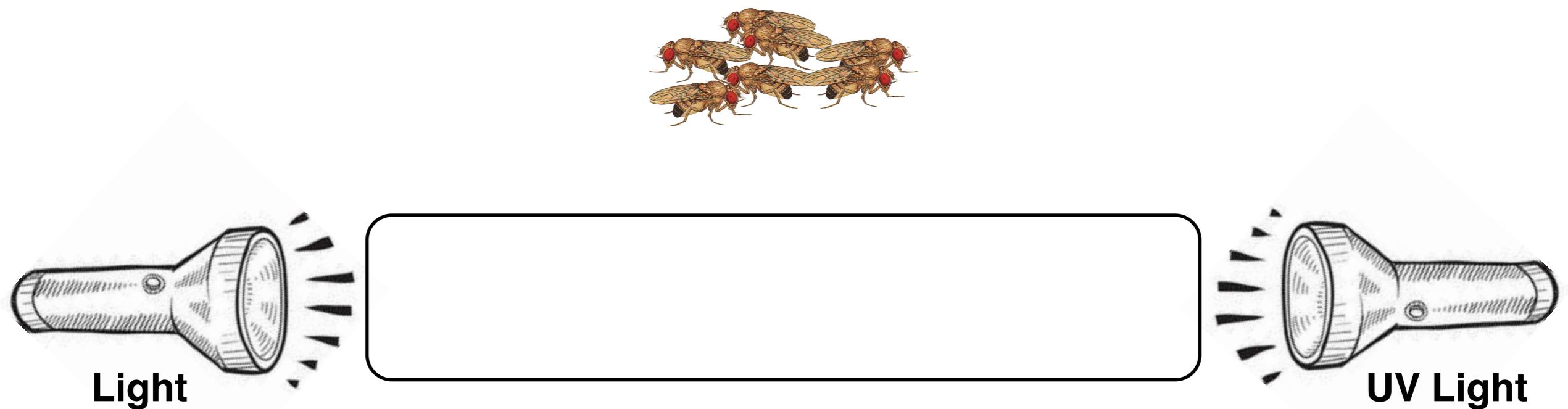


Dark



Light

# A simple behavioral selection

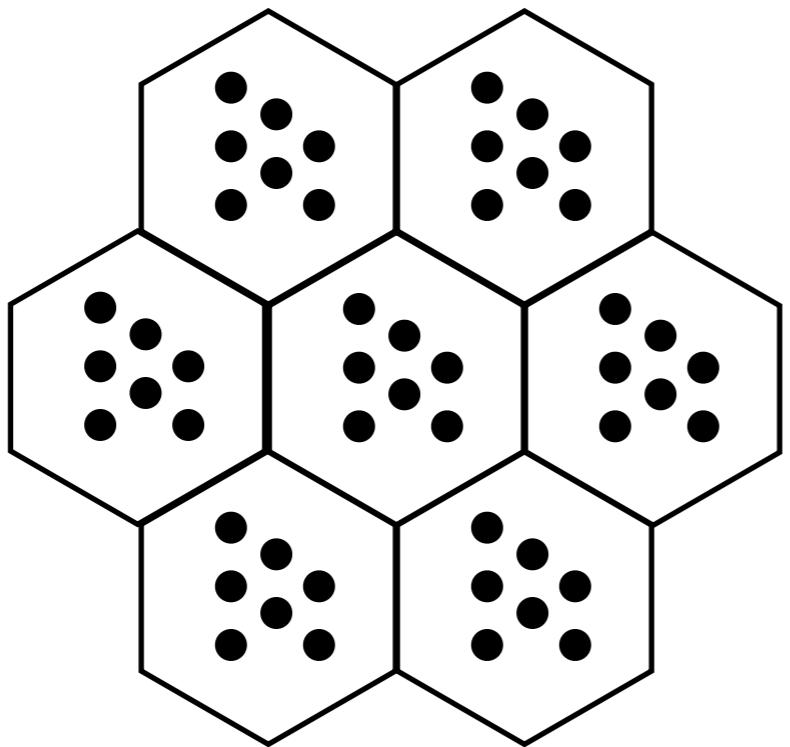




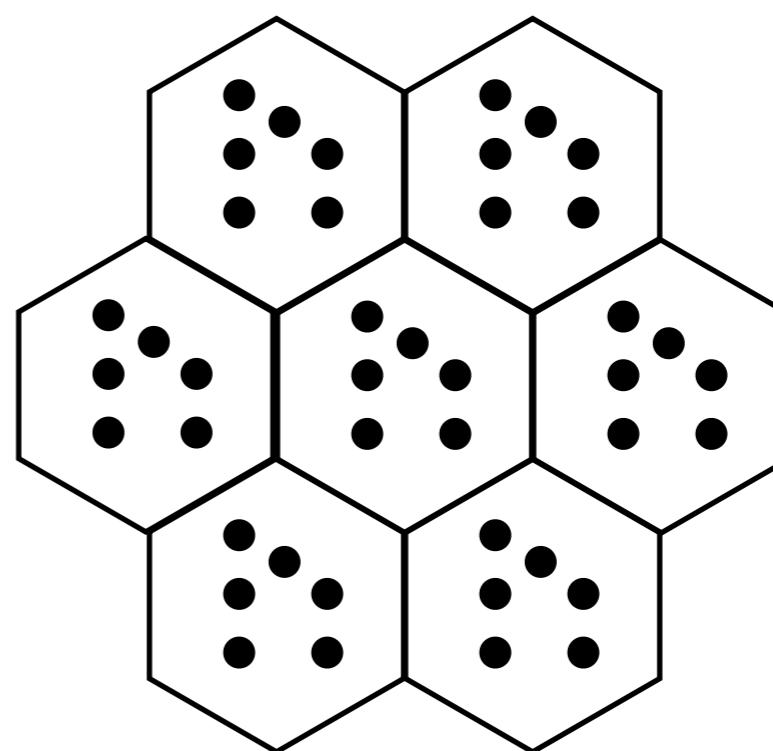
**Gerry Rubin**

# Other UV blind mutants

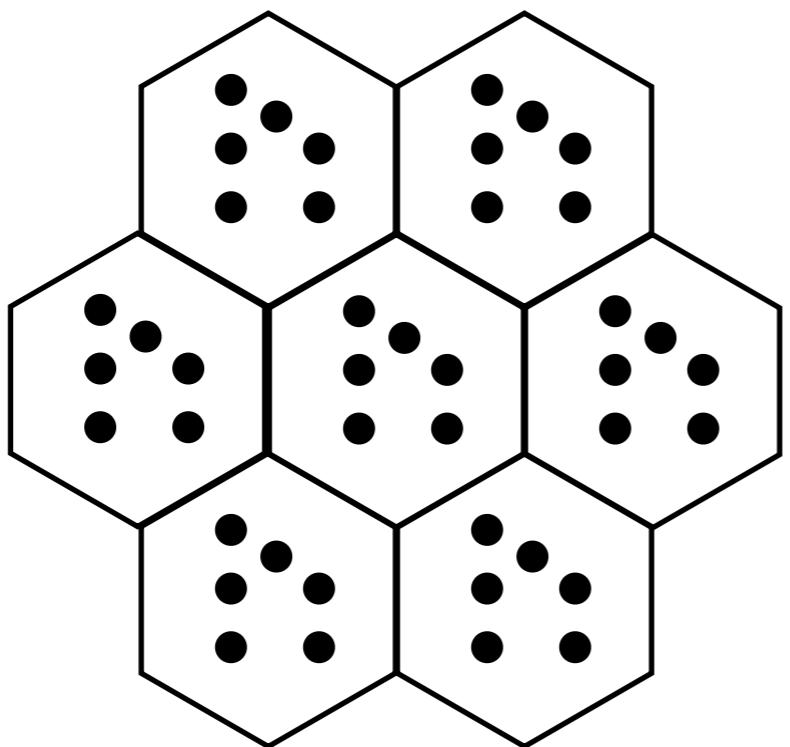
Wild-type



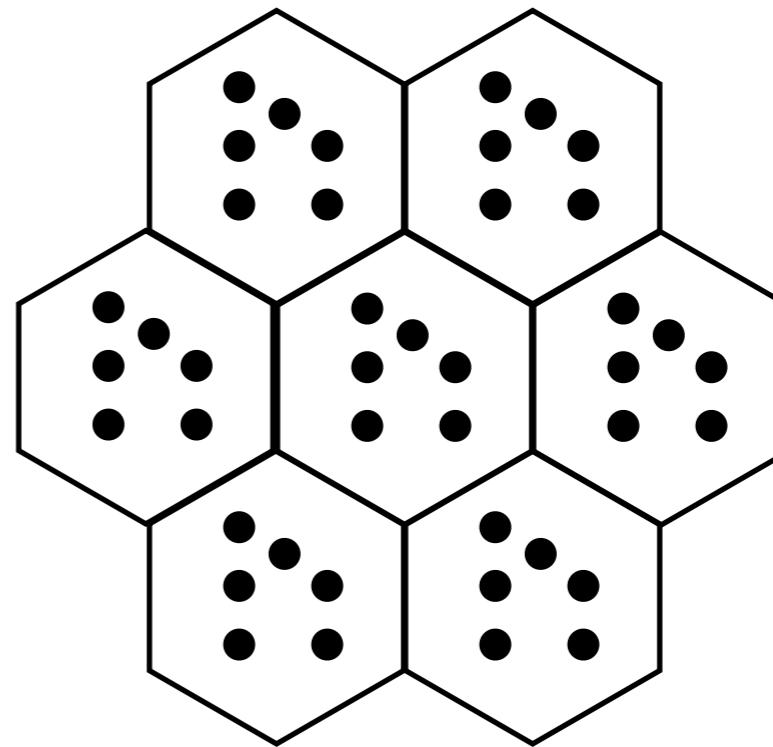
*sevenless* (UV blind)



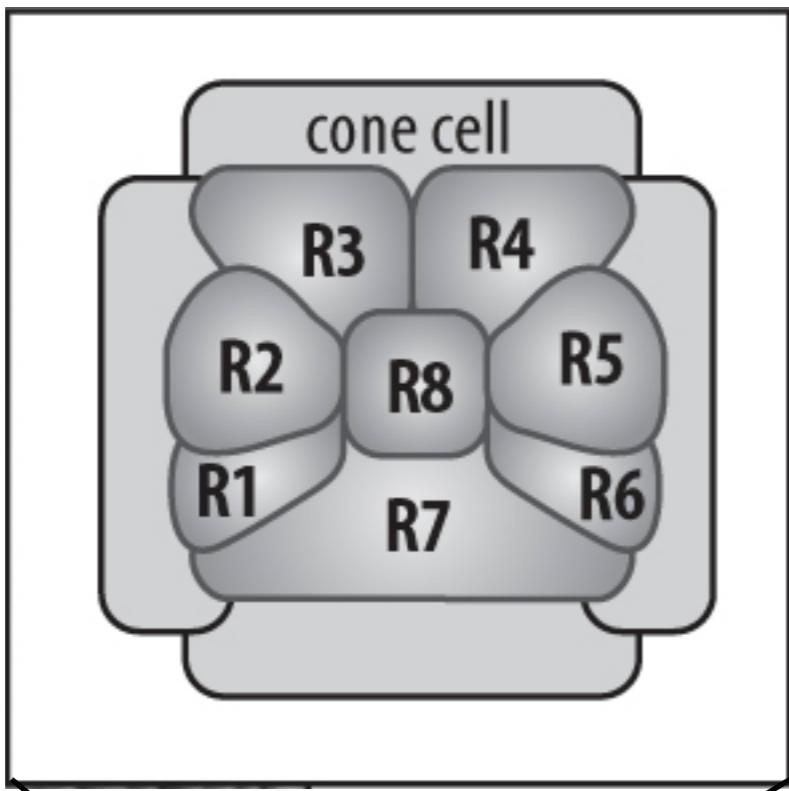
*bride of sevenless* (UV blind)



*seven-in-absentia* (UV blind)



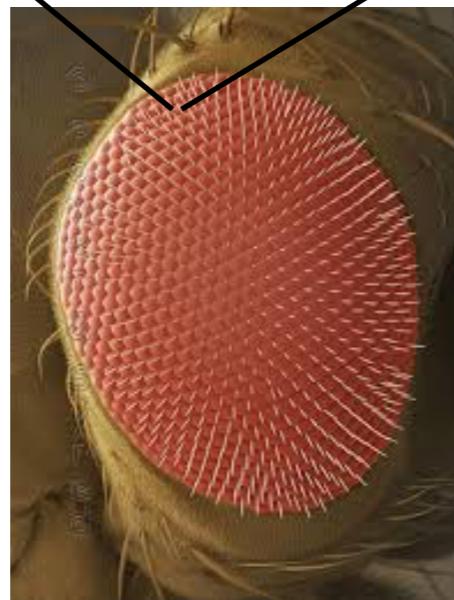
# Development of an ommatidium



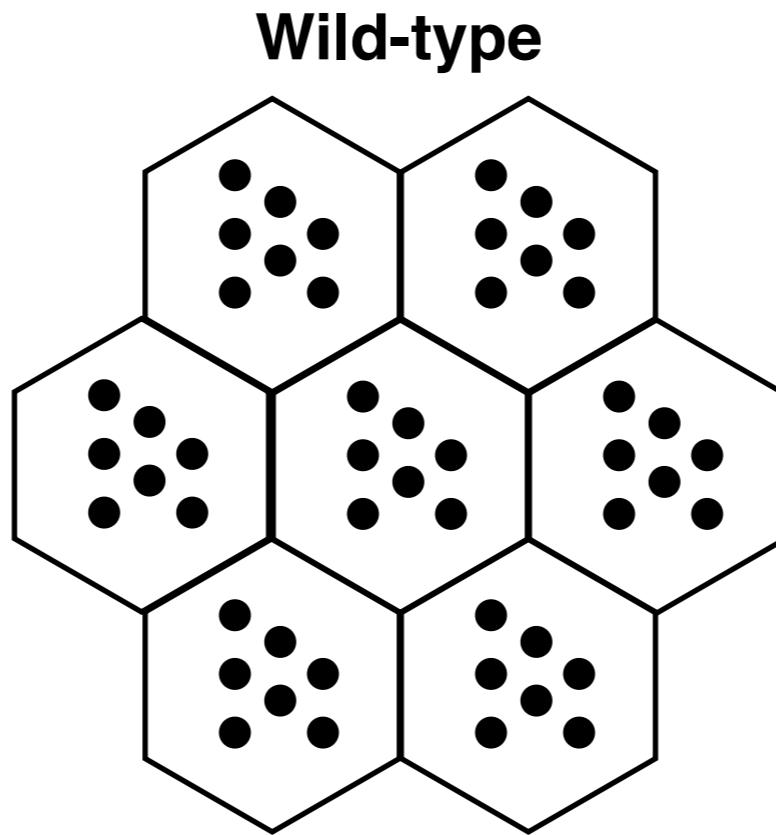
R8 born first

R1-R6 born after

R7 last to be born



# Is the function of *sev*, *sina*, or *boss* required in the R7 cell?



Function in R7 is considered cell autonomous

Function in any cell besides R7 is considered cell non-autonomous

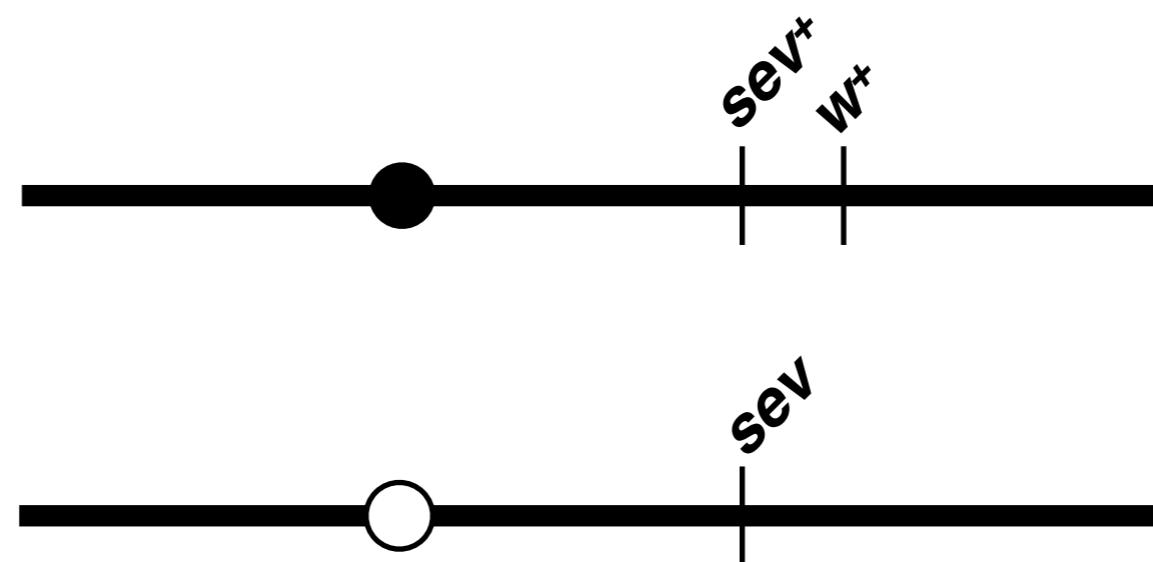
# Are genes required in ommatidia for cell viability?

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

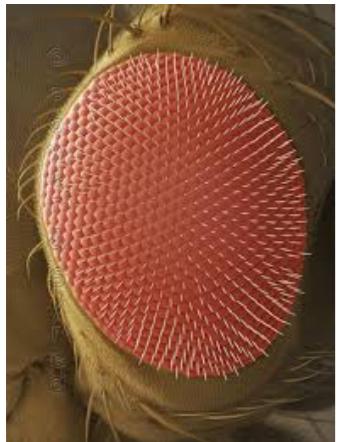


1.  $\frac{\underline{sev}}{+} ; \frac{w}{W}$

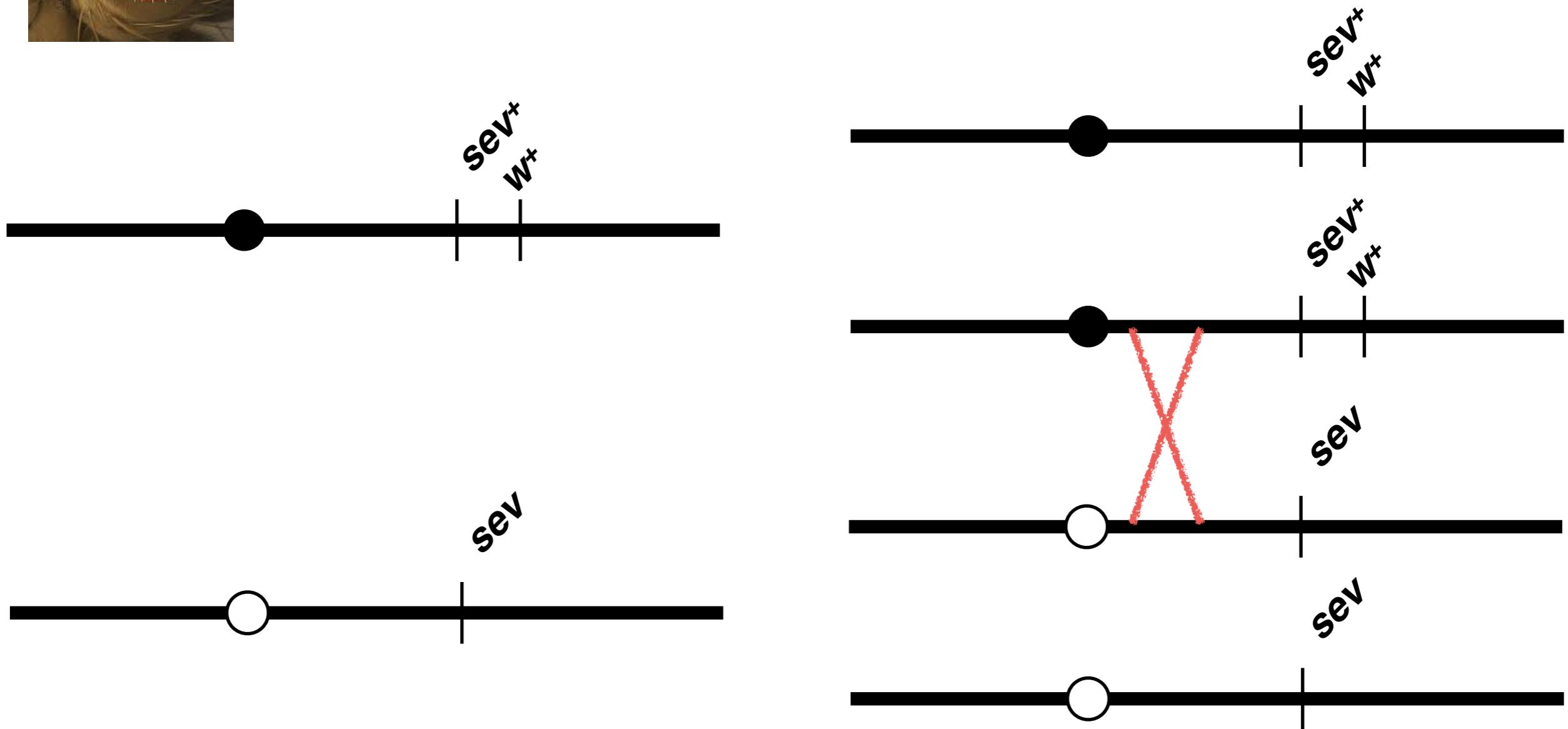
2. Use a P element with  $w^+$  distal  
to the wild-type *sev* gene



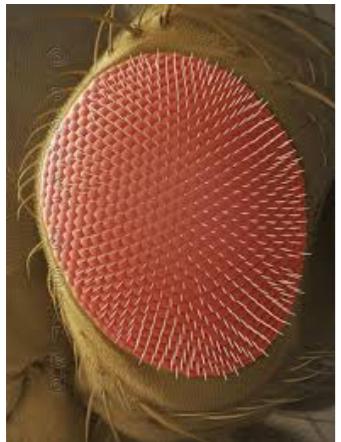
# Are genes required in ommatidia for cell viability?



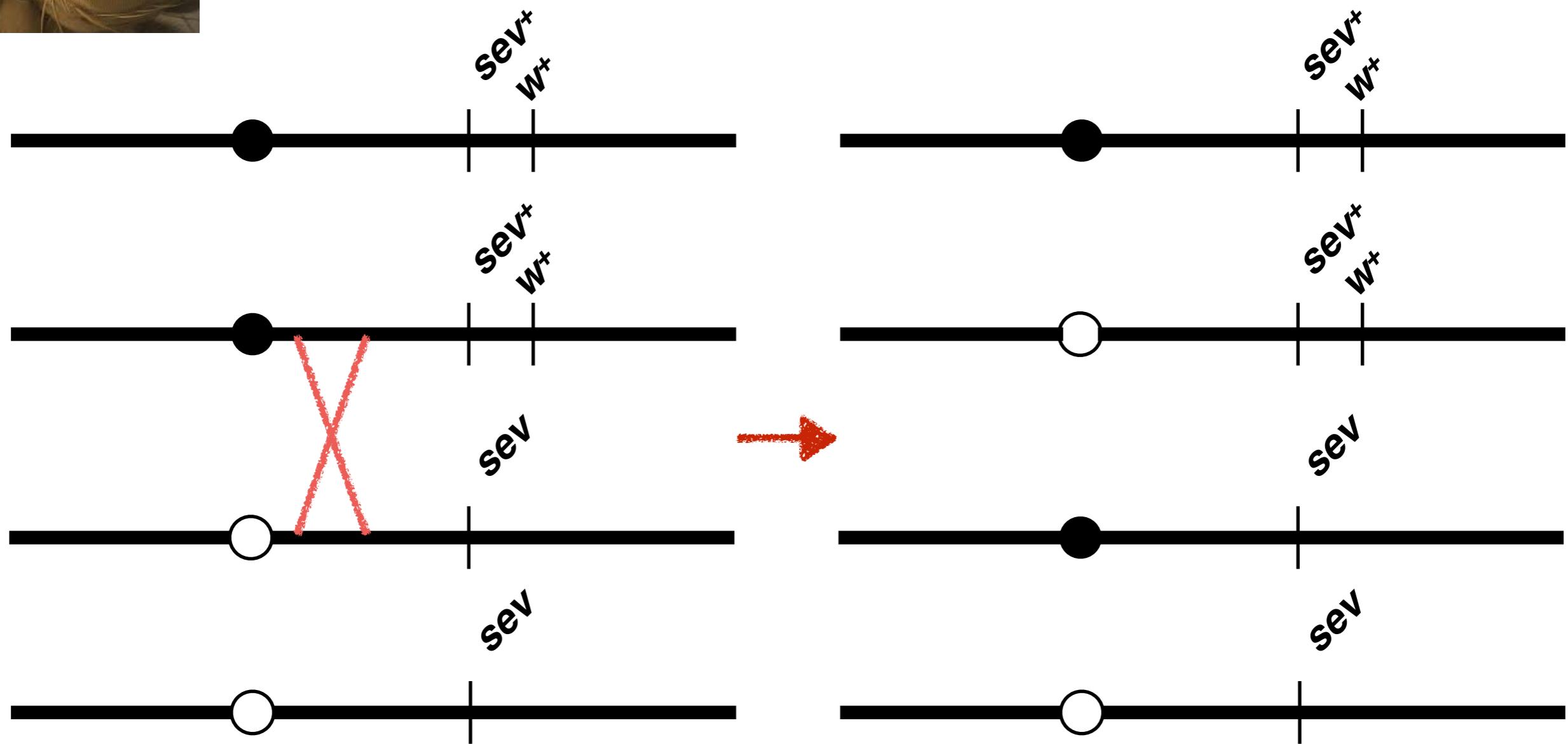
During mitosis for the cells that make up the eye, recombination can occur to repair double-strand breaks.



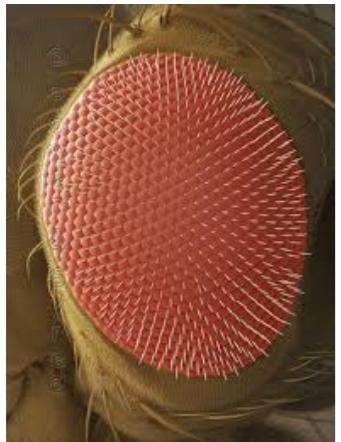
# Are genes required in ommatidia for cell viability?



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

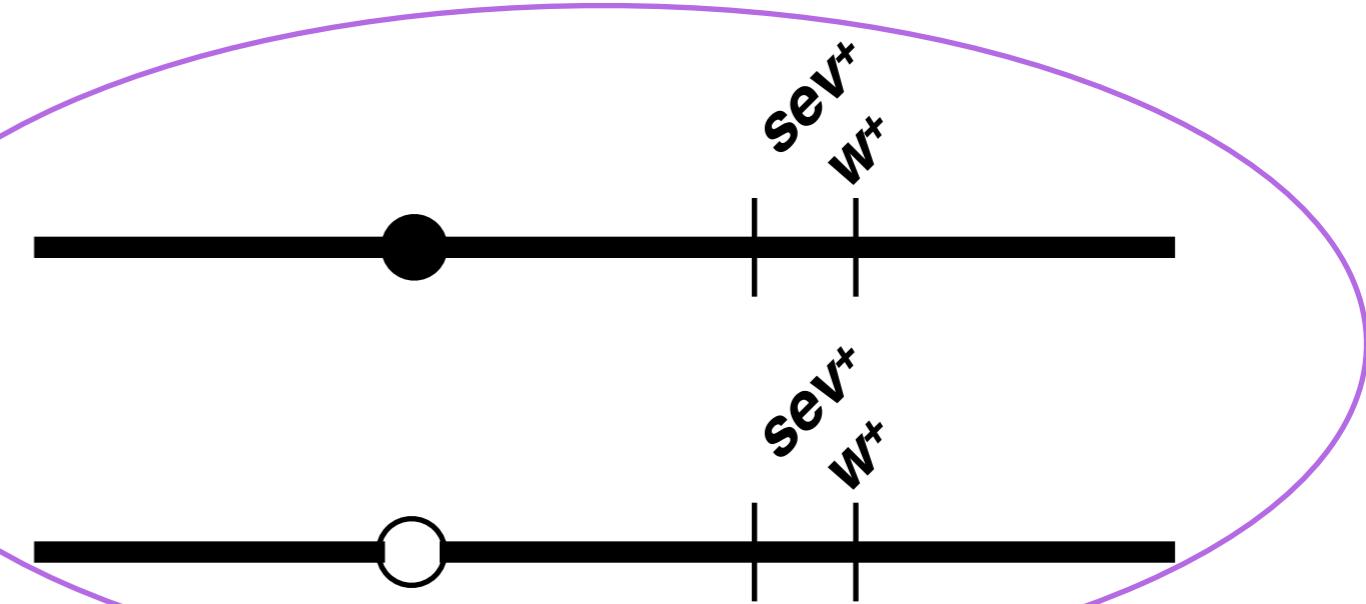


# Are genes required in ommatidia for cell viability?



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

*sev* WT and pigment



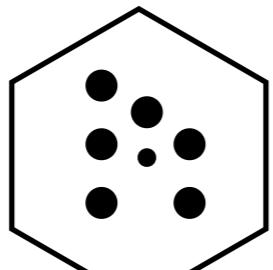
*sev*

*sev*

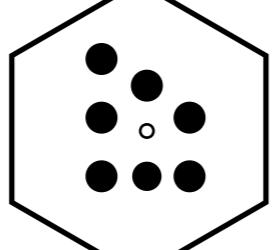
*sev* mutant  
and no pigment

**Twin spots!**

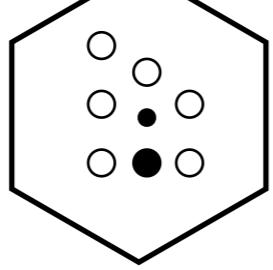
# ***sev* acts cell autonomously to regulate the R7 fate**



R7 cell *white* and *sev* mutant

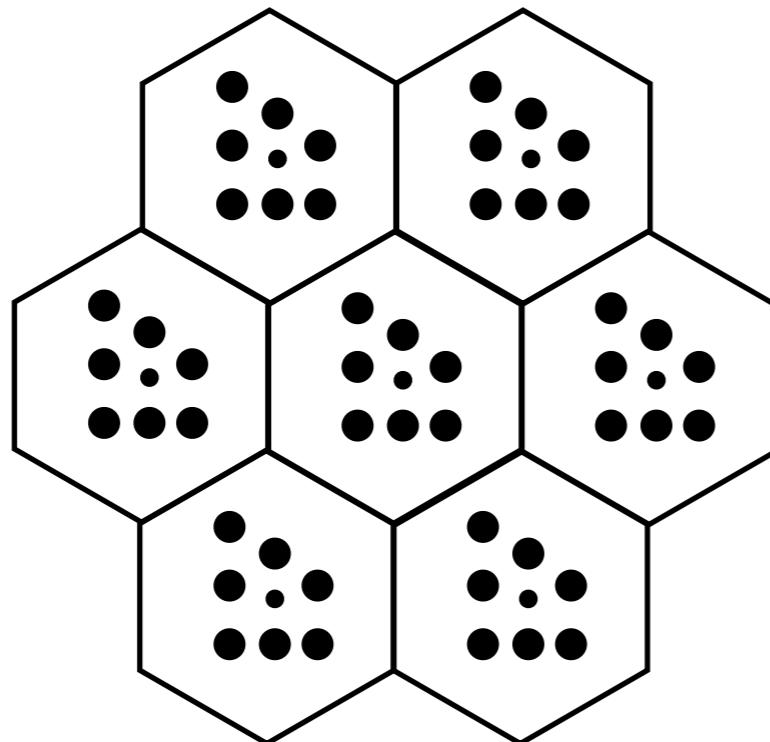


R8 cell *white* and *sev* mutant

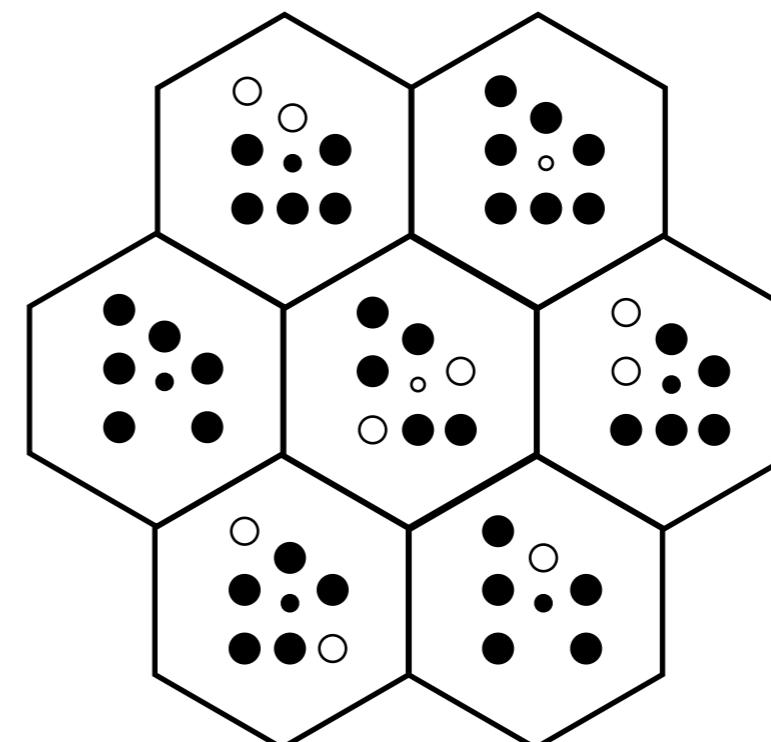


R1-R6 cells *white* and *sev* mutant

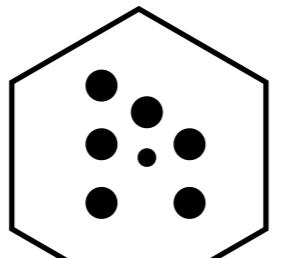
Wild-type



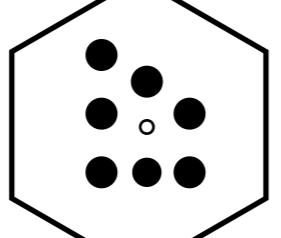
*sev* mutant



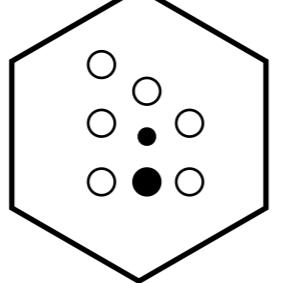
# ***boss* and *sev* are required in different R cells for R7 fate**



R7 cell *white* and *sev* mutant

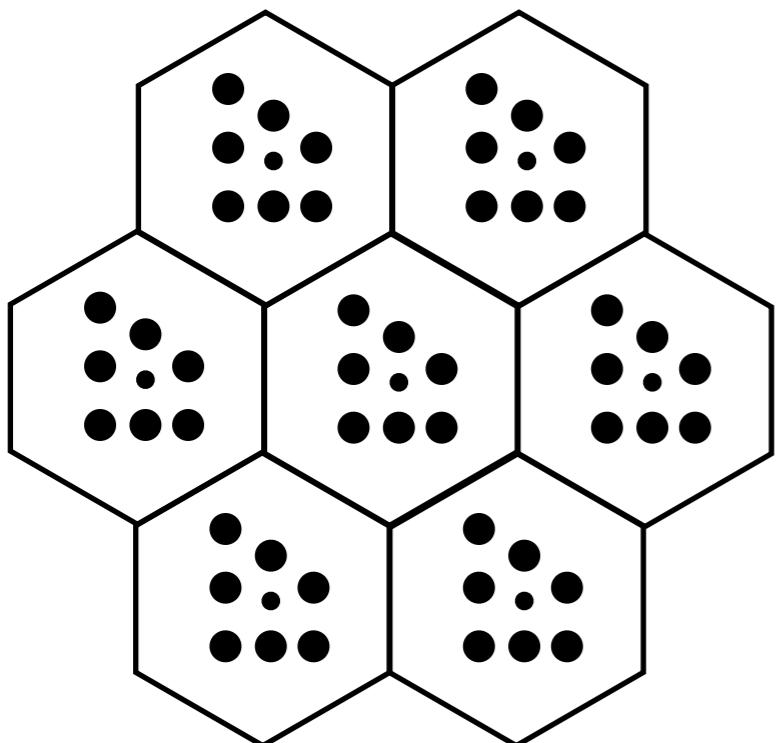


R8 cell *white* and *sev* mutant

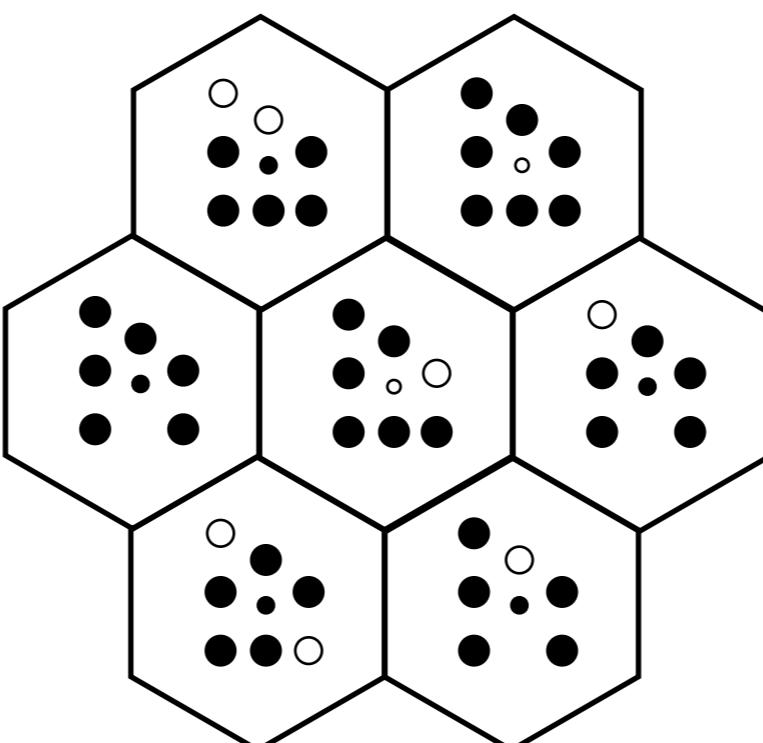


R1-R6 cells *white* and *sev* mutant

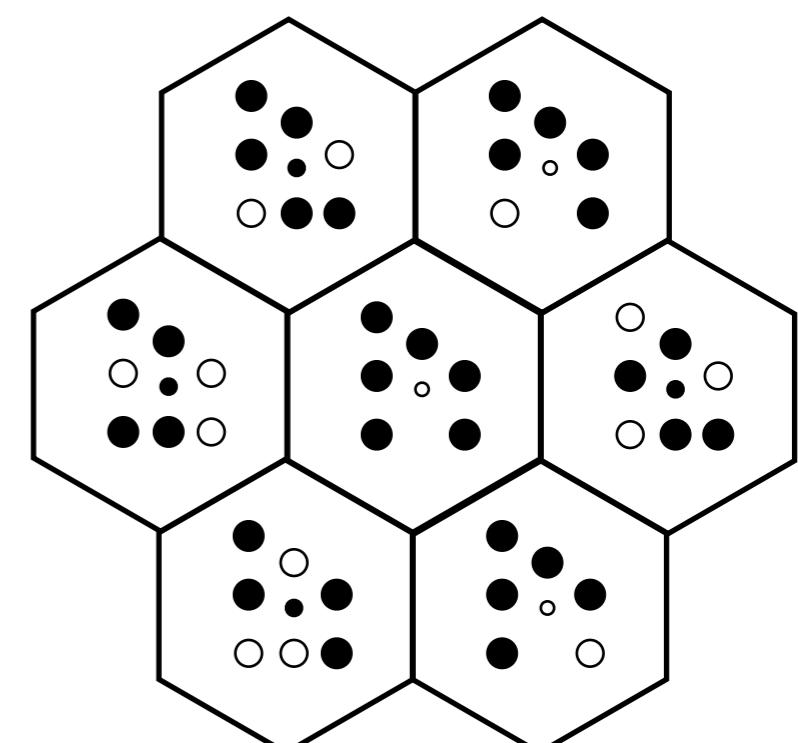
Wild-type



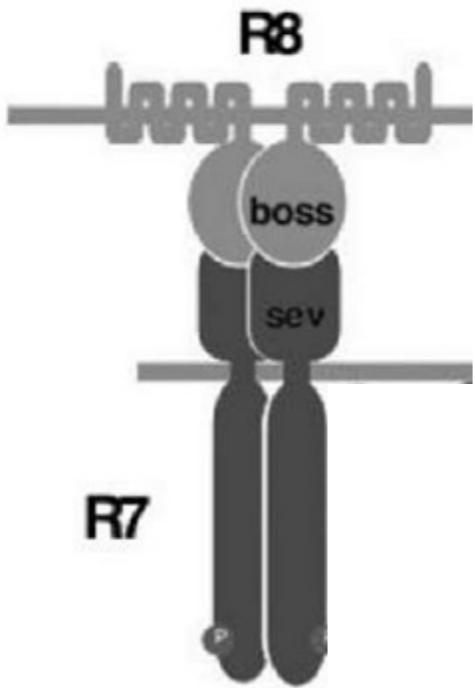
*sev* mutant



*boss* mutant

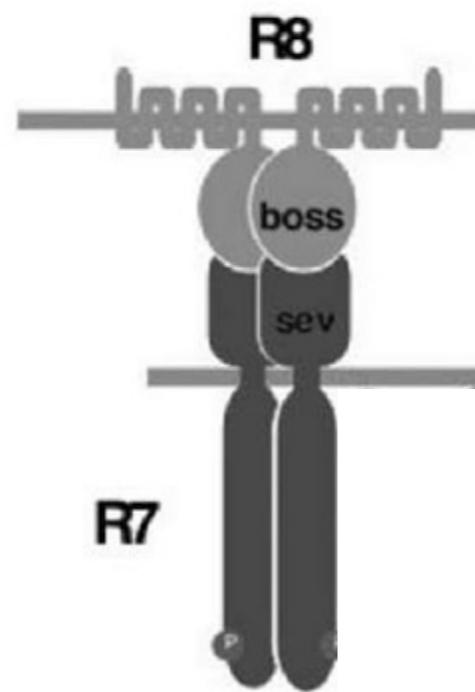
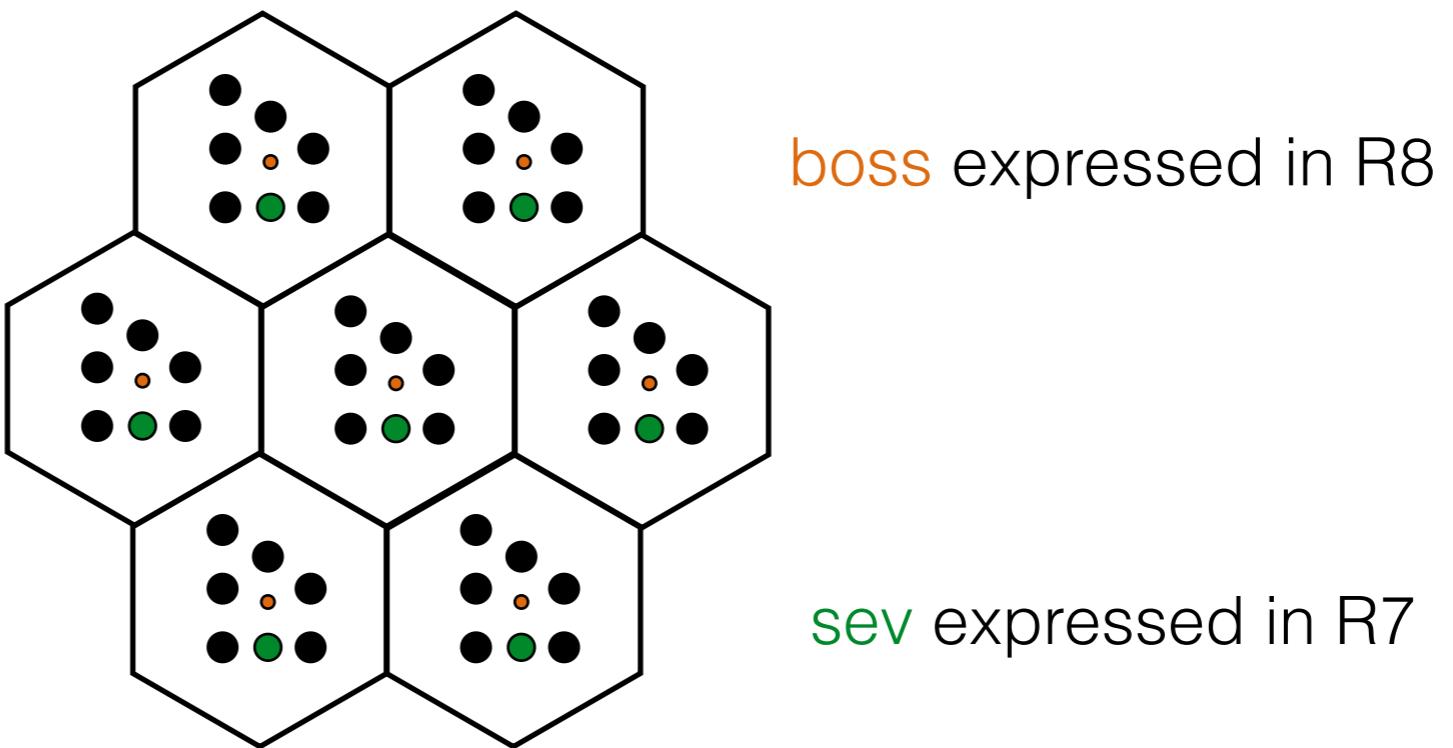


*boss* encodes  
a membrane-bound protein

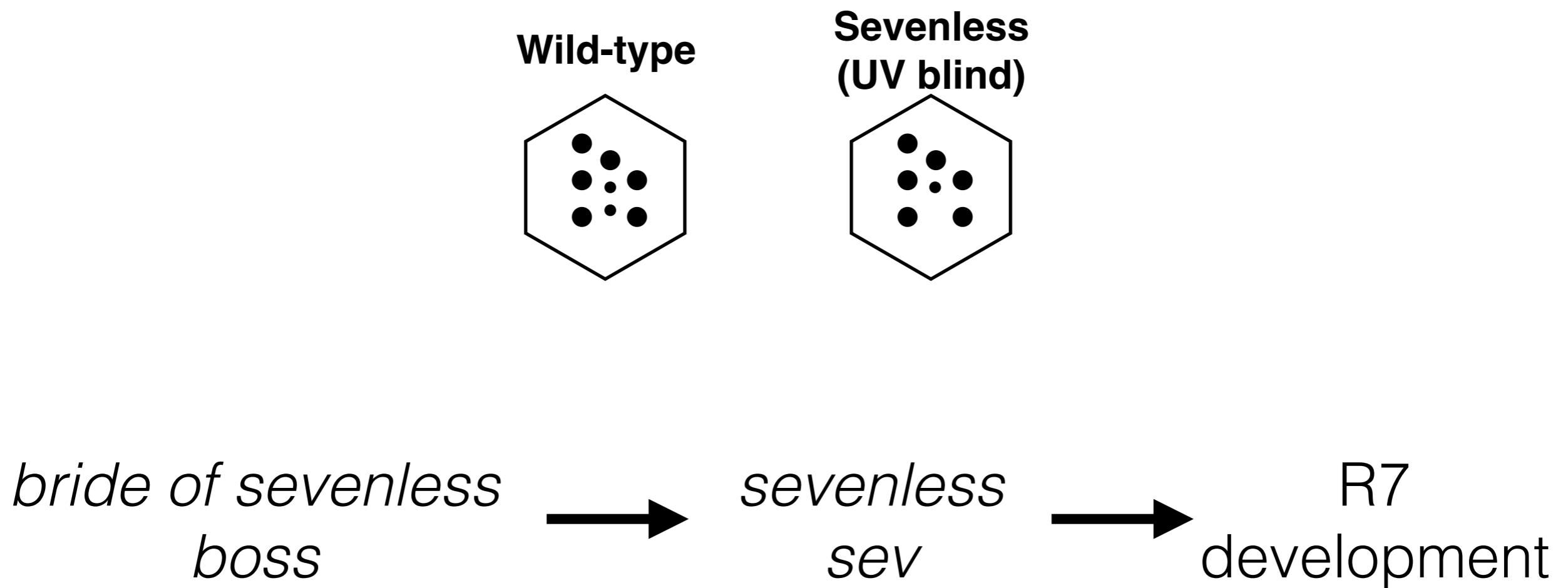


*sev* encodes  
a membrane receptor tyrosine kinase

# Expression of *sev* and *boss*



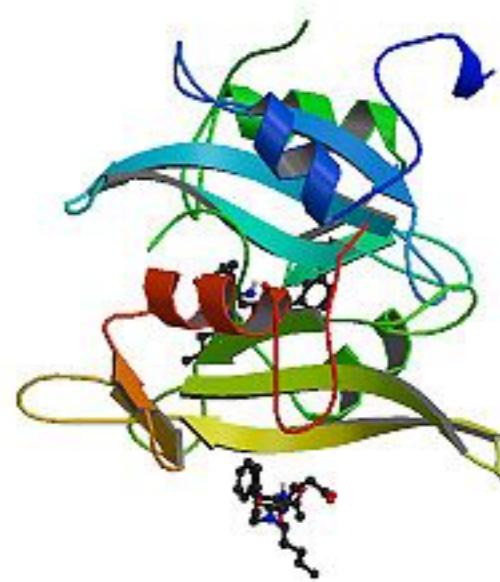
# UV blind mutants led to elements of signaling pathway



# Virus gene mutant from chicken to *Drosophila*



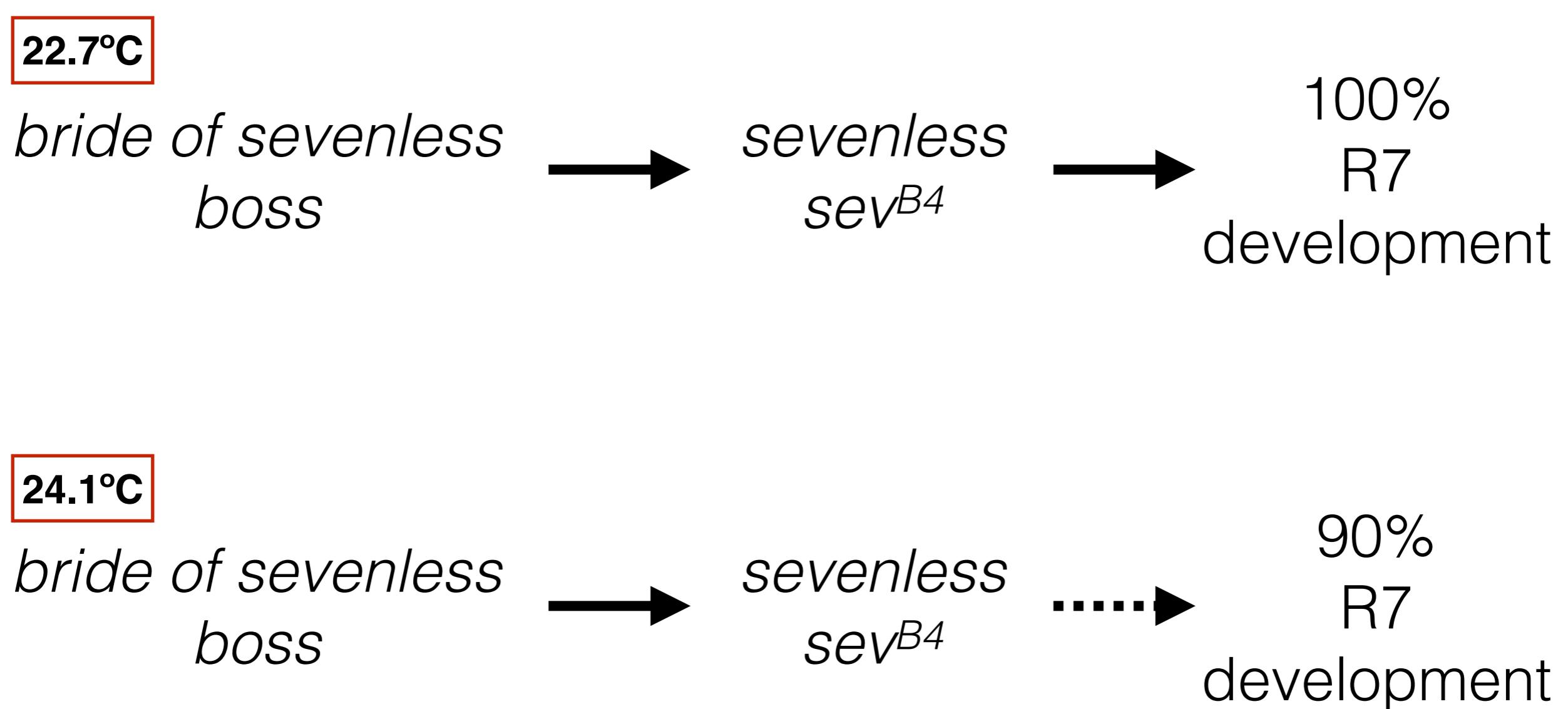
Peyton Rous discovered the first oncogenic virus in chicken



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



# **Strains used for the sensitized screen**

*sev<sup>d2</sup>* ; TM3 / CxD

*sev<sup>d2</sup>* = complete loss of *sev*

TM3 = third chromosome balancer

CxD = third chromosome balancer

P[*sev<sup>B4</sup>*]

*sev<sup>B4</sup>* = temperature-sensitive *sev* hypomorph

# Screen for dominant enhancers of sensitized phenotype

$sev^{d2}$ ; TM3 Sb P[ $sev^{B4}$ ]/ CxD

22.7°C

*bride of sevenless  
boss*



*sevenless  
 $sev^{B4}$*



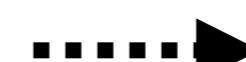
100%  
R7  
development

24.1°C

*bride of sevenless  
boss*



*sevenless  
 $sev^{B4}$*



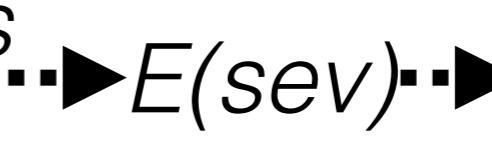
90%  
R7  
development

22.7°C

*bride of sevenless  
boss*

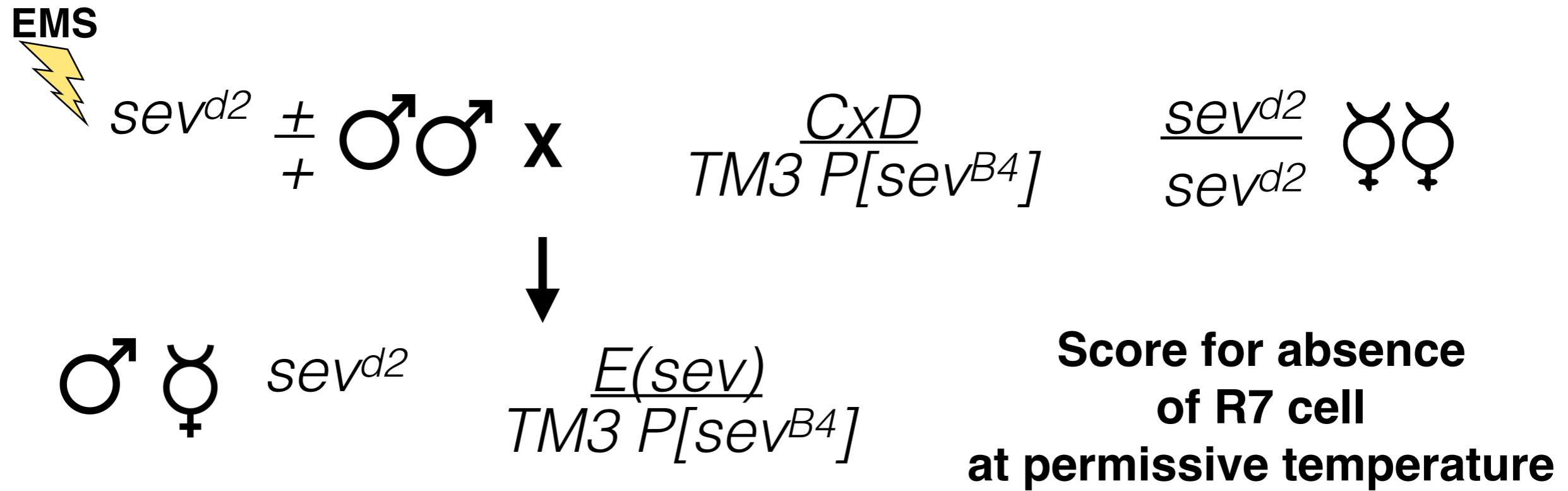


*sevenless  
 $sev^{B4}$*



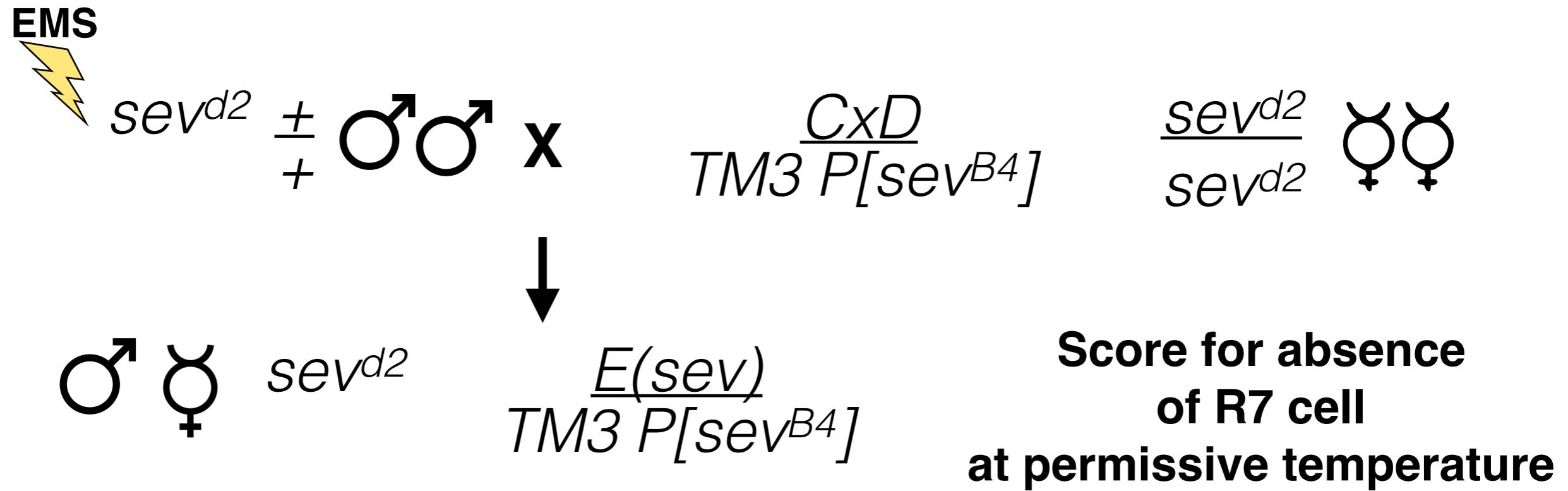
~10%  
R7  
development

# 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

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

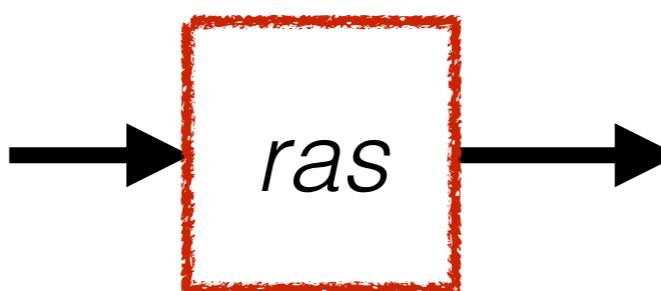
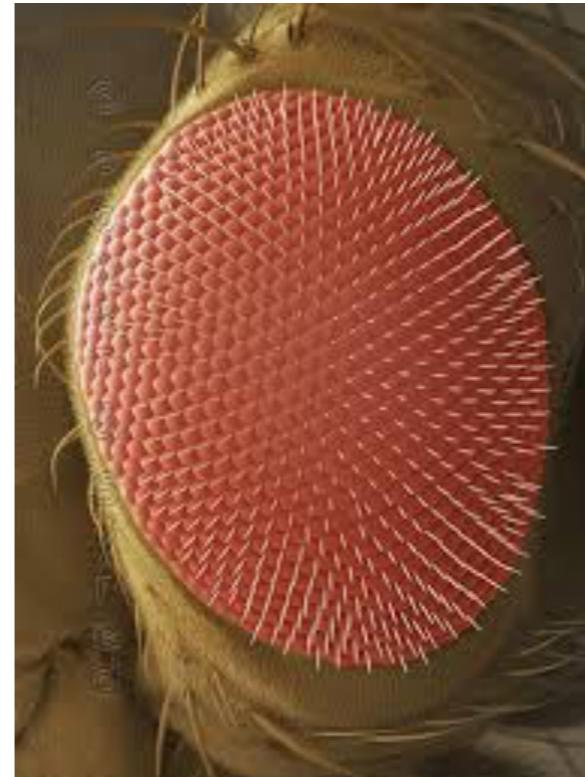
*bride of sevenless*  
*boss*



*sevenless*  
*sev*



*son of sevenless*  
*sos*

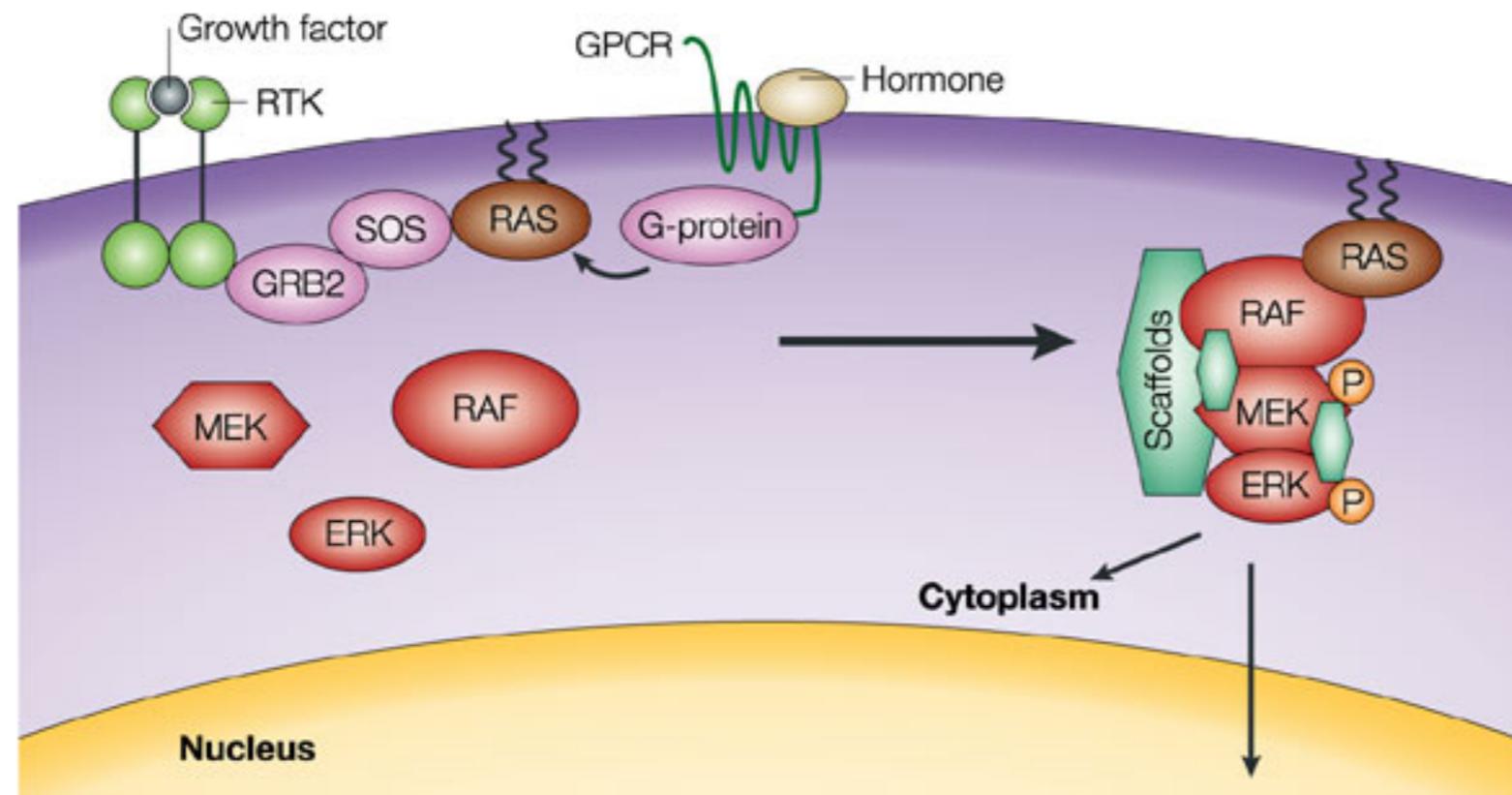


R7  
development

# **Methods to ascertain cell autonomy**

1. Expression of gene product in specific cell or tissue and look for rescue of a mutant phenotype
2. Lineage loss of unstable DNA that expresses the gene product and rescues a mutant phenotype (*C. elegans*)
3. Mitotic recombination to create clones of cells that express the gene product and rescue the mutant phenotype (*Drosophila*)

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



Nature Reviews | Molecular Cell Biology

We NEED basic research for this reason!