Bio393: Genetic Analysis

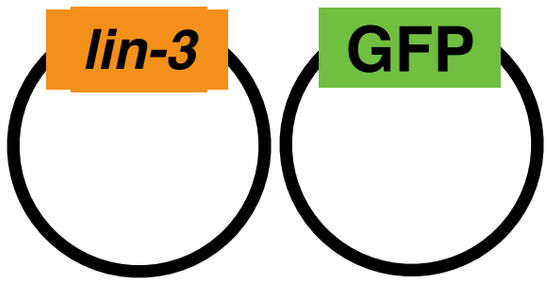
Final review session

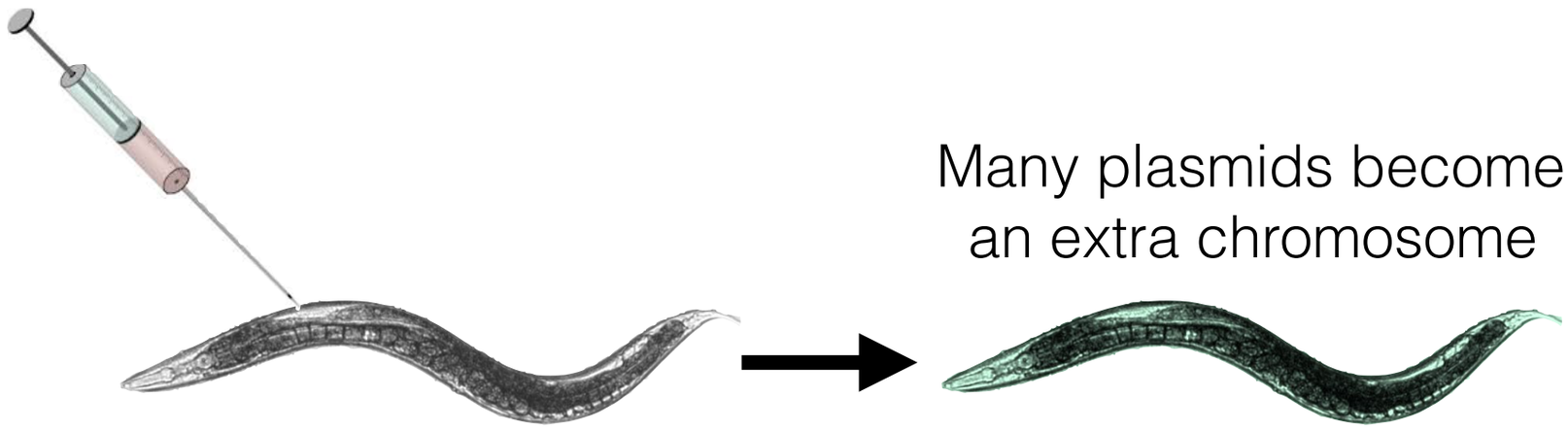
What is the logic behind cell autonomy experiments?

What can mitotic recombination experiments tell us?

Autonomy experiments tell us in what cell type a gene acts/functions in a complex animal or plant

LIN-3 is expressed in the AC; does it function there?



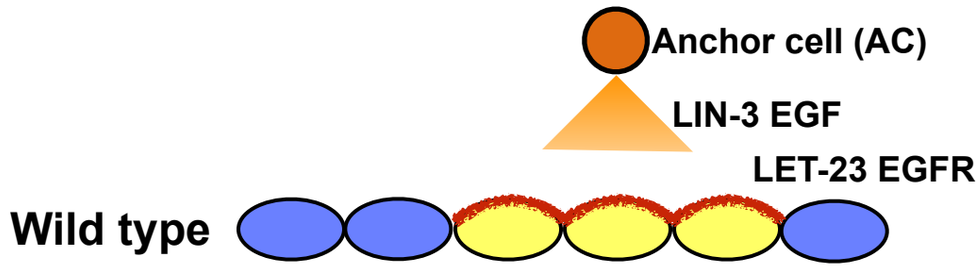


lin-3(0)
Vul

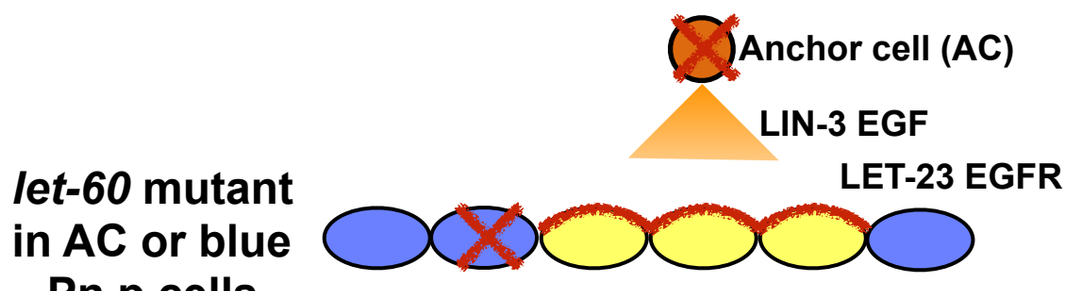
lin-3(0); lin-3(+++)
Wild-type or Muv

Genotype	Phenotype	
lin-3(0)	Vul	
lin-3(0); lin-3(+++)	Wild-type	
lin-3(0); vulval cell:lin-3(+++)	Vul	Expression of *lin-3* in vulval cells
lin-3(0); intestine:lin-3(+++)	Vul	Expression of *lin-3* in the intestine
lin-3(0); neurons:lin-3(+++)	Vul	Expression of *lin-3* in the neurons
lin-3(0); AC:lin-3(+++)	Wild-type	Expression of *lin-3* in the AC

Cell autonomy of *let-60*

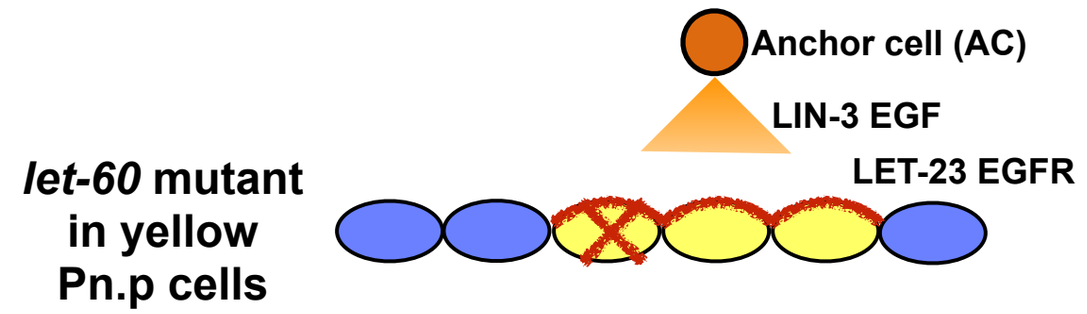


Cell autonomous action



Wild-type vulval phenotype

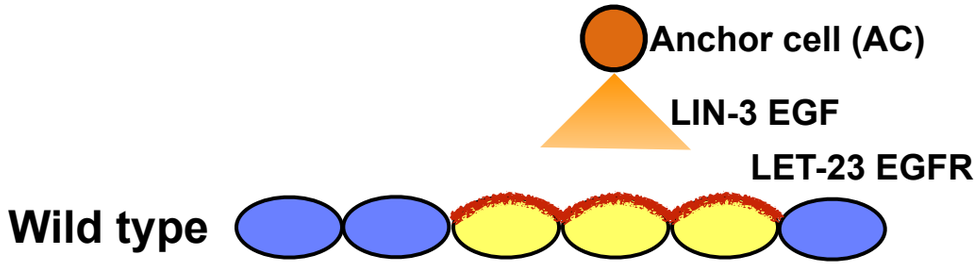
X = mutant cell



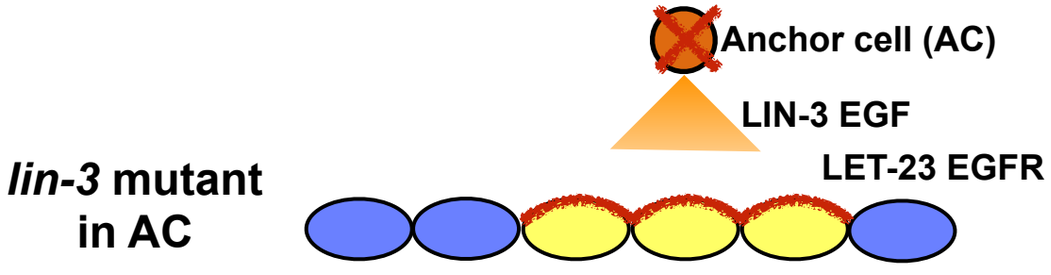
Mutant vulval phenotype

A cell autonomous trait is a trait in a multicellular organism in which only genotypically mutant cells have the mutant phenotype

Cell autonomy of *lin-3*

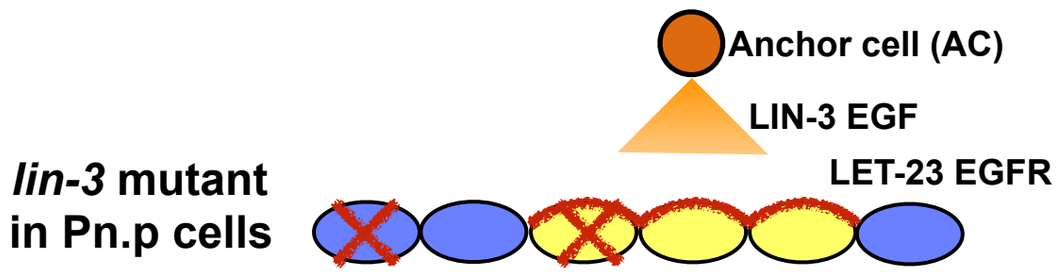


Cell non-autonomous action



Mutant vulval phenotype

= mutant cell



Wild-type vulval phenotype

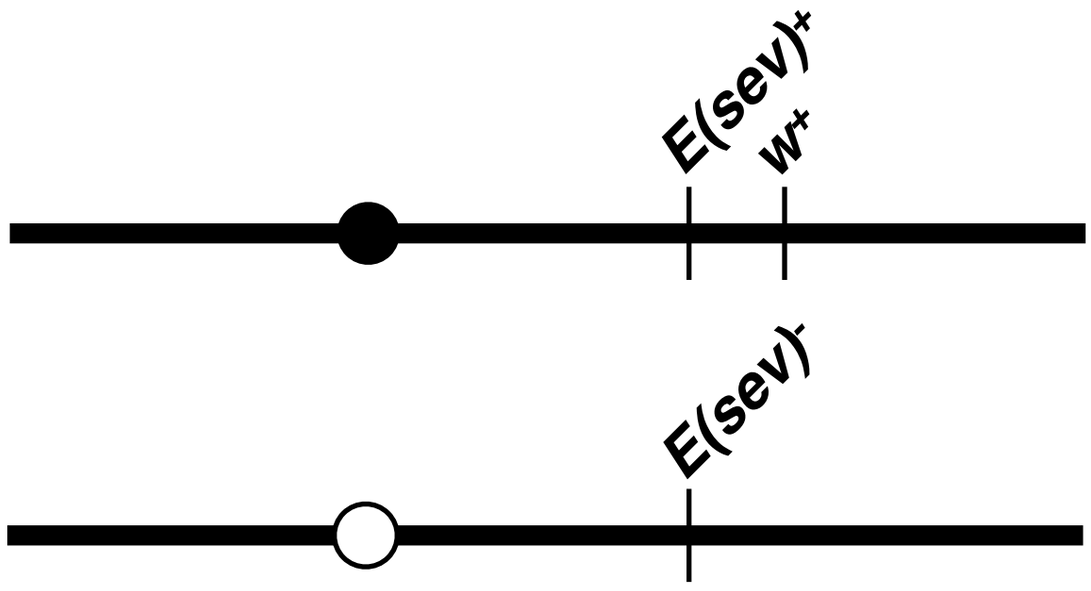
A cell autonomous trait is a trait in a multicellular organism in which only genotypically mutant cells have the mutant phenotype

Are genes required in ommatidia for cell viability?

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

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

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



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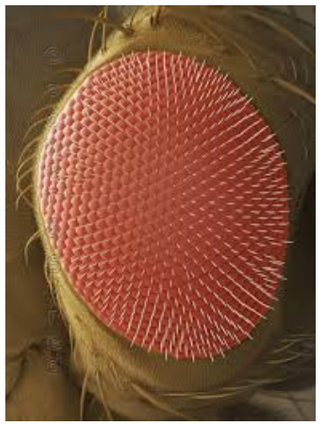
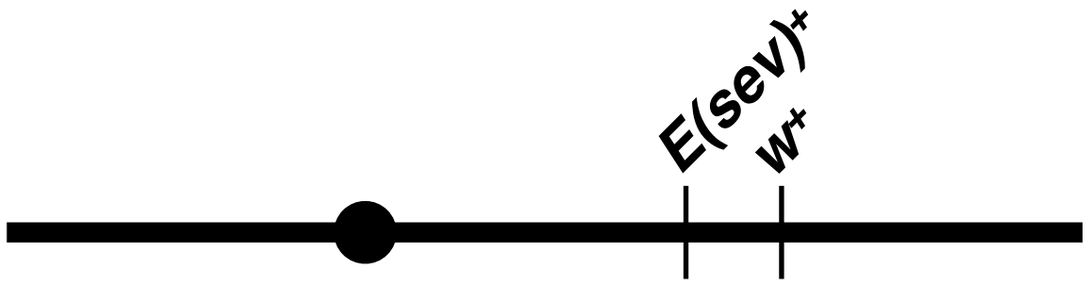
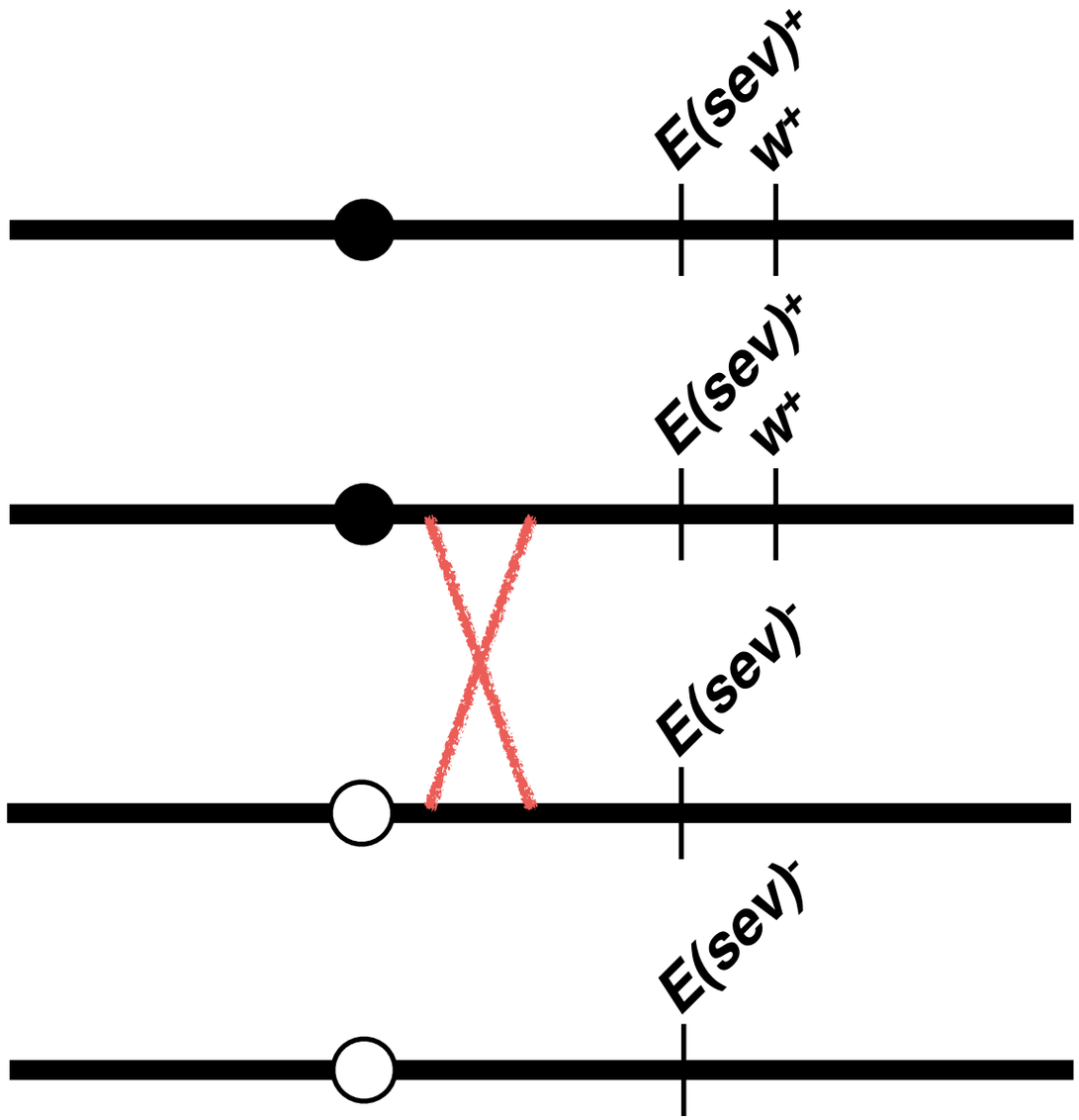


During mitosis for the cells that make up the eye, recombination can occur to repair double-strand breaks.





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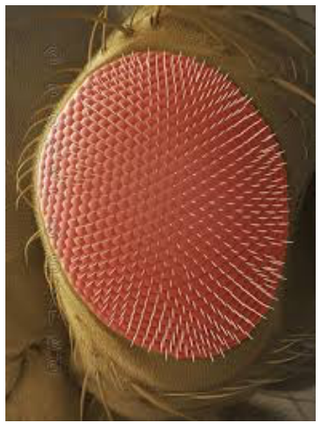

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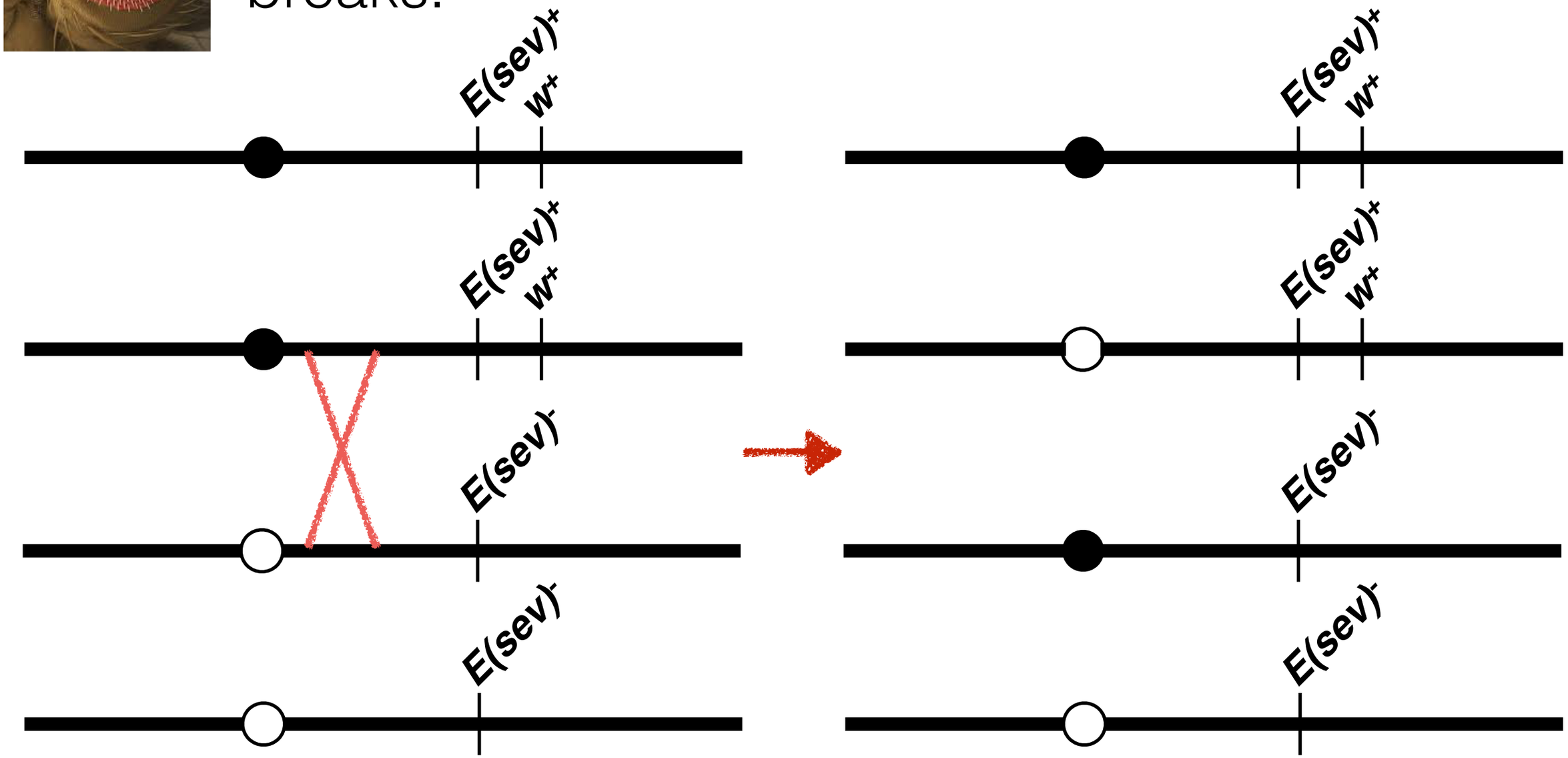

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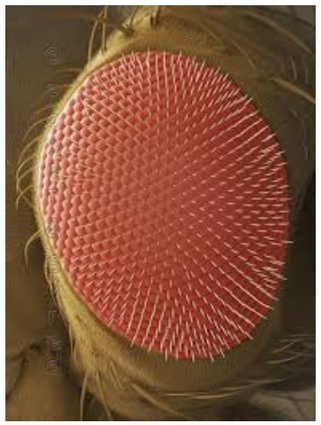

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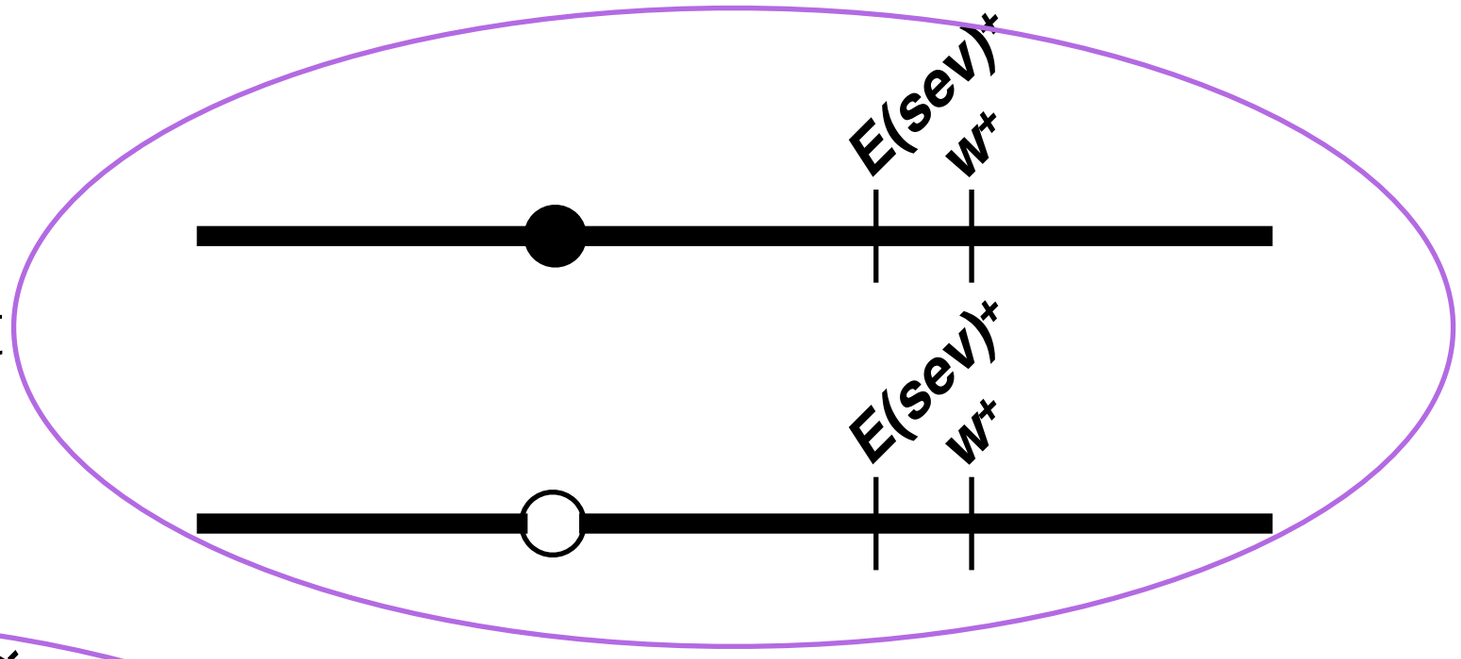
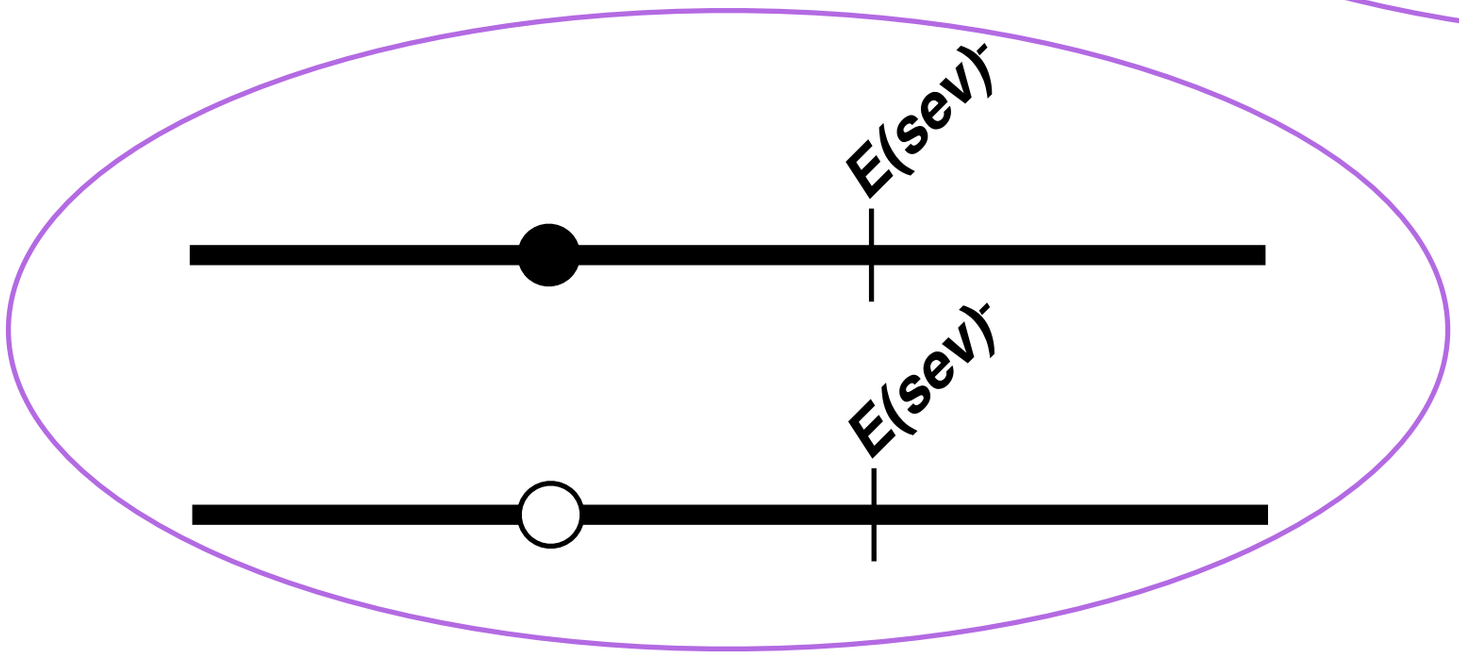
E(sev) WT and pigment

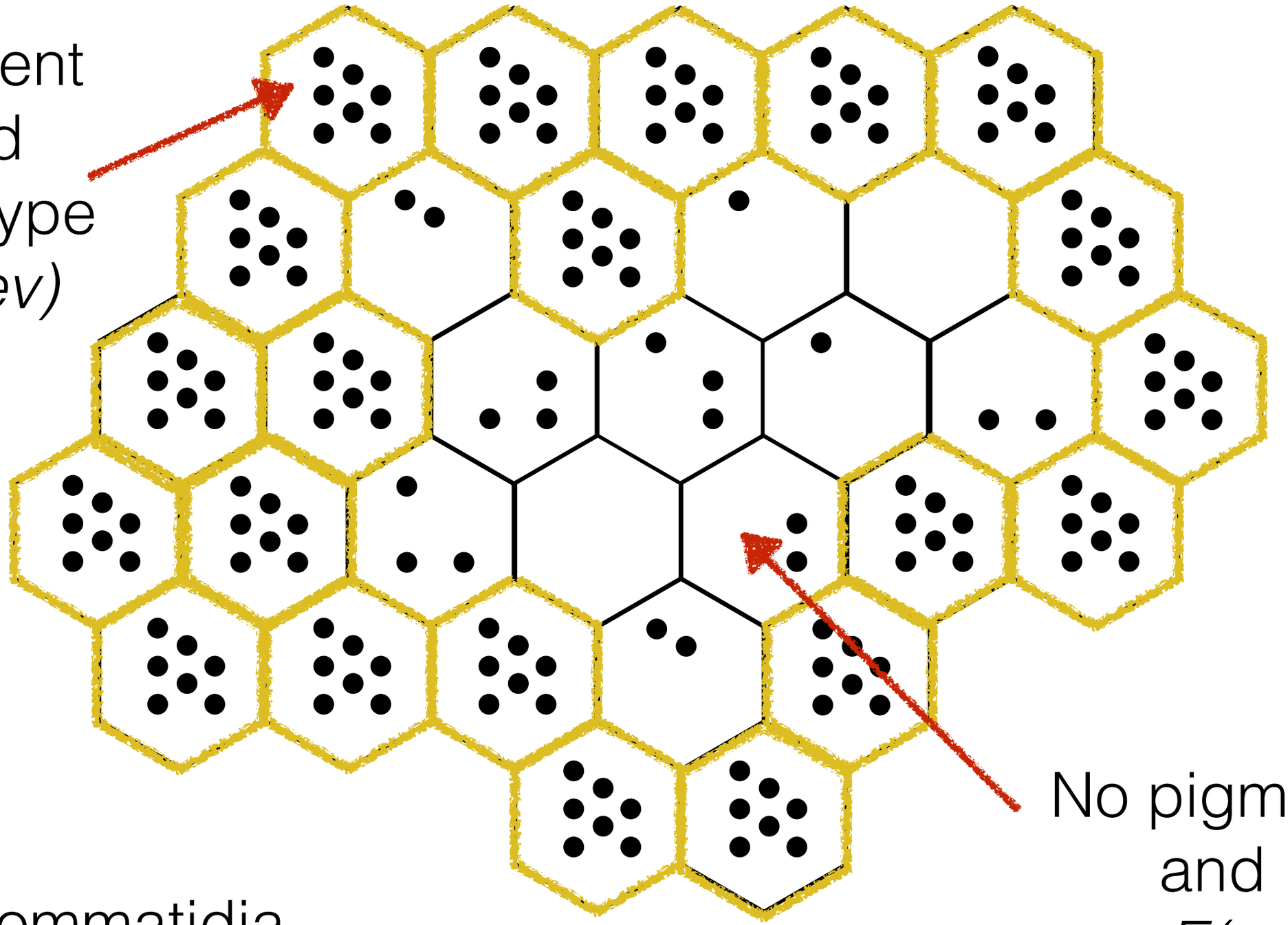




E(sev) mutant and no pigment

Are genes required in ommatidia for cell viability?

Pigment and wild-type *E(sev)*



No pigment and no *E(sev)*

Mutant ommatidia in a background of wild-type ommatidia

Behavioral genetics in non-model organisms

What is the average and standard deviation of autosome relatedness for non-twin siblings?

50% average with low standard deviation,
but what about population relatedness?

Many diseases have several varieties that carry slightly different phenotypes. To what extent does this complicate the genetic analysis of diseases?

A lot - phenotype is everything!

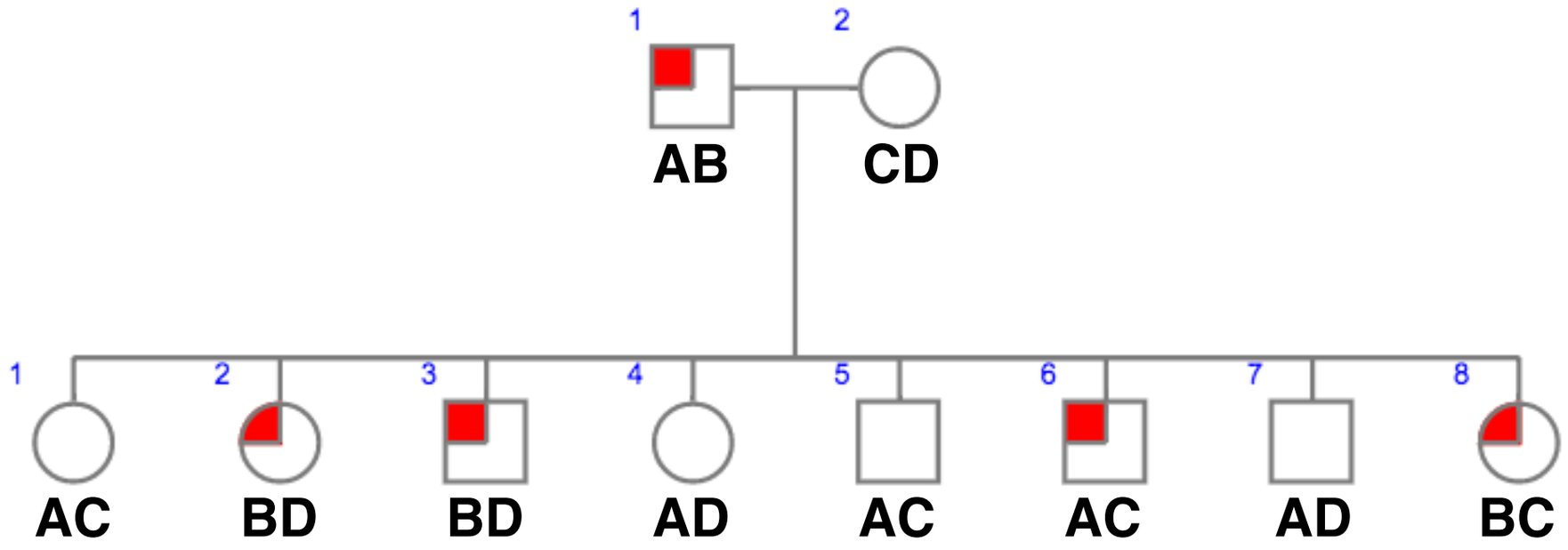
Some disease have strong environmental input.
Other diseases are caused by mutations in different genes.

How would one look at linkage of a non-autosomal dominant allele?

Most problems are autosomal dominant disorders

Problem set #3 problem #2 was X-linked recessive

Linkage is reported as a log of the odds ratio or LOD



Unphased linkage equation (each probability is of a gamete)

$$LOD = \log_{10} \frac{\frac{1}{2}((1 - \theta)^{NR} \times \theta^{R}) + \frac{1}{2}((1 - \theta)^{NR} \times \theta^{R})}{(0.5^{(NR + R)})}$$

For autosomal recessive disorder, you have twice the probabilities to calculate. Each chromosome is parental or recombinant.

Linkage disequilibrium

How to calculate LD? An example

$r^2 = (D_{AB})^2 / (p_A * (1 - p_A) * p_B * (1 - p_B))$ Remember $D_{AB} = p_{AB} - p_A * p_B$

What is the disequilibrium between two markers A and B with two forms A1 or A2 and B1 or B2?

We genotype 1000 people to get:

Haplotype	Number
A1B1	600
A1B2	100
A2B1	200
A2B2	100

Convert to numbers of individuals into haplotype frequencies:

Haplotype	Number	Frequency
A1B1	600	0.6
A1B2	100	0.1
A2B1	200	0.2
A2B2	100	0.1

How to calculate LD? An example

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Frequencies of haplotypes:

Haplotype	Number	Frequency
A1B1	600	0.6
A1B2	100	0.1
A2B1	200	0.2
A2B2	100	0.1

Convert to frequencies of alleles:

Allele	Number	Frequency
A1	700	0.7
A2	300	0.3
B1	800	0.8
B2	200	0.2

$p_{A1} = p(A1B1) + p(A1B2)$
$p_{A2} = 1 - p_{A1}$
$p_{B1} = p(A1B1) + p(A2B1)$
$p_{B2} = 1 - p_{B1}$

How to calculate LD? An example

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Convert to frequencies of alleles:

$p_{A1} = p(A1B1) + p(A1B2)$
$p_{A2} = 1 - p_{A1}$
$p_{B1} = p(A1B1) + p(A2B1)$
$p_{B2} = 1 - p_{B1}$

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$D_{AB} = 0.6 - 0.7 * 0.8 = 0.04$

$r^2 = 0.04^2 / (0.7 * 0.3 * 0.8 * 0.2) = 0.048$

Anything else?