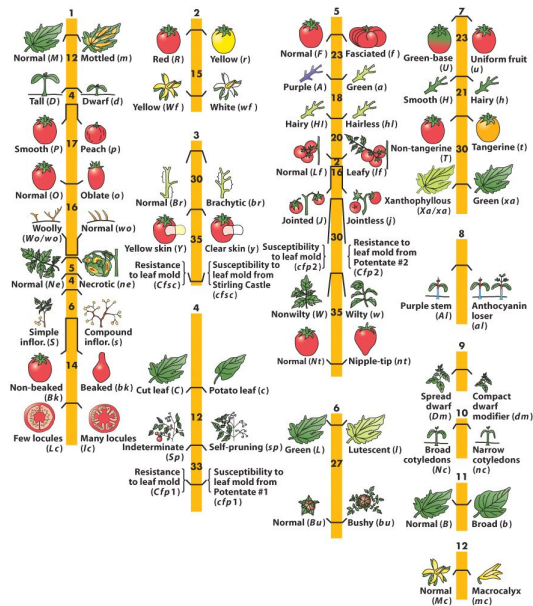


Transmission patterns of linked genes



Linkage, recombination and gene mapping

Why are linkage relationships important?

Linkage and independent assortment
- statistical tests of hypotheses

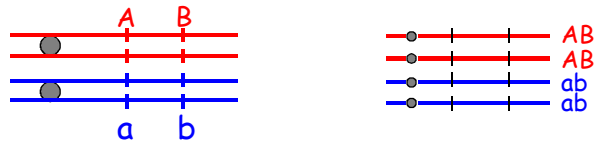
Recombination mapping - visible markers
- detection
- calculation of genetic distance
- genetic maps vs physical maps
- correcting map distances

Transmission patterns of linked genes

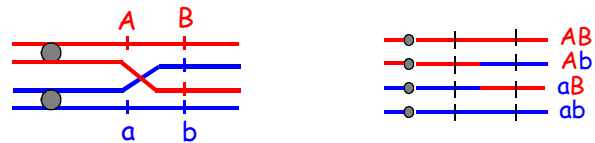
alleles of genes on the same chromosome
tend to be inherited as a group, especially
when close together

new combinations of alleles at different loci
are produced by recombination

No Recombination



With Recombination



Transmission patterns of linked genes

alleles of genes on the same chromosome
tend to be inherited as a group, especially
when close together

new combinations of alleles at different loci
are produced by recombination

*for a given pair of loci, product of most meioses
will be non-recombinant (parental)

*recombination detectable only in individuals
heterozygous at all loci

in crosses, identify linked loci by non-mendelian ratios

- 2 common classes (*parentals*)
- 2 uncommon classes (*recombinants*)

Bateson and Punnet's discovery of genetic linkage

flower color: purple (P) or red (p) both were autosomal with
pollen shape: long(L) or round (l) complete dominance

but, dihybrid crosses produced anomalous F₂ ratios

Phenotype	Genotype	Number of Progeny	
		Observed	Expected (9:3:3:1 ratio)
Purple, long	<i>P-L-</i>	4831	(6952)(9/16) = 3910.5
Purple, round	<i>P-ll</i>	390	(6952)(3/16) = 1303.5
Red, long	<i>ppL-</i>	393	(6952)(3/16) = 1303.5
Red, round	<i>ppll</i>	1338	(6952)(1/16) = 434.5
		6952	6952.0

Bateson and Punnet's data do not fit the expected F₂ ratio

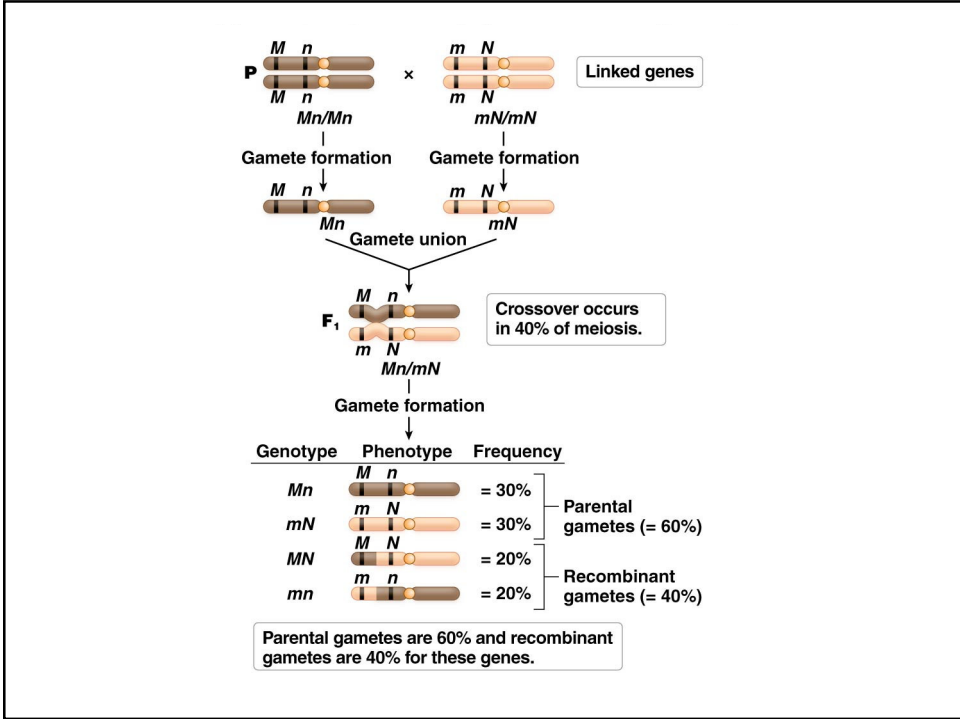
$$\chi^2_{\text{dof}} = \sum \frac{(\text{observed number} - \text{expected number})^2}{(\text{expected number})}$$

$$= \frac{(4831-3910.5)^2}{3910.5} + \frac{(390-1303.5)^2}{1303.5} + \frac{(393-1303.5)^2}{1303.5} + \frac{(1338-434.5)^2}{434.5}$$

$$= 216.68 + 640.19 + 635.99 + 1878.74$$

$$= 3371.6 \quad \text{degrees of freedom} = 4 - 1 = 3$$

$$\text{critical value} = 7.82, \quad p \ll 0.05$$



Drosophila melanogaster:

autosomal, recessive traits: ebony body (*e*)
spineless bristle (*sp*)

testcross: $e/+ \ sp/+ \ \text{♀} \times \ e/e \ sp/sp \ \text{♂}$

♂ gamete	♀ gamete	phenotype	exp <i>f</i>	obs <i>f</i>
$e \ sp$	$e \ sp$	ebony spineless		
$e \ sp$	$+ \ +$	wild type		
$e \ sp$	$e \ +$	ebony		
$e \ sp$	$+ \ sp$	spineless		

-independent assortment

$AaBb \longrightarrow$ types of gametes??

$pr(AB) = pr(ab) = pr(Ab) = pr(aB) = \frac{1}{4}$

testcross: $e/+ \ sp/+ \ ♀ \times \ e/e \ sp/sp \ ♂$

↓

$♂$ gamete	$♀$ gamete	phenotype	exp f	obs f
$e \ sp$	$e \ sp$	ebony spineless	250	59
$e \ sp$	$+ \ +$	wild type	250	71
$e \ sp$	$e \ +$	ebony	250	430
$e \ sp$	$+ \ sp$	spineless	250	440

parentals

recombinants

determining the recombination distance between genes:

RF = frequency of recombination

$$RF = \frac{\text{number of recombinant offspring}}{\text{total number of offspring}}$$

$$RF = (71 + 59)/1000$$

$$RF = 130/1000 = 0.13$$

$$\begin{aligned} \text{map distance} &= RF \times 100 = \text{map units (cM)} \\ 0.13 \times 100 &= 13 \text{ m.u.} \end{aligned}$$

Notation:

initial (null) hypothesis is that genes are unlinked

$e/e; sp/sp$ or $e/+; sp/+$

for genes known to be linked

$e\ sp/e\ sp$ or $e\ sp/++$ or $e\ +/+ sp$

σ^r gamete	♀ gamete	phenotype	exp f	obs #
$e\ sp$	$e\ sp$	ebony spineless	250	59
$e\ sp$	$++$	wild type	250	71
$e\ sp$	$e\ +$	ebony	250	440
$e\ sp$	$+ sp$	spineless	250	430

obs	e	+	tot
sp	59	430	489
+	440	71	511
tot	499	501	1000

exp	e	+	tot
sp	244	245	489
+	255	256	511
tot	499	501	1000

testing for linkage with the chi-square test

H_0 : genes are assorting independently

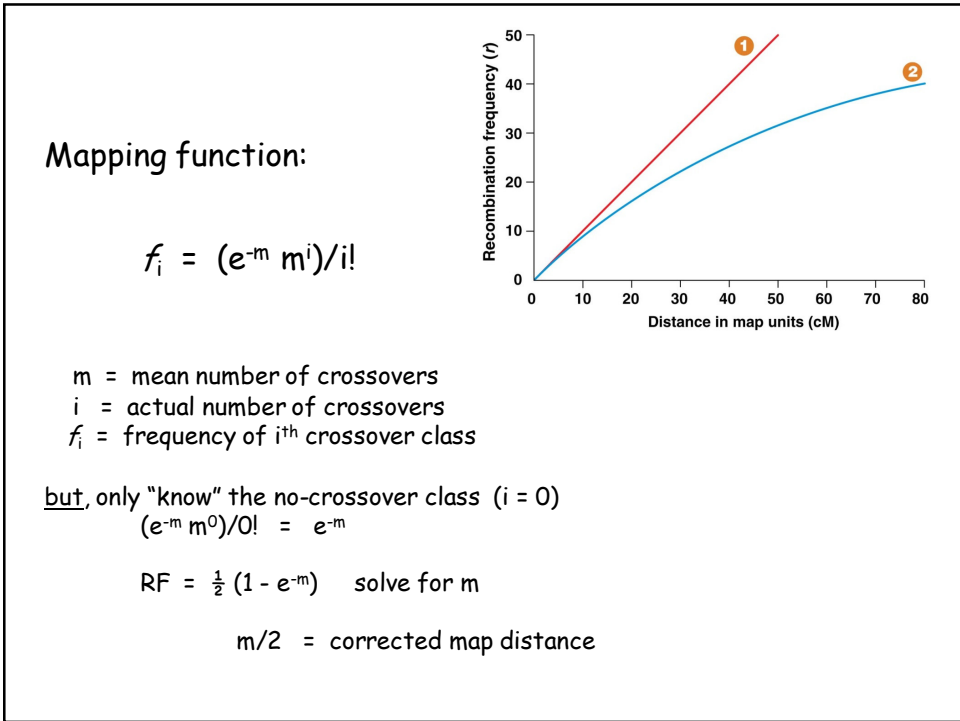
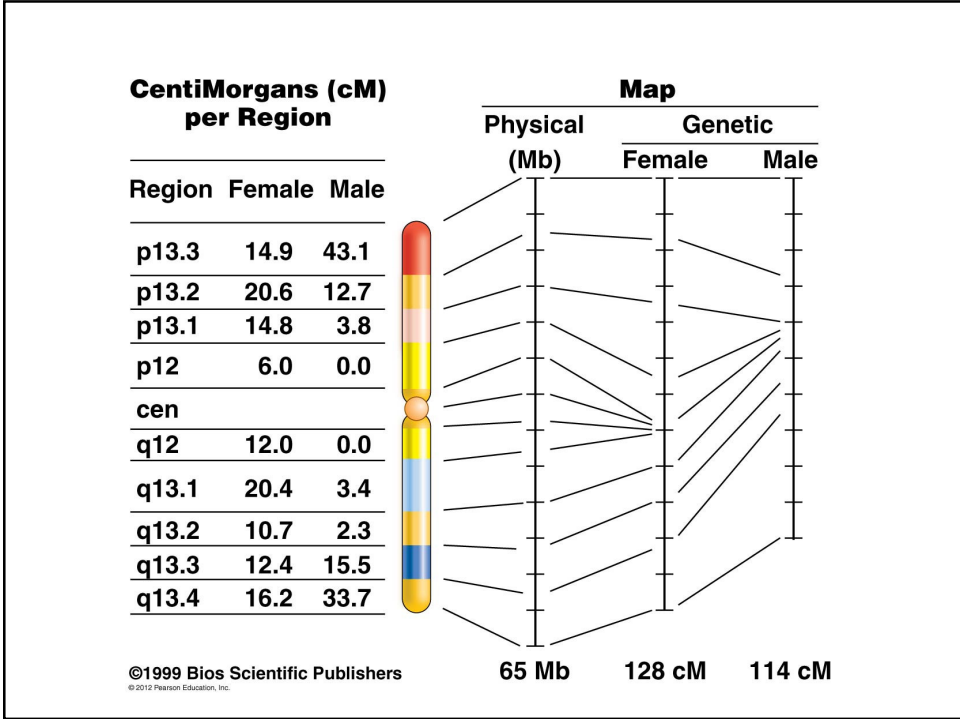
$$\chi^2_{\text{dof}} = \sum \frac{(\text{observed number} - \text{expected number})^2}{(\text{expected number})}$$

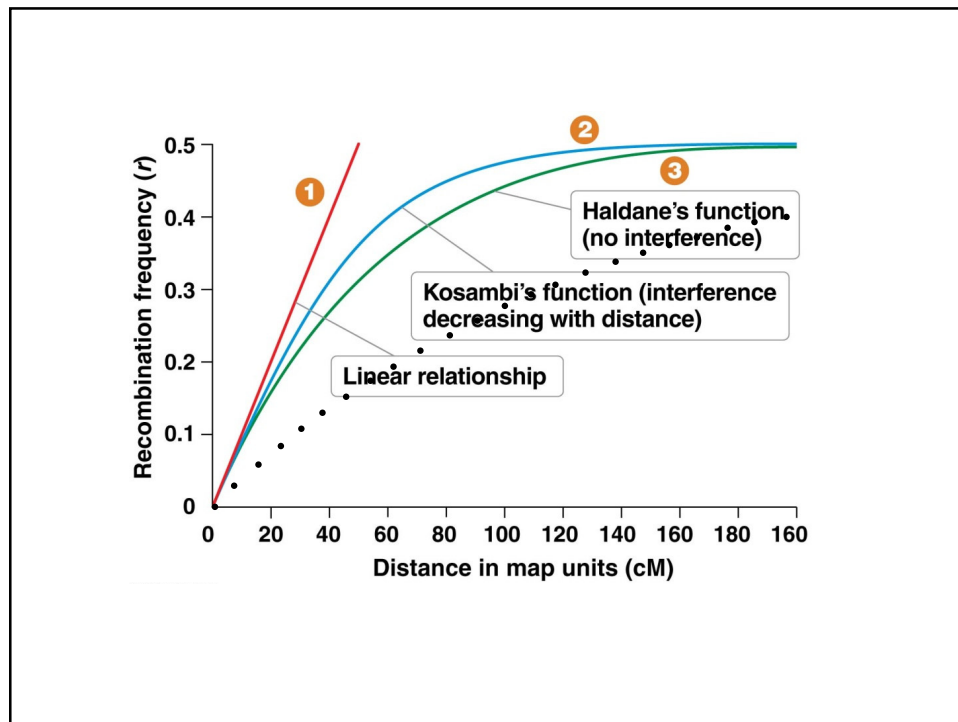
$$\begin{aligned} \chi^2_1 &= \frac{(430-245)^2}{245} + \frac{(71-256)^2}{256} + \frac{(59-244)^2}{244} + \frac{(440-255)^2}{255} \\ &= 139.7 + 133.7 + 134.7 + 134.2 \\ &= 542.3 \quad p \lll 0.05 \end{aligned}$$

σ^{r} gamete	f gamete	phenotype	exp f	obs #
<i>e sp</i>	<i>e sp</i>	ebony spineless	0.25	59 1
<i>e sp</i>	+ +	wild type	0.25	71 1
<i>e sp</i>	<i>e</i> +	ebony	0.25	430 4
<i>e sp</i>	+ <i>sp</i>	spineless	0.25	440 4

effects of sample size !

$$\text{Chi-square} = 3.60 \quad 0.05 < p < 0.10$$





mapping cross with visible markers: ≥ 3 loci

test cross: heterozygous female,
homozygous recessive male

linkage if two common offspring types

determine parental genotypes

calculate RF values (map distances) for pairs of genes

determine gene order (map)

σ^7 gametes	f gametes	progeny phenotype	#progeny	
ju str pi	ju + +	javelin	294	parentals
ju str pi	+ str pi	striped, pink	287	
ju str pi	ju str pi	javelin, striped, pink	140	recombinant
ju str pi	+ + +	wild type	139	
ju str pi	+ + pi	pink	66	
ju str pi	ju str +	javelin, striped	65	
ju str pi	ju + pi	javelin, pink	4	double crossover
ju str pi	+ str +	striped	5	

Take-home points

spatial arrangement of genes

- gene interactions
- genome evolution
- crop improvement

transmission patterns of linked genes

- most offspring will inherit the allele combinations present in their parents
- recombination is rare, detect numerically

from testcross progeny

- parental allele combinations (on the chromosome)
- genetic distance between linked loci
- gene order (genetic map)
- test with chi-square

linkage analysis is limited to genes that are close together
(non-linear relationship between estimated and actual distance);
mapping functions can improve estimates of genetic distance