



Ligaçāo e Mapeamento Cromossômico

LOCOS DE CARACTERÍSTICAS QUANTITATIVAS

HERANÇA QUANTITATIVA

Onde estão os genes que contribuem com as características quantitativas?

MAPEAMENTO CROMOSSÔMICO

LOCOS DE CARACTERÍSTICAS QUANTITATIVAS

MAPEAMENTO DE QTLs

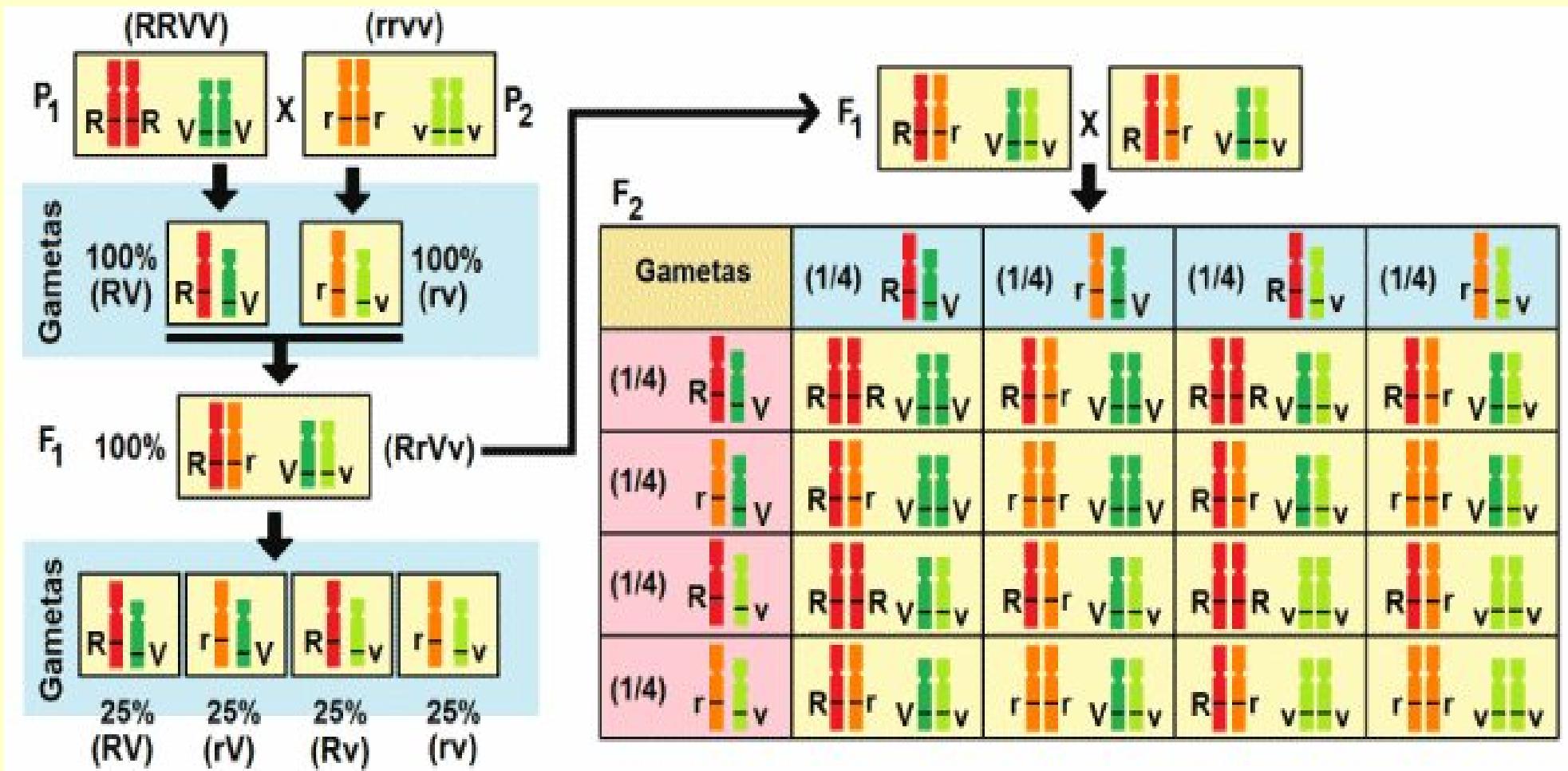
REQUER:

1. Cruzamento que resultará em uma população segregante;
2. Encontrar regiões conhecidas no genoma (mapa de ligação);
3. Correlação entre a característica fenotípica e as regiões genômicas

**MAPEAMENTO BASEADO EM
DESEQUILÍBRIO DE LIGAÇÃO**

Mas o que é um mapa de ligação?

SEGREGAÇÃO INDEPENDENTE



DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS

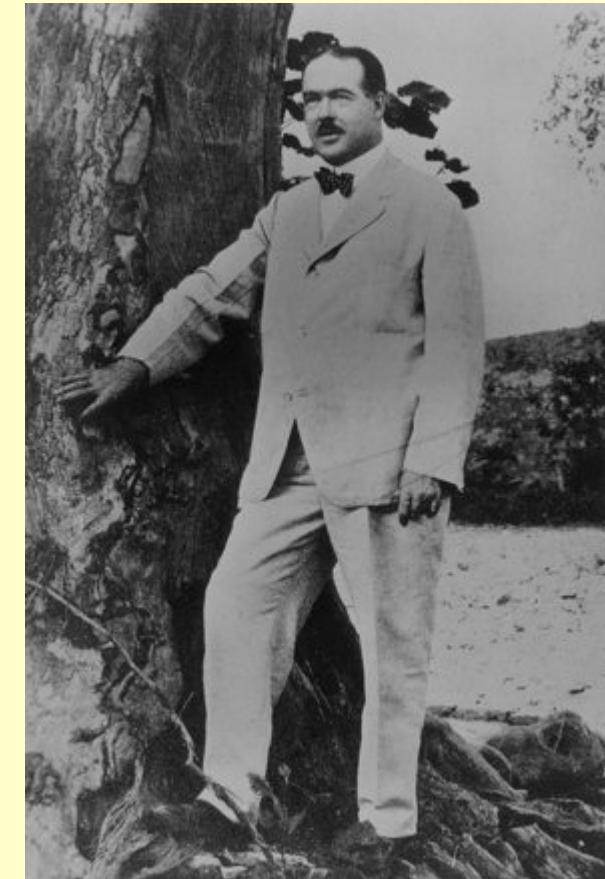
Segregação independente

vs

Desequilíbrio de ligação

Walter Sutton (1903)

- Há mais que um par de fatores nos cromossomos
- Se os cromossomos retém permanentemente suas individualidades, então todos os [alelo]morfos representados por qualquer cromossomo devem ser herdados juntos



Bateson, Saunders
e Punnett (1906)



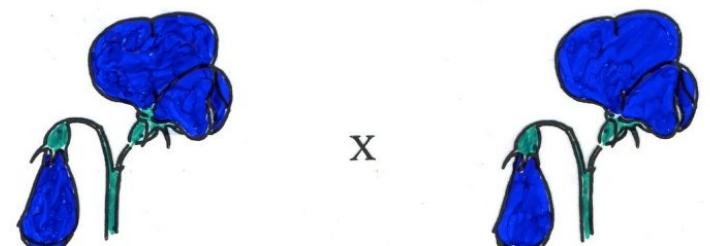
Ervilha-de-cheiro
(Lathyrus odoratus)

P



X

F₁



X

F₂



3

:

1

Ervilha-de-cheiro (*Lathyrus odoratus*)

Bateson, Saunders
e Punnett (1906)

Ervilha-de-cheiro
(*Lathyrus odoratus*)

P



X



F₁



X



F₂



3

:

1

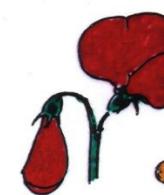
Ervilha-de-cheiro

(*Lathyrus odoratus*)

P



X



F₁



Esperado

9

3

3

1

Encontrado

11,8

1

1

3,26

Acoplamento e repulsão

Ervilha-de-cheiro
(*Lathyrus odoratus*)

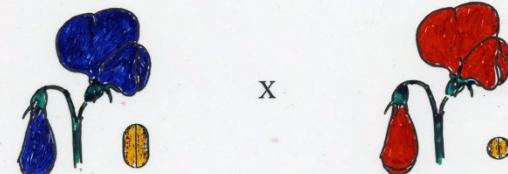
P



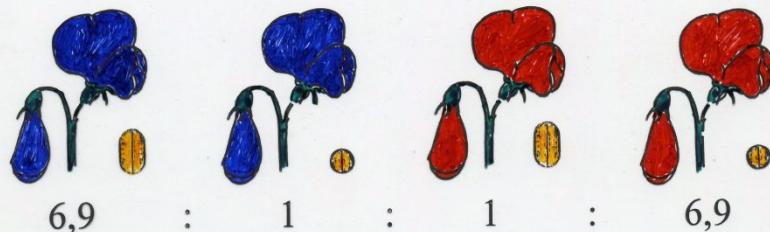
F₁



Cruzamento-teste

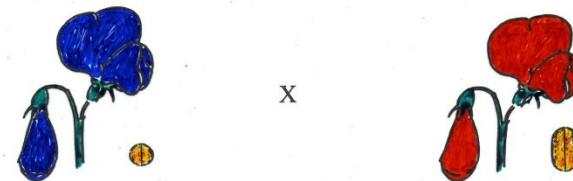


F₁

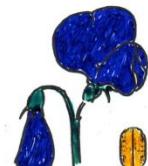


Ervilha-de-cheiro
(*Lathyrus odoratus*)

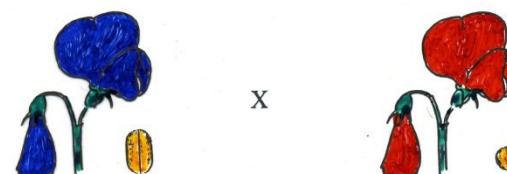
P



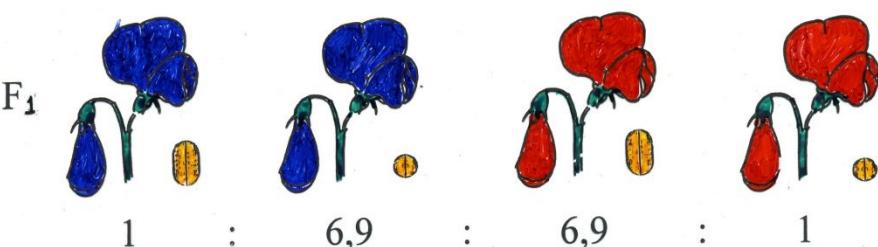
F₁



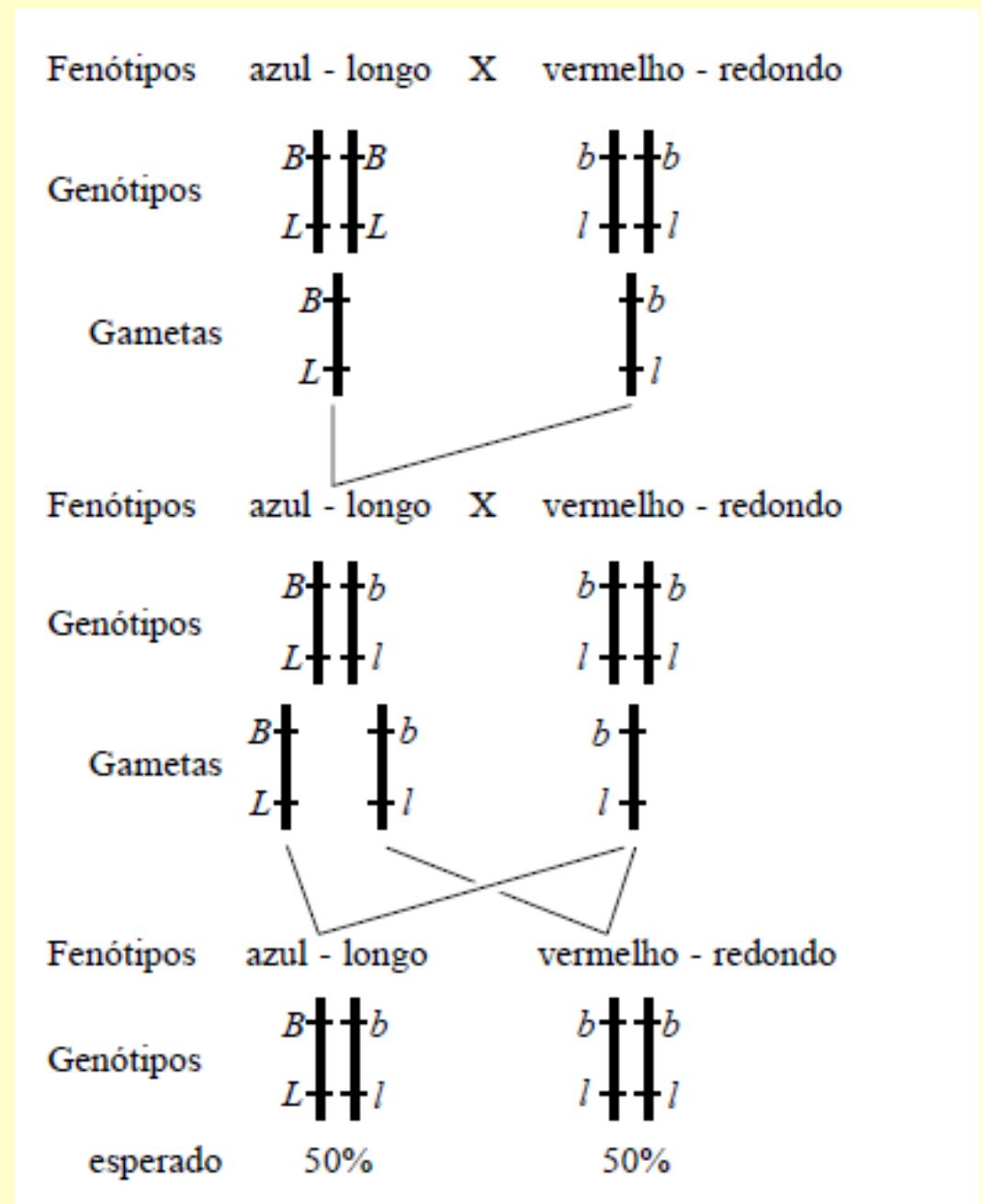
Cruzamento-teste



F₁

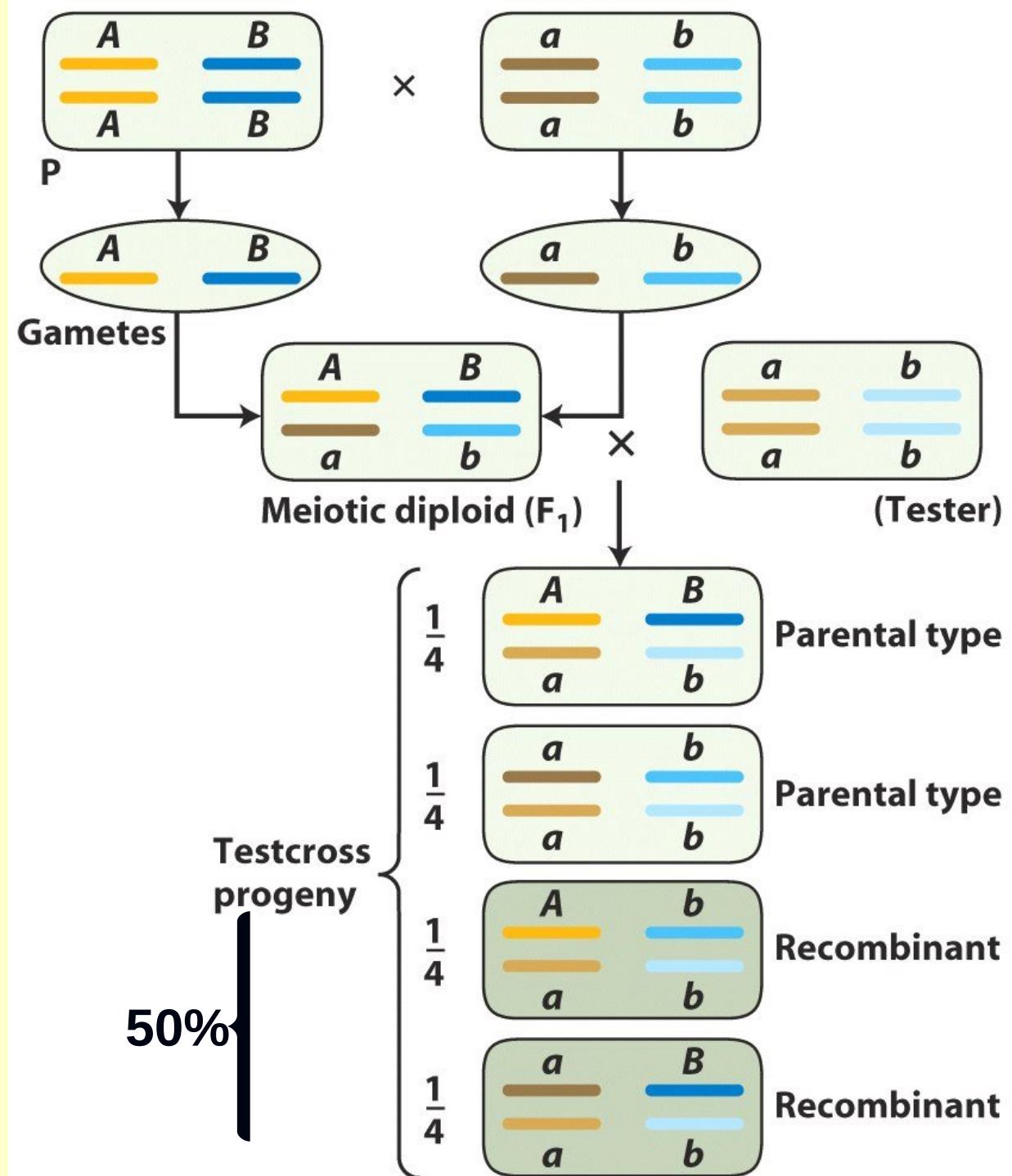


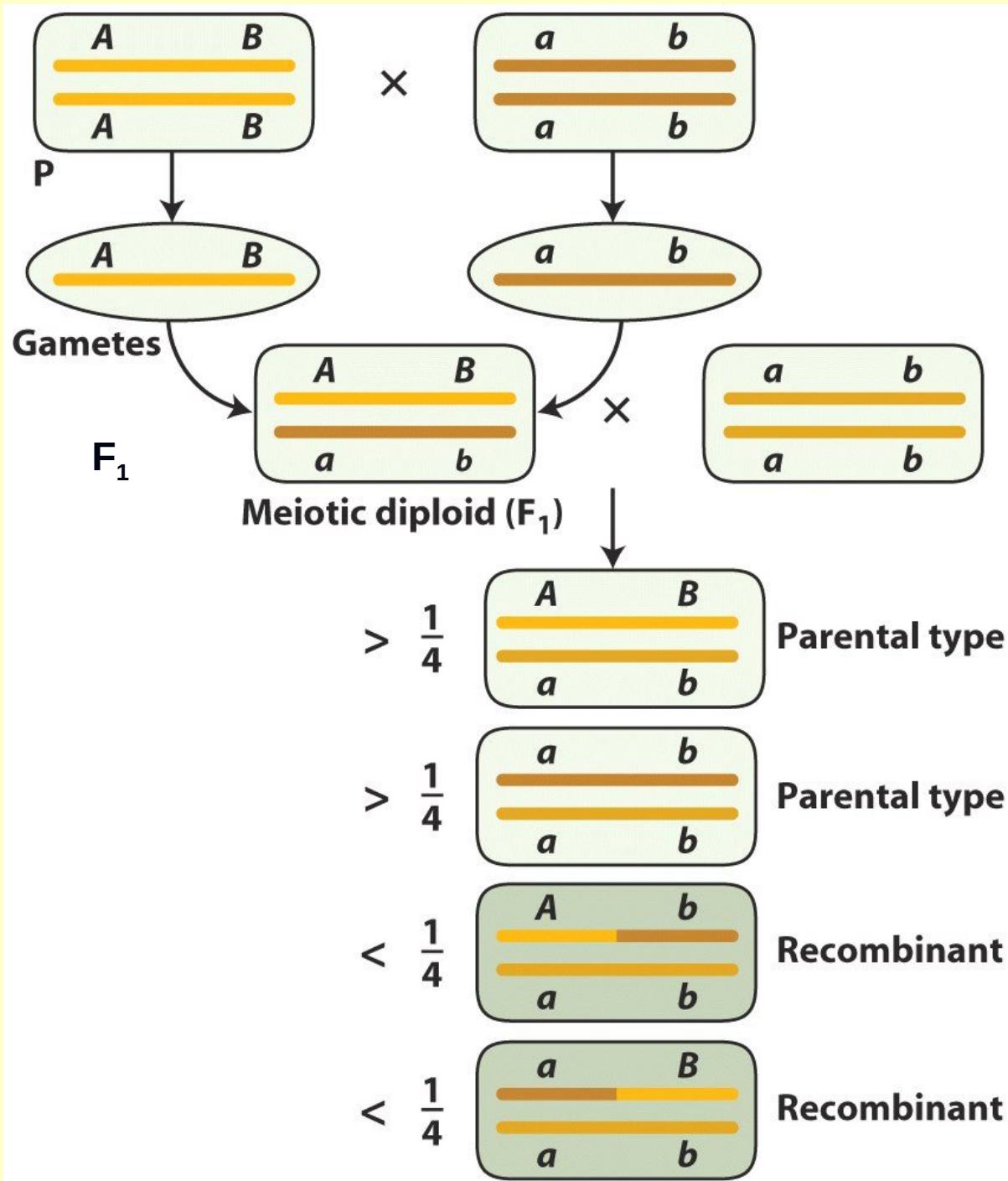
Testando a hipótese de Sutton de ligação total entre fatores



Ou seja, a hipótese de Sutton explica o acoplamento, mas...

cruzamento
teste

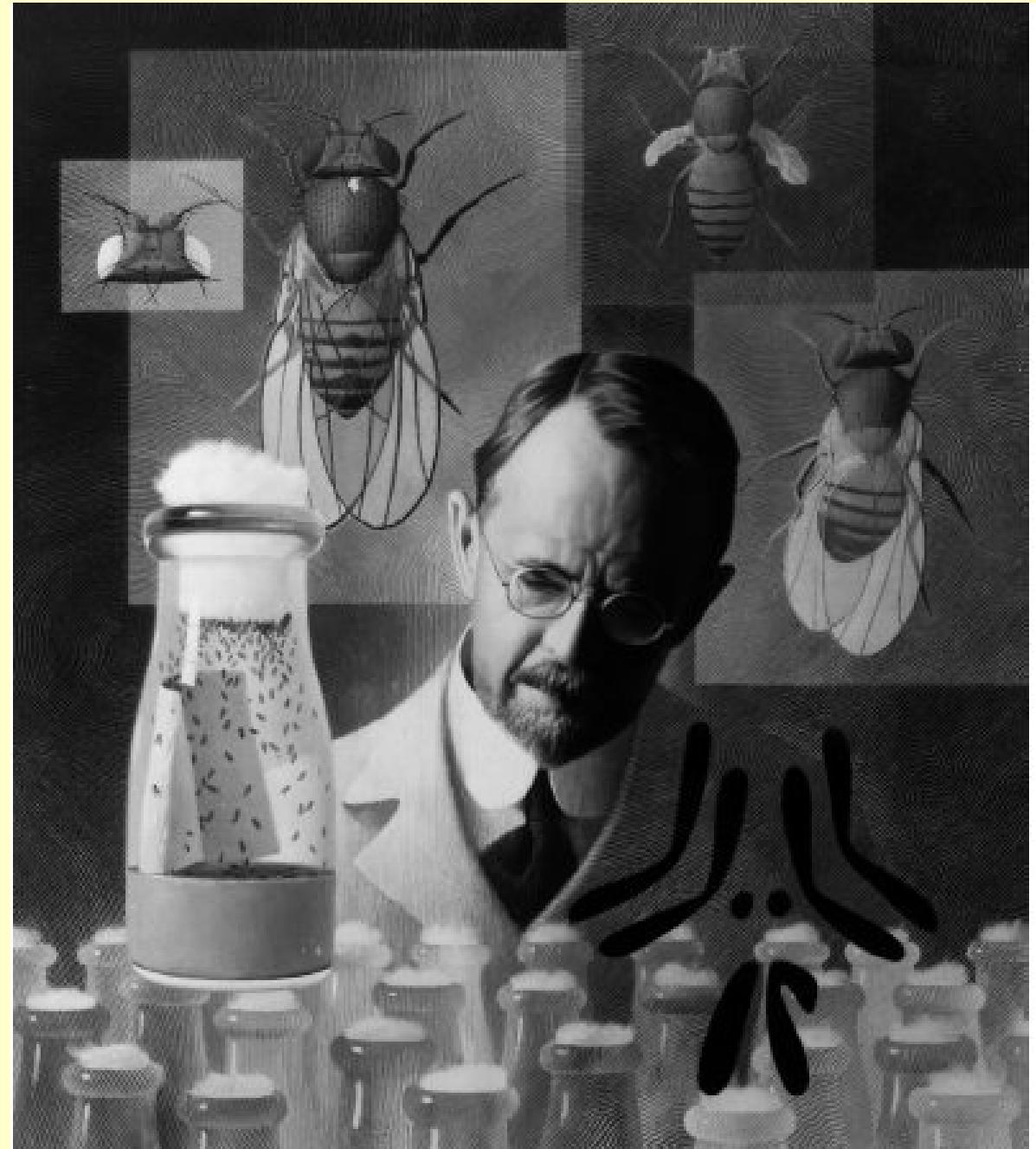




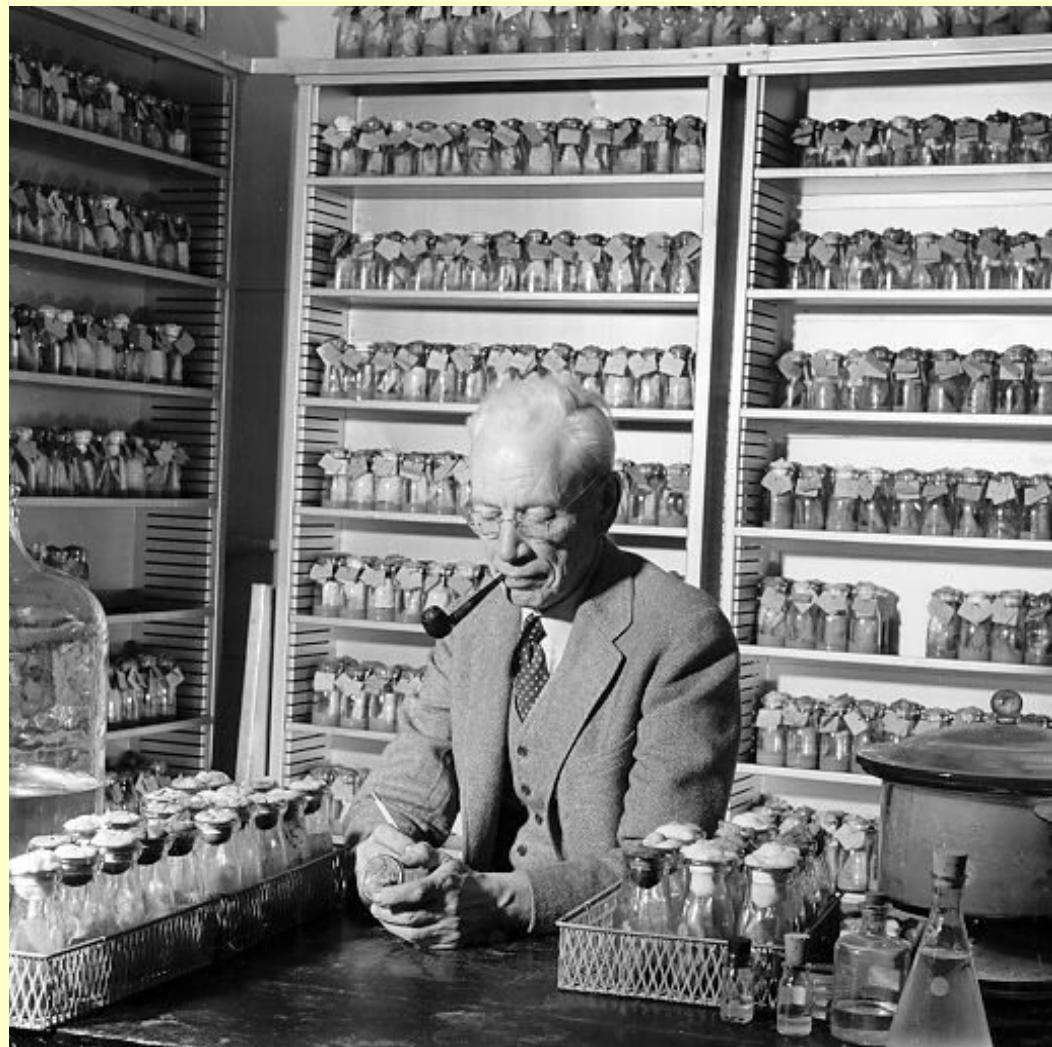
**Thomas Hunt
Morgan**

Nobel 1933

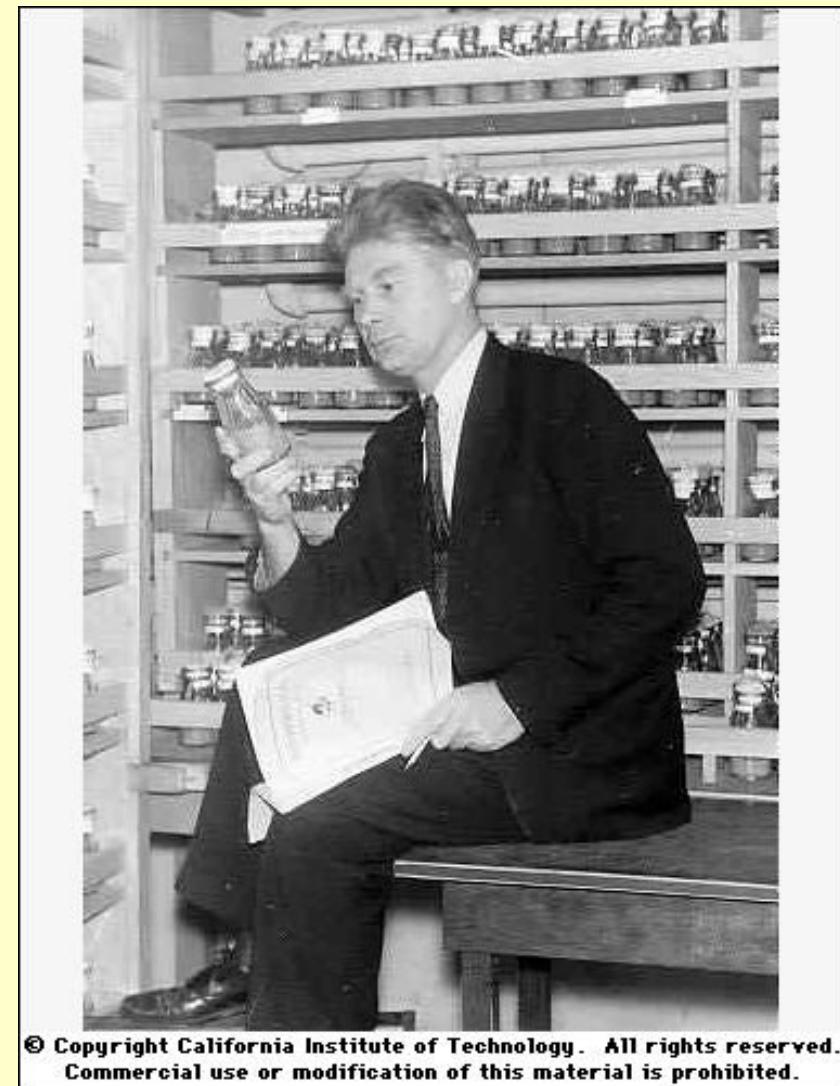
“The lord of the fly”



No “fly lab”



Alfred H. Sturtevant

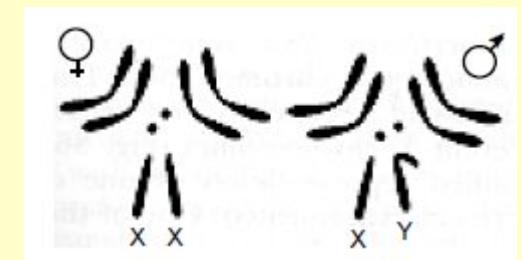
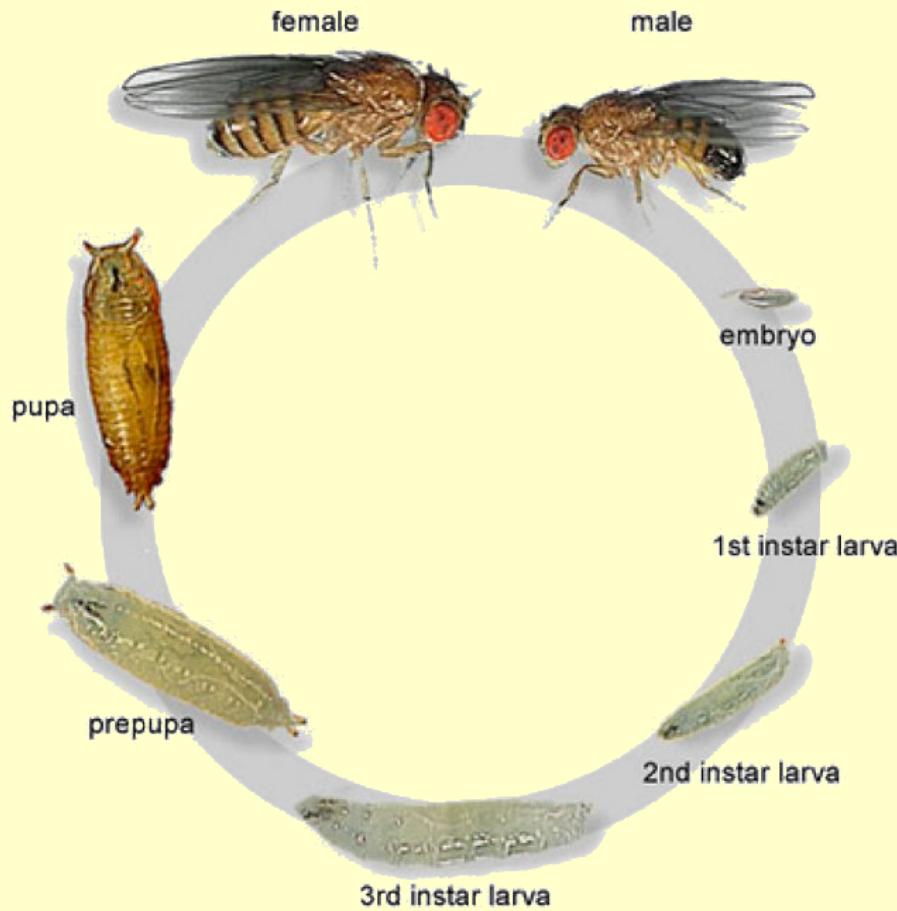


Calvin Bridges

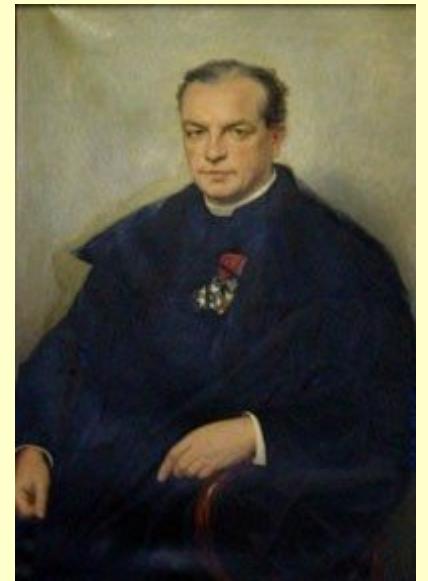
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DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS



Em 1909 – Teoria de Quiasmatipia por Frans Alfons Jansseen

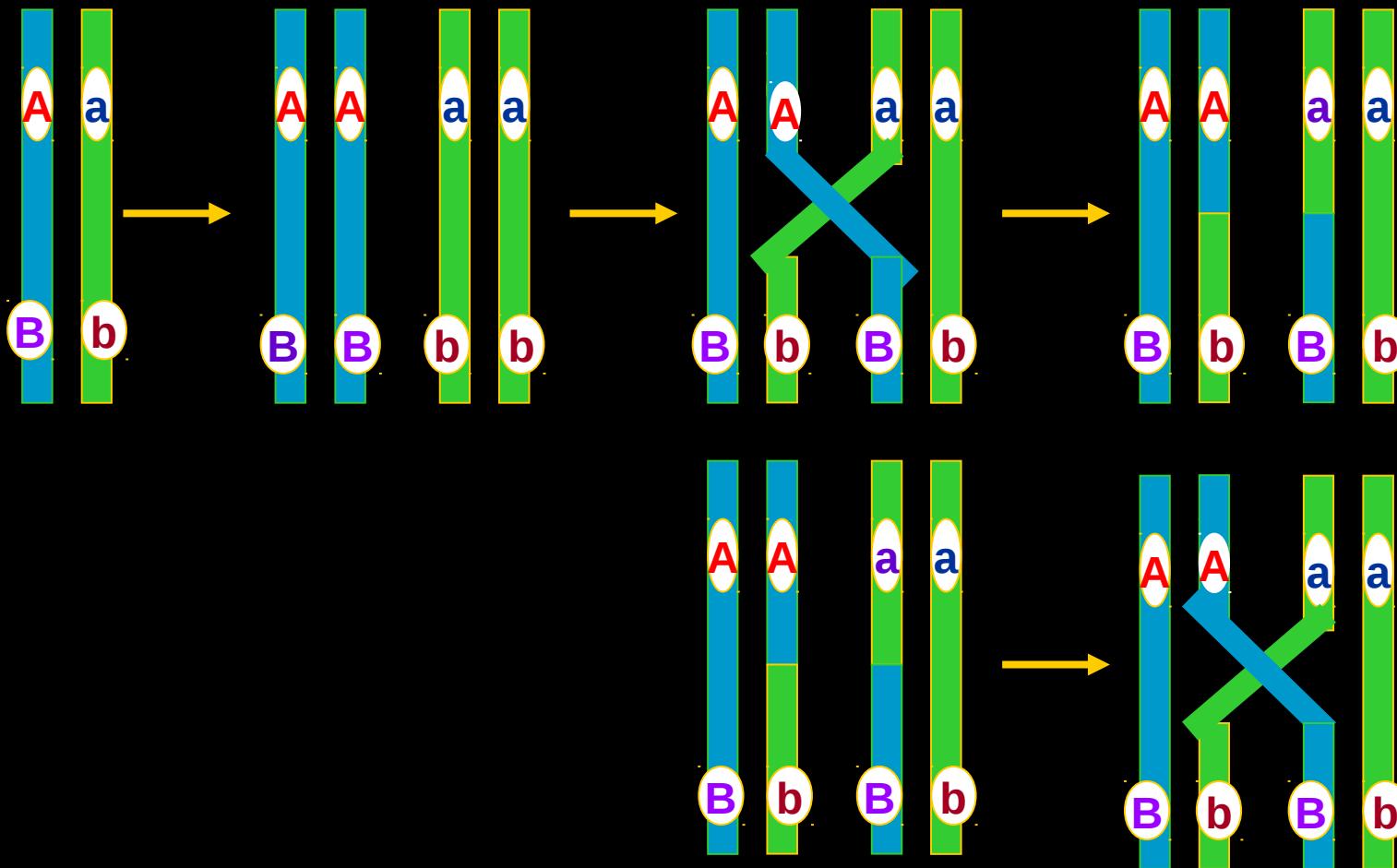


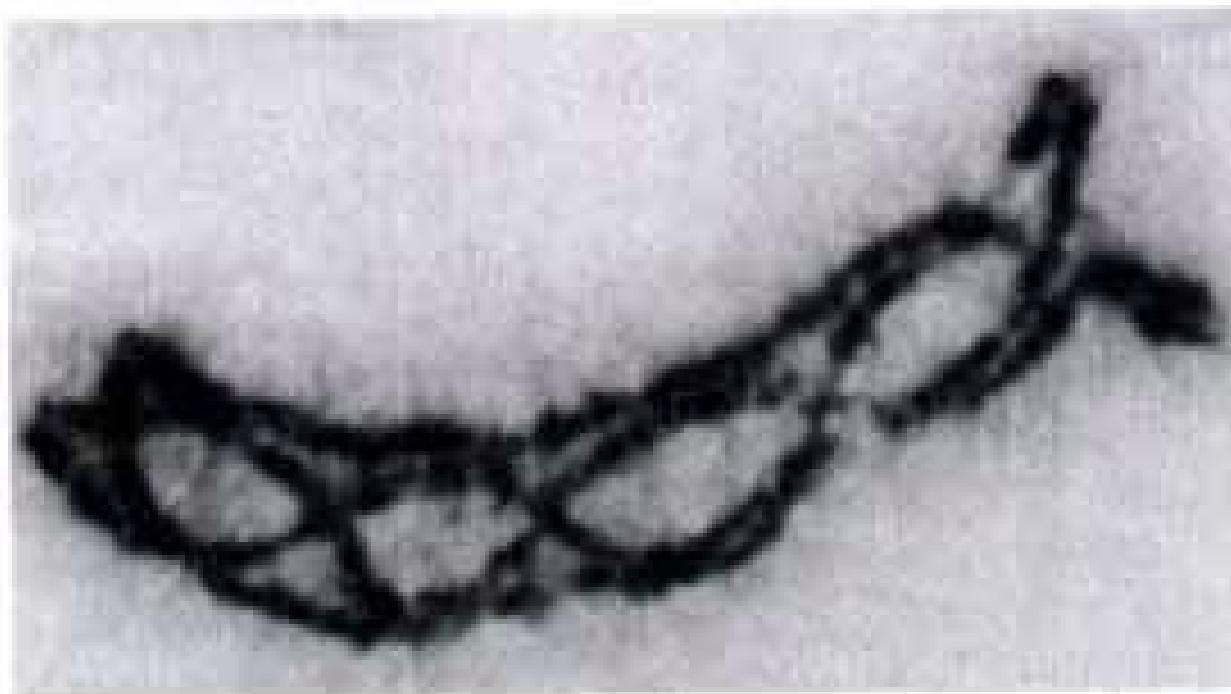
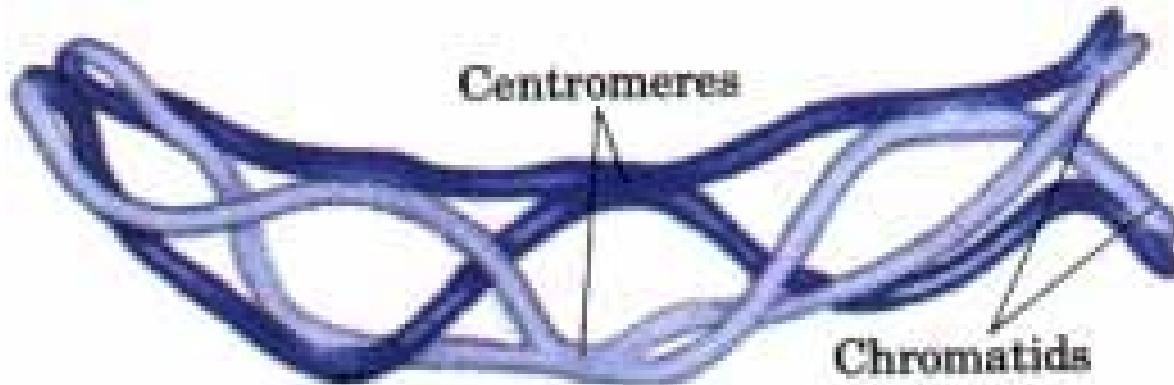
Na meiose as cromátides se enrolam e se quebram

Esse mosaicos formam “novas” cromátides

Uma hipótese correta baseada em interpretações erradas!!

Teoria de Quiasmatipia





(a)

$2 \mu\text{m}$

Primeiro mapa de ligação

GRUPO I

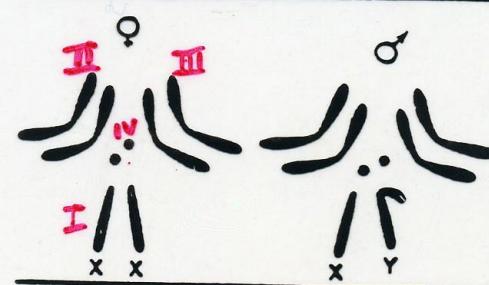
Nome	Região afetada
Abnormal	Abdome
Bar	Olhos
Bifid	Veias das asas
Bow	Asas
Cherry	Cor dos olhos
Chrome	Cor do corpo
Cleft	Nervuras das asas
Club	Asas
Depressed	Asas
Dotted	Tórax
Facet	Omatídos
Furrowed	Olhos
Fused	Veias das asas
Green	Cor do corpo
Jaunty	Asas
Lemon	Cor do corpo
Lethals. 13	Morte
Miniature	Asas
Notch	Veias das asas
Reduplicated	Pernas
Ruby	Cor dos olhos
Rudimentary	Asas
Sable	Cor do corpo
Shifted	Veias das asas
Short	Asas
Skee	Asas
Spoon	Asas
Spot	Cor do corpo
Tan	Antenas
Truncate	Asas
Vermilion	Cor dos olhos
White	Cor dos olhos
Yellow	Cor do corpo

GRUPO II

Nome	Região Afetada
Antlered	Asas
Apterous	Asas
Arc	Asas
Balloon	Veias das asas
Black	Cor do corpo
Blistered	Asas
Comma	Tórax
Confluent	Veias das asas
Cream II	Cor dos olhos
Curved	Asas
Dachs	Pernas
Extra vein	Veias das asas
Fringed	Asas
Jaunty	Asas
Limited	Faixa abdominal
Littlecrossover	Cromossomo II
Morula	Omatídos
Olive	Cor do corpo
Plexus	Veias das asas
Purple	Cor dos olhos
Speck	Tórax
Strap	Asas
Streak	Padrão do tórax
Trefoil	Padrão do tórax
Truncate	Asas
Vestigial	Asas

GRUPO III

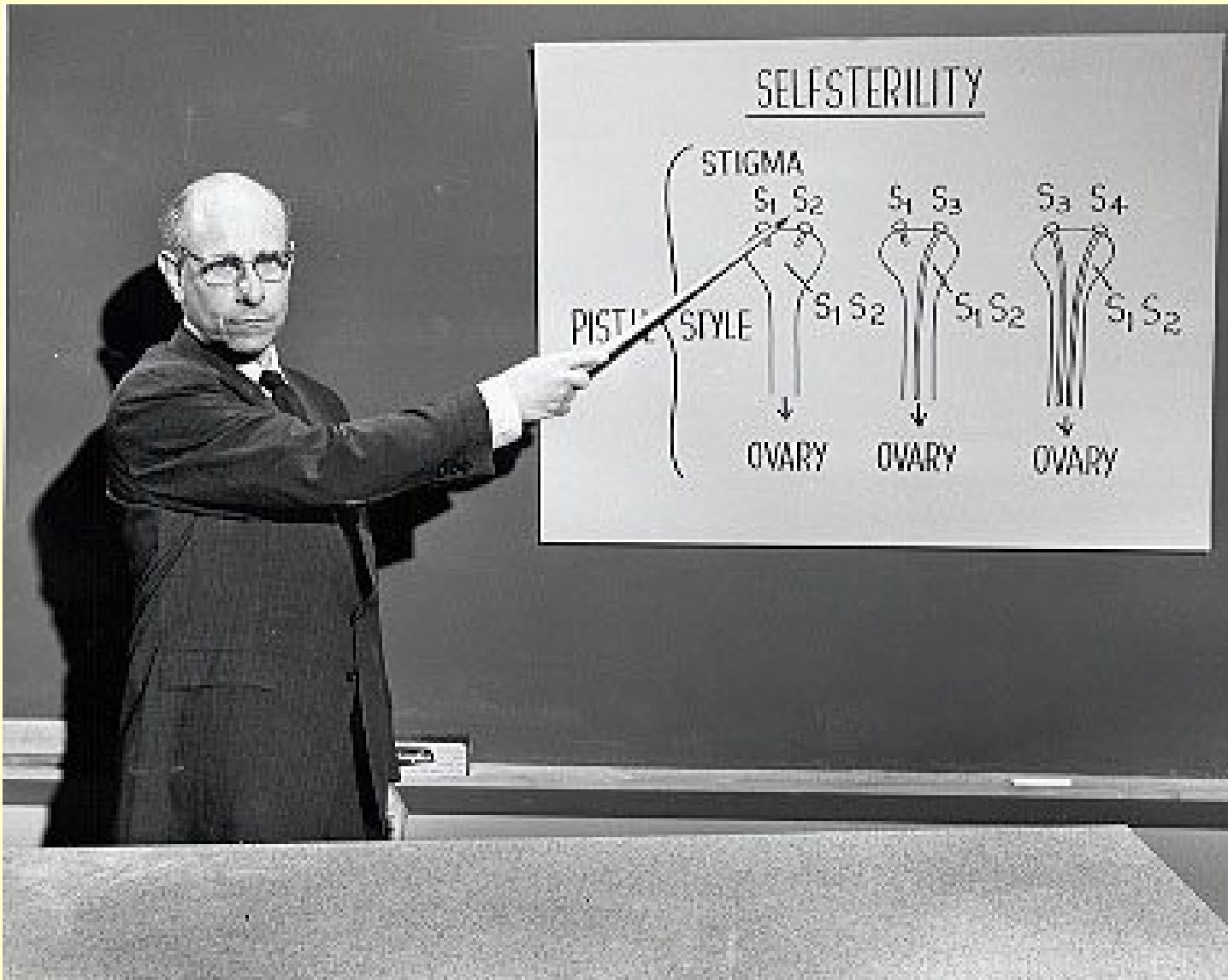
Nome	Região Afetada
Band	Padrão do tórax
Beaded	Asas
Cream III	Cor dos olhos
Deformed	Olhos
Dwarf	Tamanho do corpo
Ebony	Cor do corpo
Giant	Tamanho do corpo
Kidney	Olhos
Low crossing	Cromossomo III
-over	Cor dos olhos
Maroon	Cor dos olhos
Peach	Cor dos olhos
Pink	Cor dos olhos
Rough	Olhos
Safranin	Cor dos olhos
Sepia	Cor dos olhos
Sooty	Cor do corpo
Spineless	Cerdas
Spread	Asas
Trident	Padrão do tórax
Truncate intensf.	Asas
Whitehead	Cor periocelar
White ocelli	Ocelos

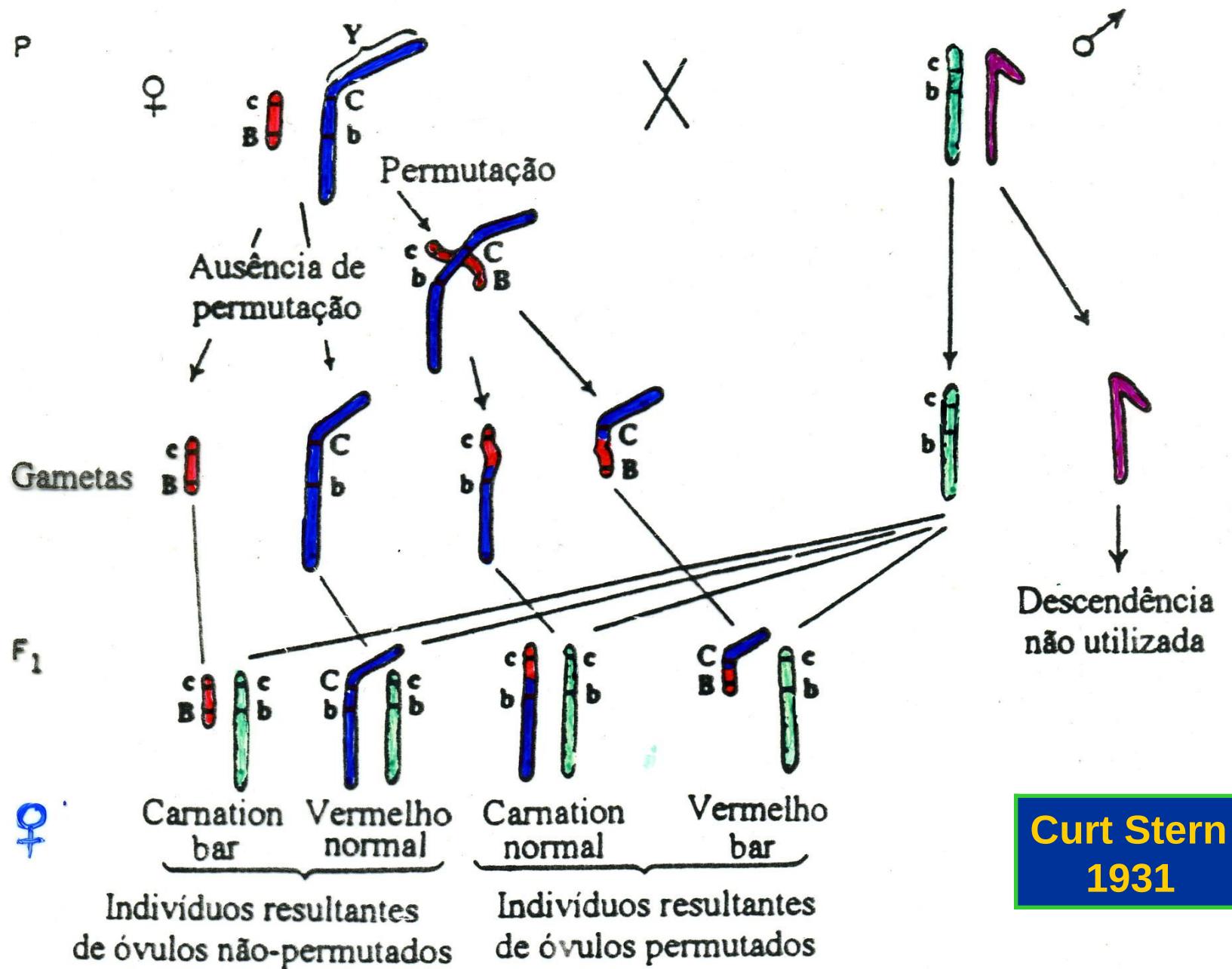


GRUPO IV

Nome	Região Afetada
Bent	Asas
Eyeless	Olhos

Curt Stern (1902-1981)





27.000 larvas, das quais 367 foram analisadas

MAPAS DE LIGAÇÃO

Morgan, em 1910

Hipótese: “os fatores estariam localizados em lugares definidos nos cromossomos e dispostos em uma ordem linear.”

Então:

“para um determinado segmento de um par de cromossomos homólogos qualquer, a probabilidade de haver uma permutação entre suas cromátides não-irmãs dependeria do comprimento desse segmento.”

Sturtevant fez a seguinte dedução, 1912-1913

“Se a hipótese de Morgan estiver correta, a proporção de recombinantes pode ser usada como um indicador da distância entre dois fatores quaisquer.”

DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS



Dois genes autossônicos:

GENE 1 -> cor do olho
pr roxo; *pr⁺* vermelho

GENE 2 -> comprimento da asa
vg vestigial; *vg⁺* normal

TIPO SELVAGEM DOMINANTE

DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

P

pr/pr . vg/vg x pr⁺/pr⁺ . vg⁺/vg⁺

Gametas

pr . vg

pr⁺ . vg⁺

F1 dihíbridos

pr⁺/pr . vg⁺/vg

DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS

Cruzamento pr^+/pr . vg^+/vg x pr/pr . vg/vg
teste

DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS

Cruzamento pr^+/pr . vg^+/vg x pr/pr . vg/vg
teste

Classes de gametas	$\text{pr}^+ . \text{vg}^+$ $\text{pr} . \text{vg}$ $\text{pr}^+ . \text{vg}$ $\text{pr} . \text{vg}^+$
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DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS

Cruzamento pr^+/pr . vg^+/vg x pr/pr . vg/vg
teste

Classes de gametas	$\text{pr}^+ . \text{vg}^+$	1339
	$\text{pr} . \text{vg}$	1195
	$\text{pr}^+ . \text{vg}$	151
	$\text{pr} . \text{vg}^+$	154

DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

Cruzamento pr^+/pr . vg^+/vg x pr/pr . vg/vg
teste

Classes de gametas	$\text{pr}^+ . \text{vg}^+$	1339
	$\text{pr} . \text{vg}$	1195
	$\text{pr}^+ . \text{vg}$	151
	$\text{pr} . \text{vg}^+$	154

Desvio drástico da razão
1:1:1:1

Seria possível explicar
esse resultado?

DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS

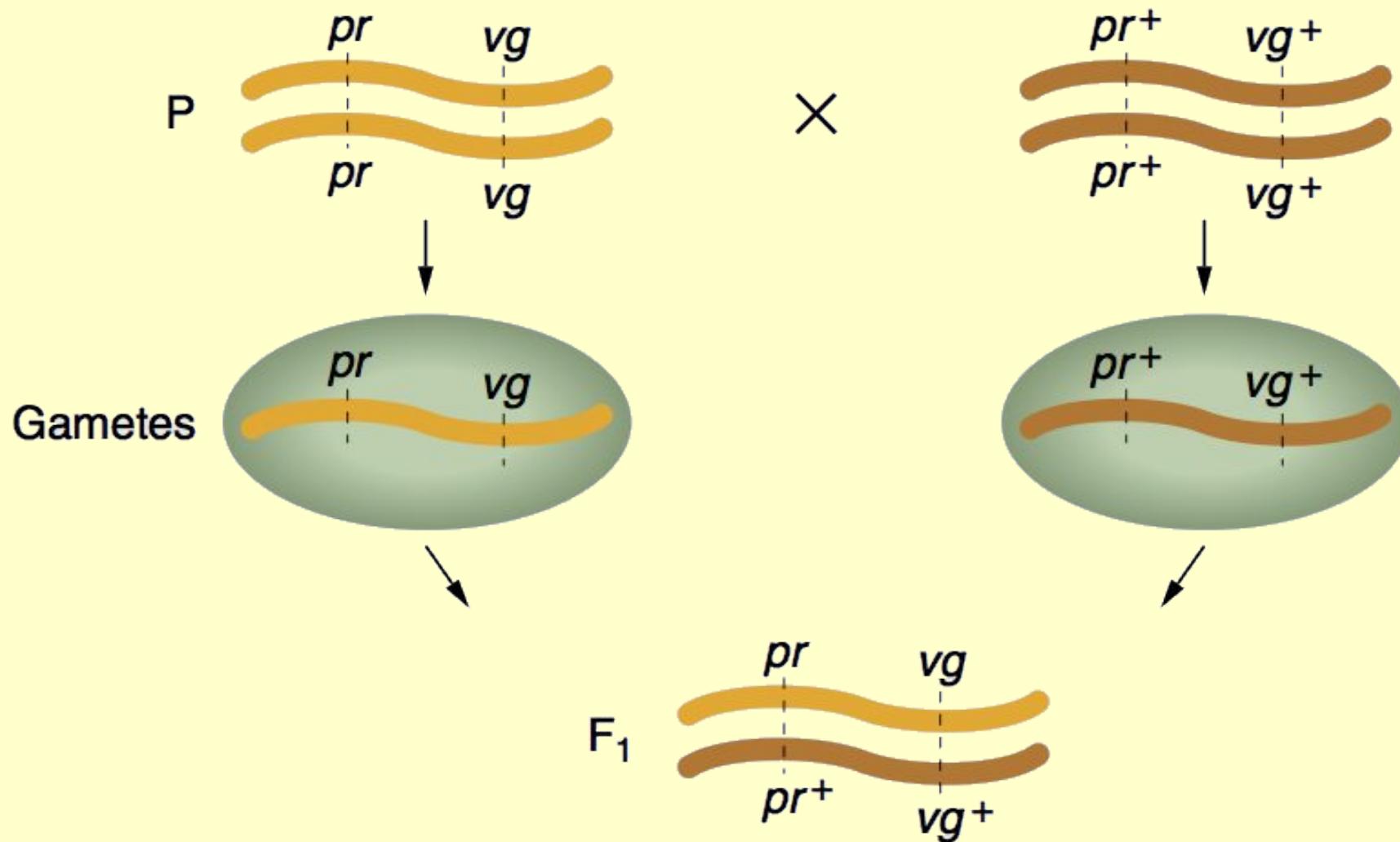
Outro cruzamento $\text{pr}^+/\text{pr}^+ . \text{vg}/\text{vg}$ x $\text{pr}/\text{pr} . \text{vg}^+/\text{vg}^+$

F1 $\text{pr}^+/\text{pr} . \text{vg}^+/\text{vg}$

Classes de gametas	$\text{pr}^+ . \text{vg}^+$	157
	$\text{pr} . \text{vg}$	146
	$\text{pr}^+ . \text{vg}$	965
	$\text{pr} . \text{vg}^+$	1.067

DESEQUILÍBRIO DE LIGAÇÃO

GENES LIGADOS



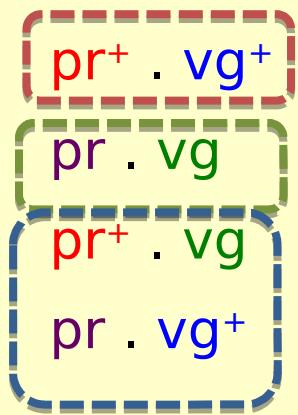
DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

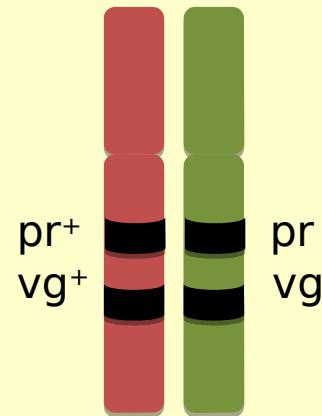
Cruzamento
teste

$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas



1339
1195
151
154



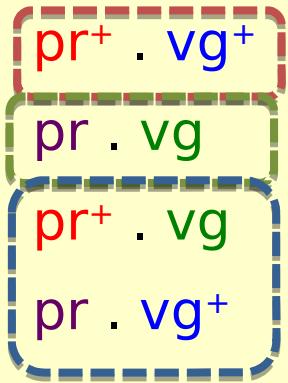
DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

Cruzamento
teste

$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas

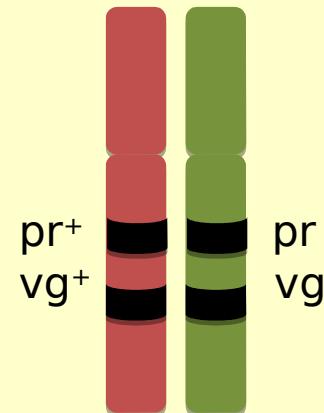


1339

1195

151

154



Recombinantes

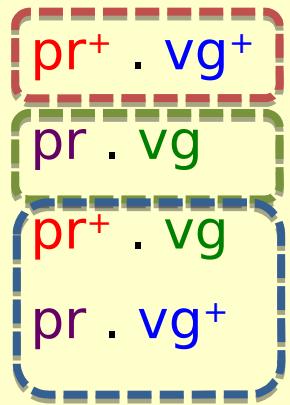
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GENES LIGADOS

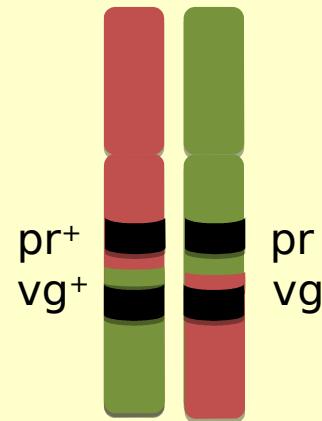
Cruzamento
teste

$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas



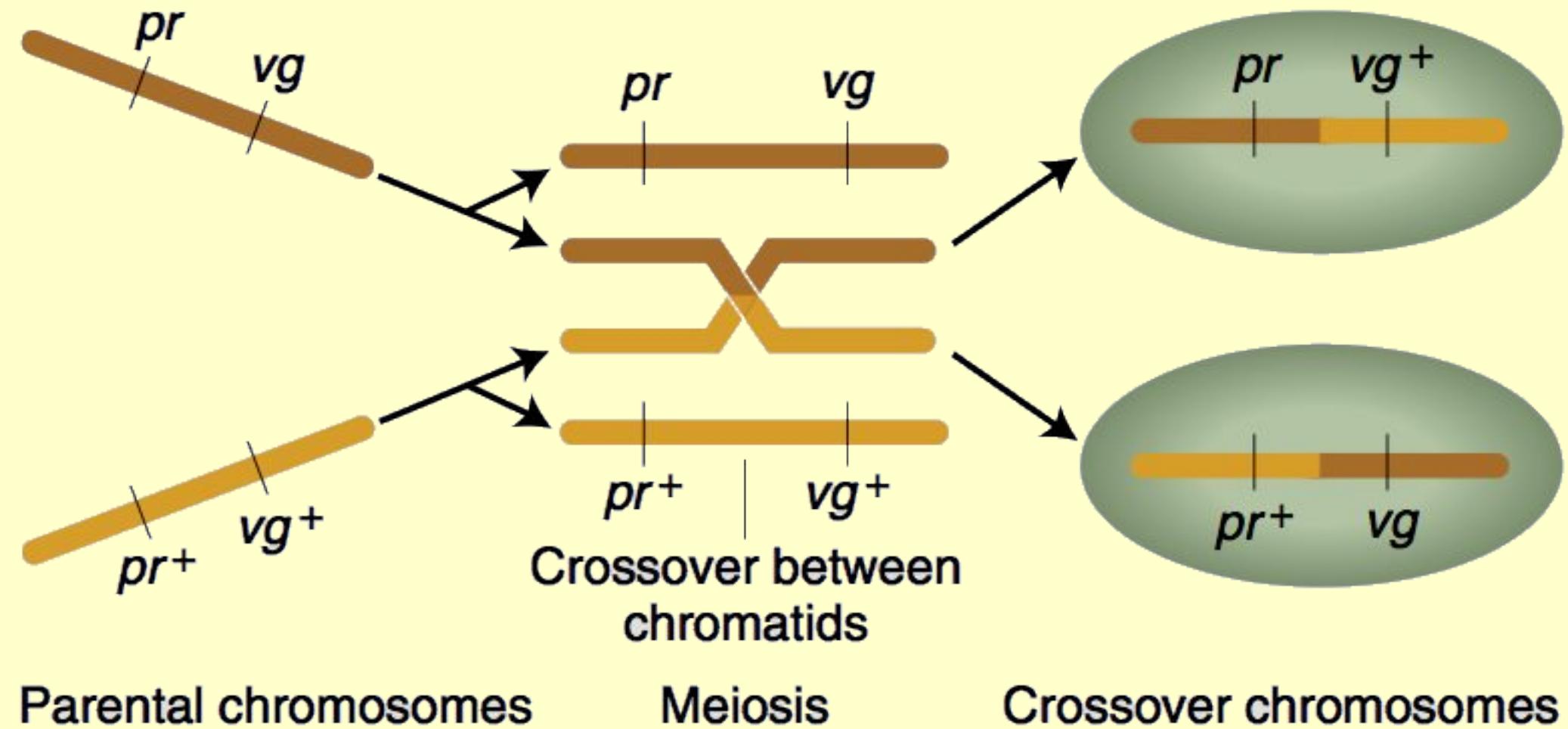
1339
1195
151
154



Recombinantes

RECOMBINAÇÃO

GENES LIGADOS



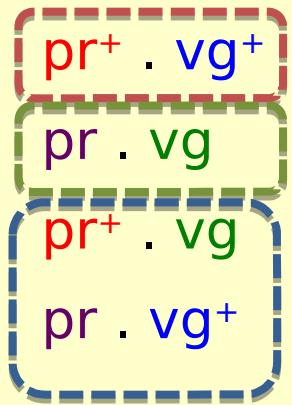
DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

Cruzamento
teste

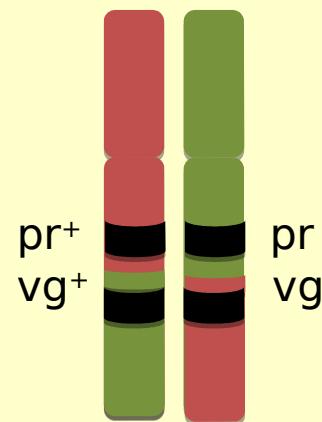
$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas



1339
1195
151
154

Recombinantes



Qual é a frequência de
recombinação neste cruzamento?

DESEQUILÍBRIOS DE LIGAÇÃO

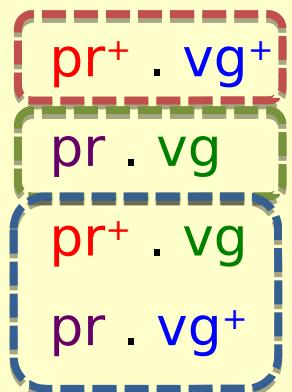
GENES LIGADOS

Cruzamento
teste

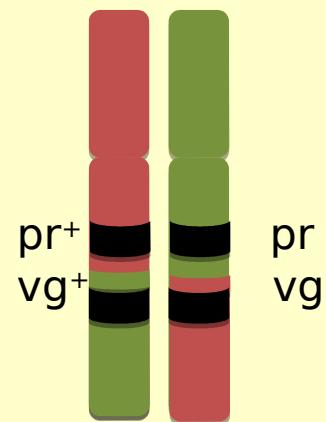
$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas

Recombinantes



1339
1195
151
154
2839



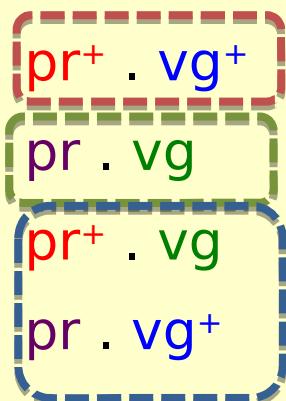
DESEQUILÍBRIOS DE LIGAÇÃO

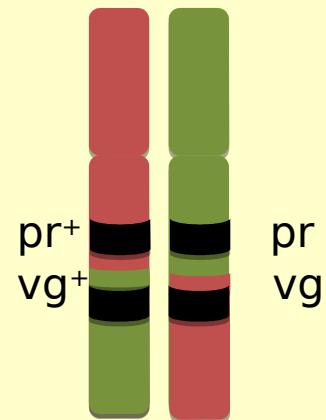
GENES LIGADOS

Cruzamento
teste

$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas

	<u>Recombinantes</u>	<u>2839</u>
$pr^+ . vg^+$	1339	
$pr . vg$	1195	
$pr^+ . vg$	151	
$pr . vg^+$	154	



$$F_R = 151 + 154 / 2839 * 100 = 10,7 \%$$

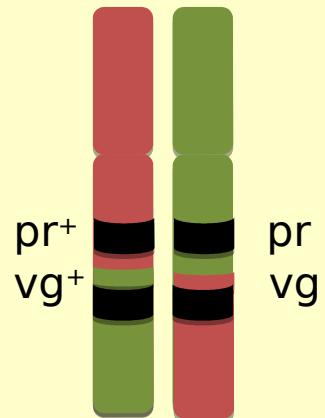
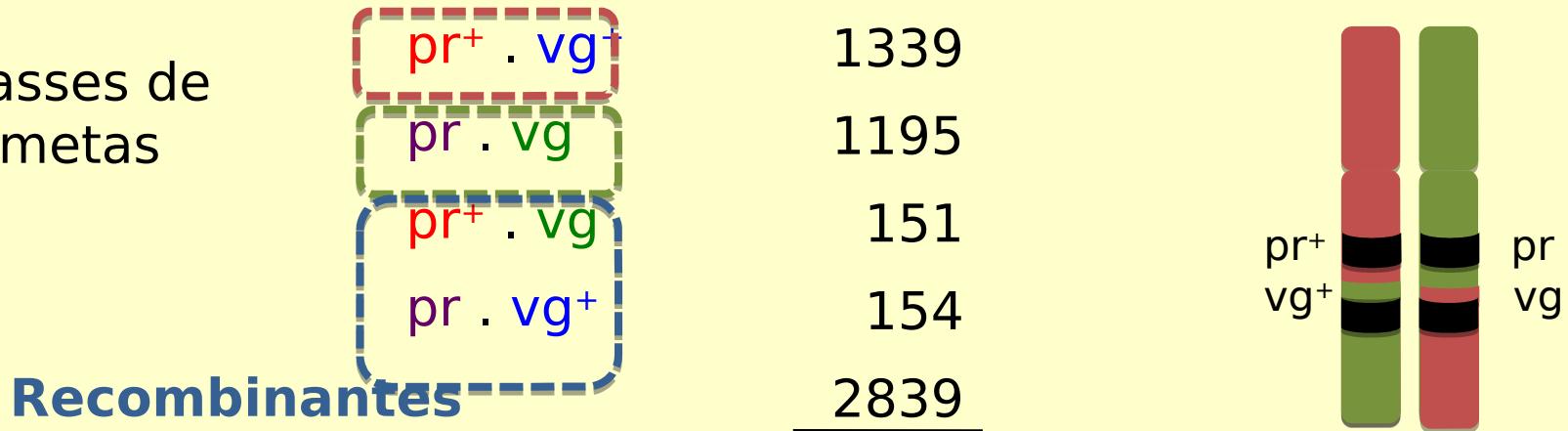
DESEQUILÍBRIOS DE LIGAÇÃO

GENES LIGADOS

Cruzamento
teste

$pr^+/pr \cdot vg^+/vg \times pr/pr \cdot vg/vg$

Classes de
gametas



BASE DO
MAPEAMENTO
GENÉTICO

$$F_R = 151 + 154 / 2839 * 100 = 10,7 \%$$

MAPA DE LIGAÇÃO

CONSTRUINDO MAPAS LINEARES

Interestadual BR-050

CIDADES	DISTÂNCIA EM Km
Limeira - São Paulo	153
Limeira - Ribeirão Preto	166
Ribeirão Preto - Uberlândia	274
Ribeirão Preto - São Paulo	319
Uberlândia - Brasília	425
Uberlândia - Limeira	440
Uberlândia – São Paulo	593
Brasília - Ribeirão Preto	699
Brasília - Limeira	865

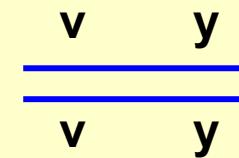
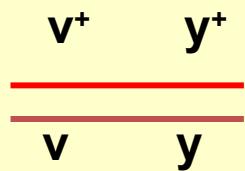
DESEQUILÍBRIO DE LIGAÇÃO

MAPAS DE LIGAÇÃO

Fêmeas selvagens

X

Machos vermillion yellow



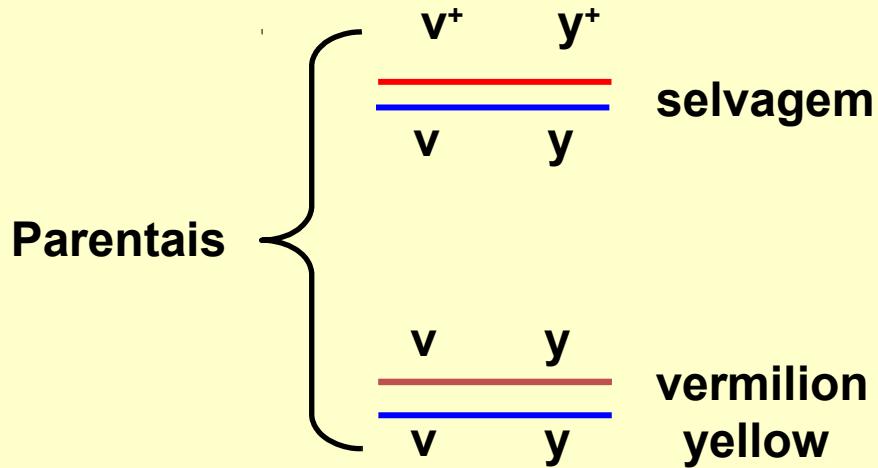
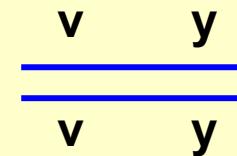
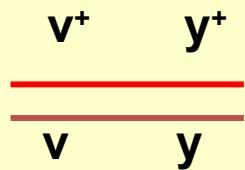
DESEQUILÍBRIOS DE LIGAÇÃO

MAPAS DE LIGAÇÃO

Fêmeas selvagens

X

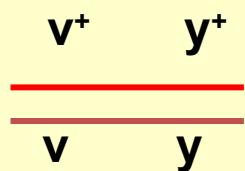
Machos vermillion yellow



DESEQUILÍBRIOS DE LIGAÇÃO

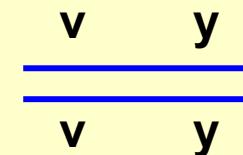
MAPAS DE LIGAÇÃO

Fêmeas selvagens

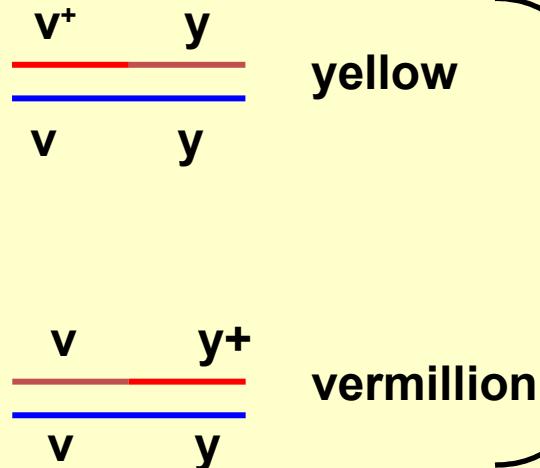
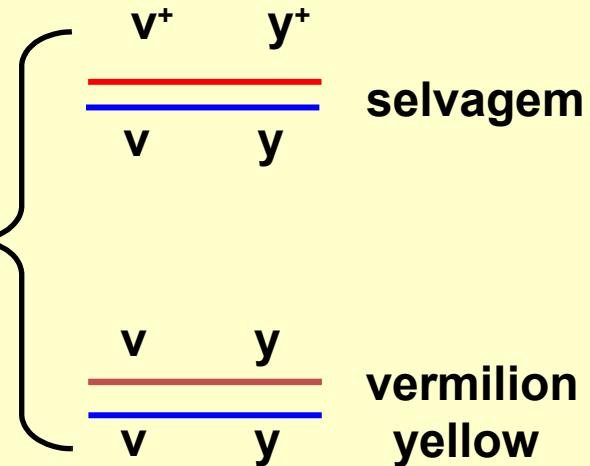


X

Machos vermillion yellow



Parentais



Recombinantes

30%

MAPA DE LIGAÇÃO

CROMOSSOMO X DE *Drosophila melanogaster*



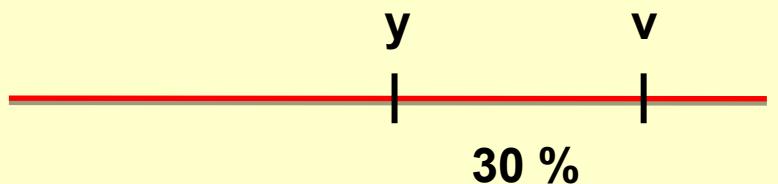
Olho vermillion *v*



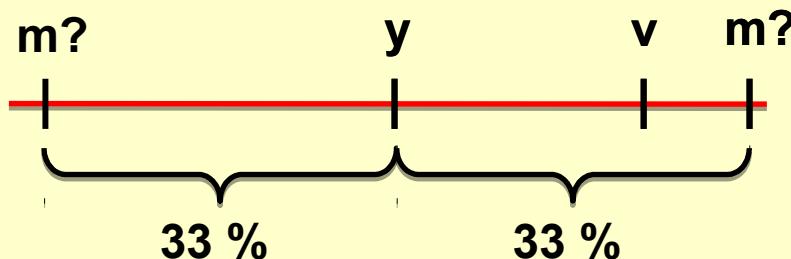
Corpo yellow *y*

MAPA DE LIGAÇÃO

CROMOSSOMO X DE *Drosophila melanogaster*



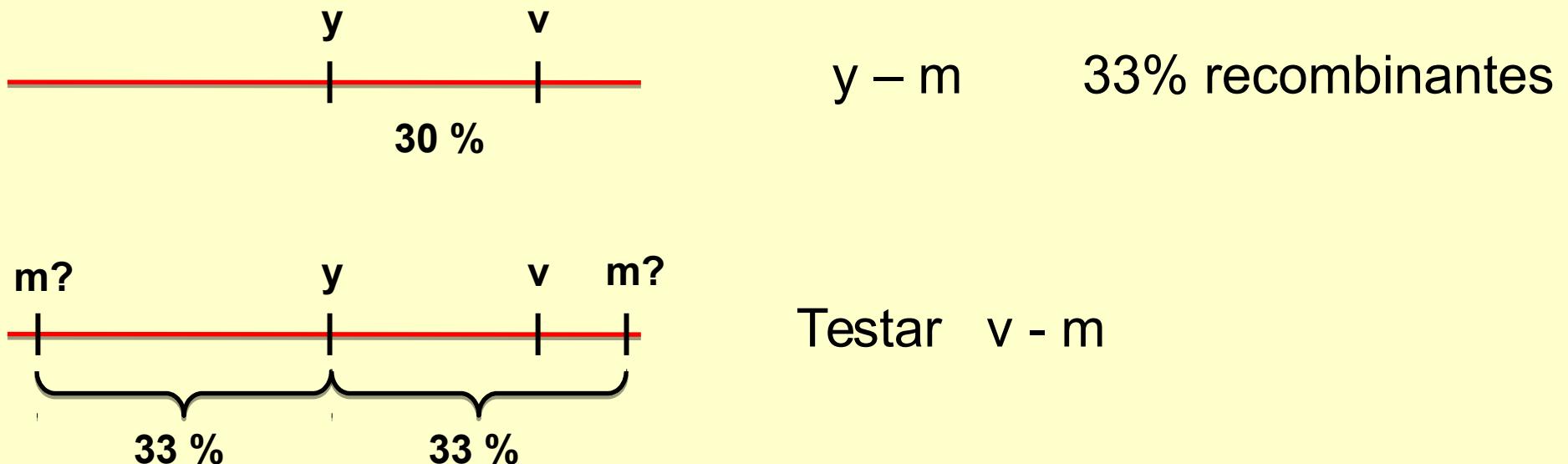
y – m 33% recombinantes



Asas miniature *m*

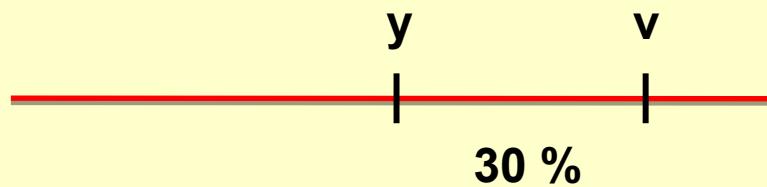
MAPA DE LIGAÇÃO

CROMOSSOMO X DE *Drosophila melanogaster*

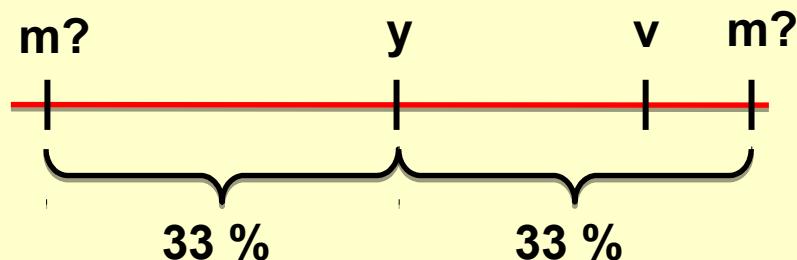


MAPA DE LIGAÇÃO

CROMOSSOMO X DE *Drosophila melanogaster*



y – m 33% recombinantes

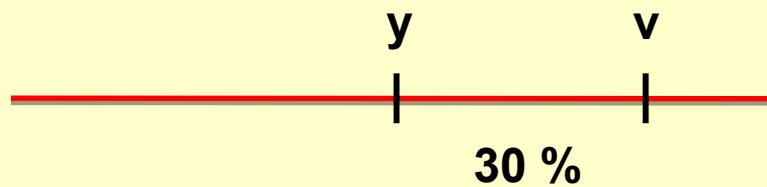


Testar v - m

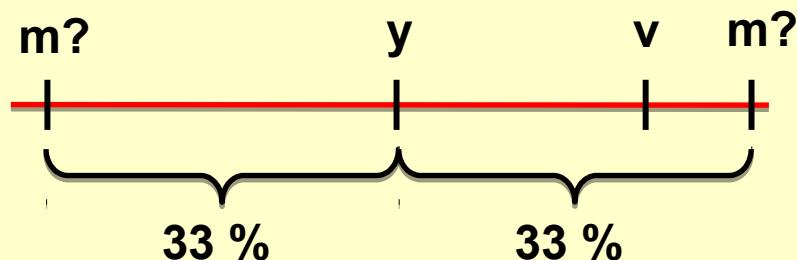
v – m = 3% recombinantes

MAPA DE LIGAÇÃO

CROMOSSOMO X DE *Drosophila melanogaster*



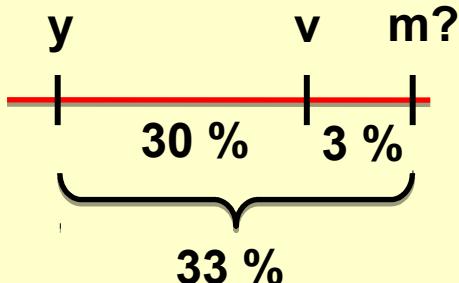
y – m 33% recombinantes



Testar v - m

v – m = 3% recombinantes

Portanto:



DESEQUILÍBRIOS DE LIGAÇÃO

MAPAS DE LIGAÇÃO

Genes

m Miniature wings



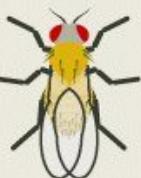
v Vermilion eyes



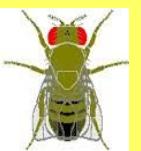
w White eyes



y Yellow body



r Rudimentary



Recombination frequencies

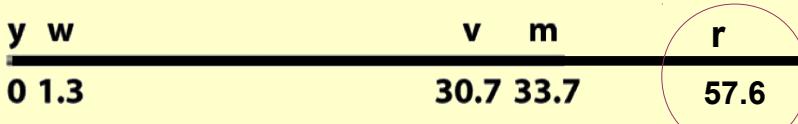
Between m and v = 3.0%

Between m and y = 33.7%

Between v and w = 29.4%

Between w and y = 1.3%

Deduced map positions

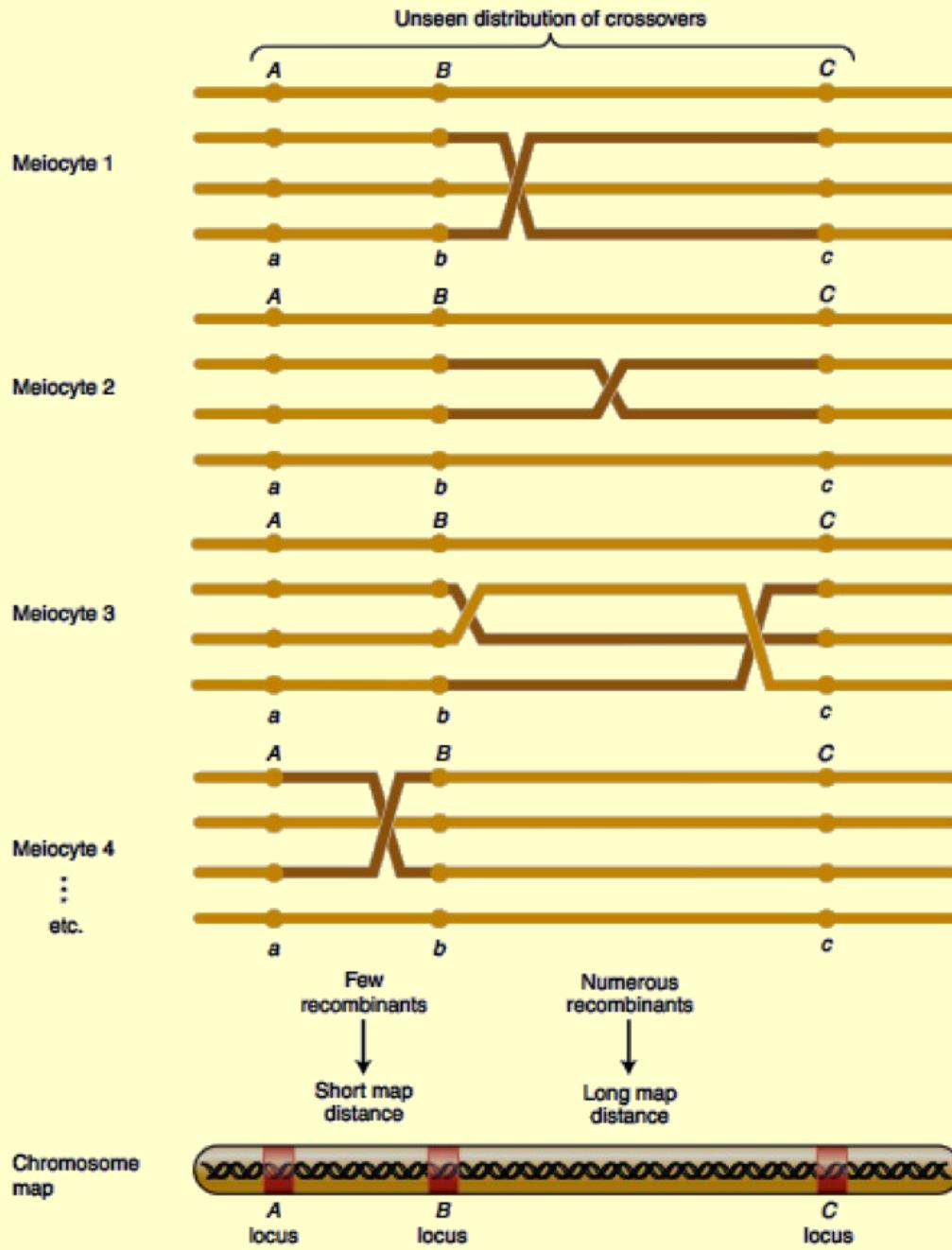


Se calculado diretamente

y-r = 55.4% ??

DESEQUILÍBRIOS DE LIGAÇÃO

MAPAS DE LIGAÇÃO



MAPA DE LIGAÇÃO

PERMUTAÇÕES DUPLAS

Como descobrir permutações duplas?

MAPA DE LIGAÇÃO

PERMUTAÇÕES DUPLAS

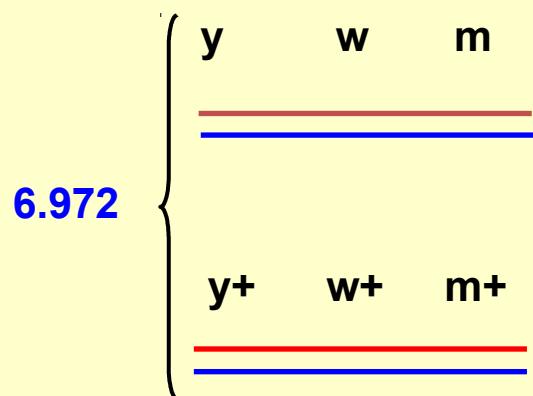


MAPA DE LIGAÇÃO

PERMUTAÇÕES DUPLAS

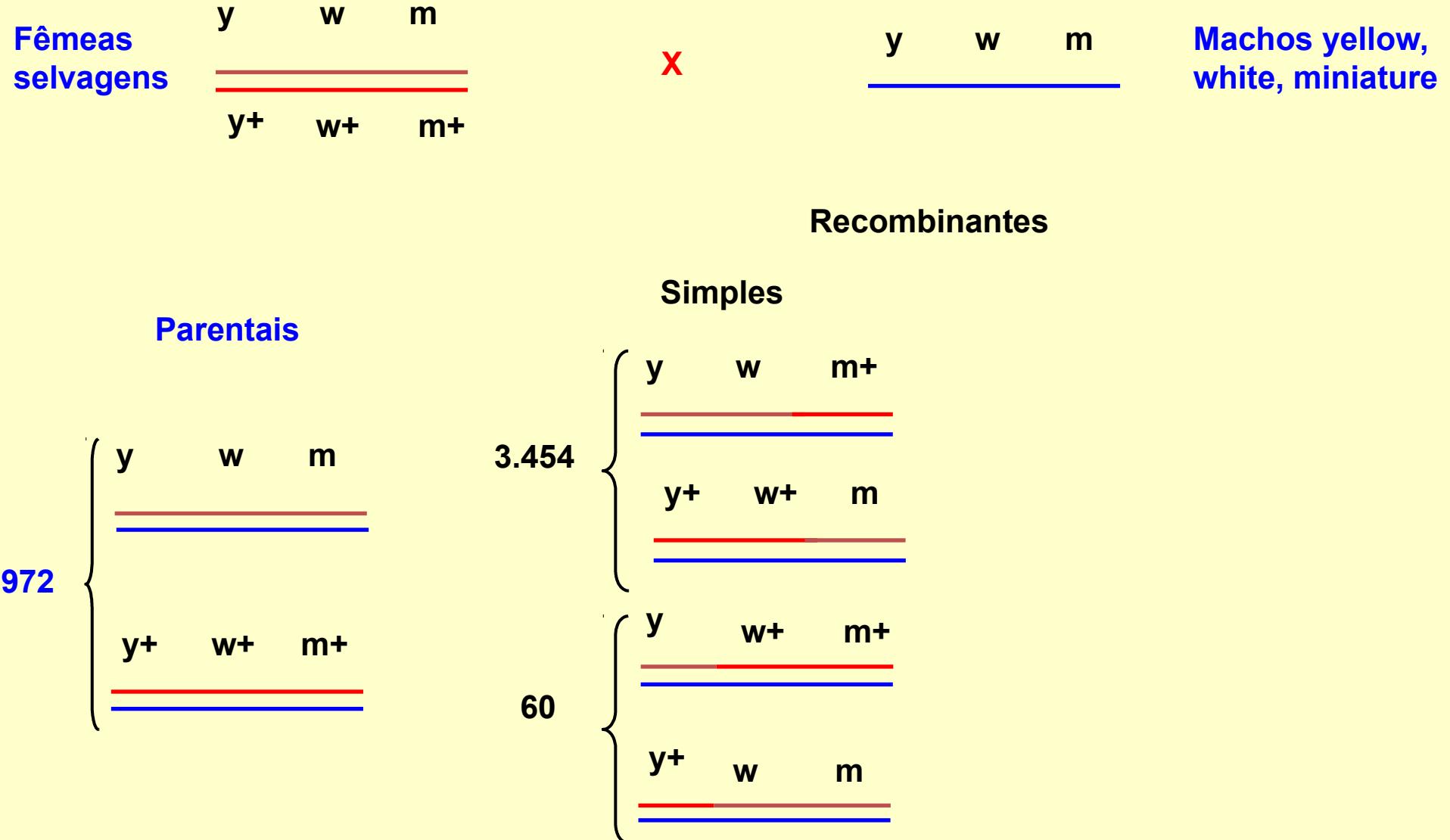


Parentais



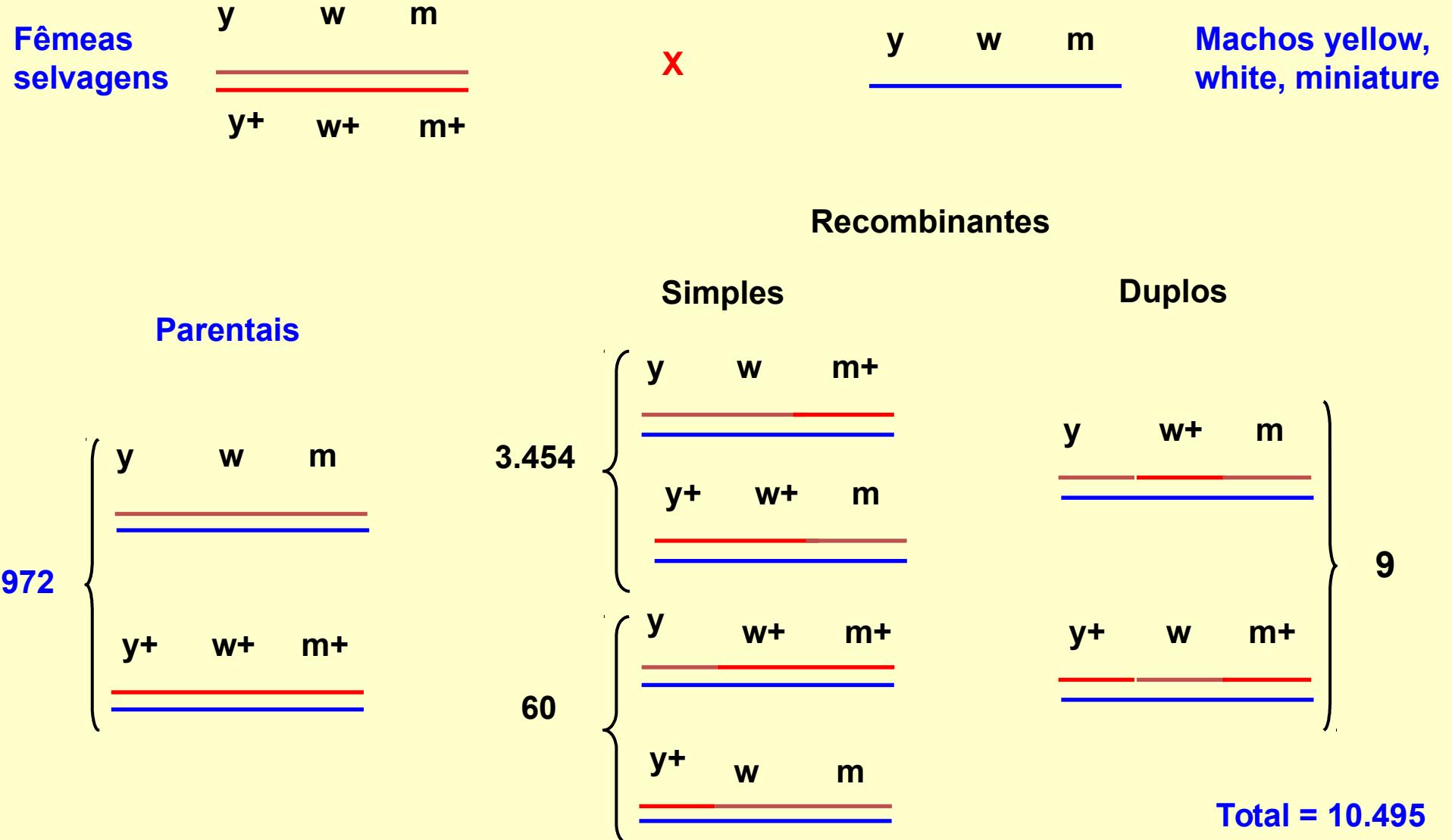
MAPA DE LIGAÇÃO

PERMUTAÇÕES DUPLAS

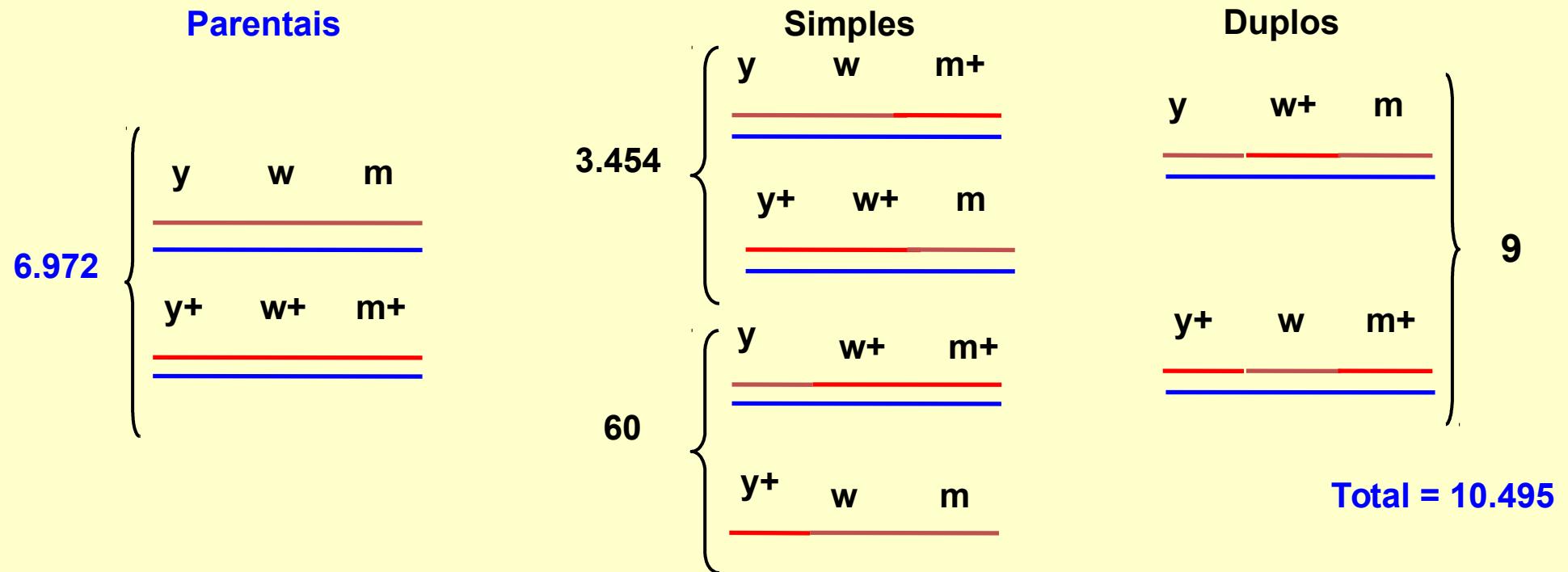


MAPA DE LIGAÇÃO

PERMUTAÇÕES DUPLAS



Recombinantes

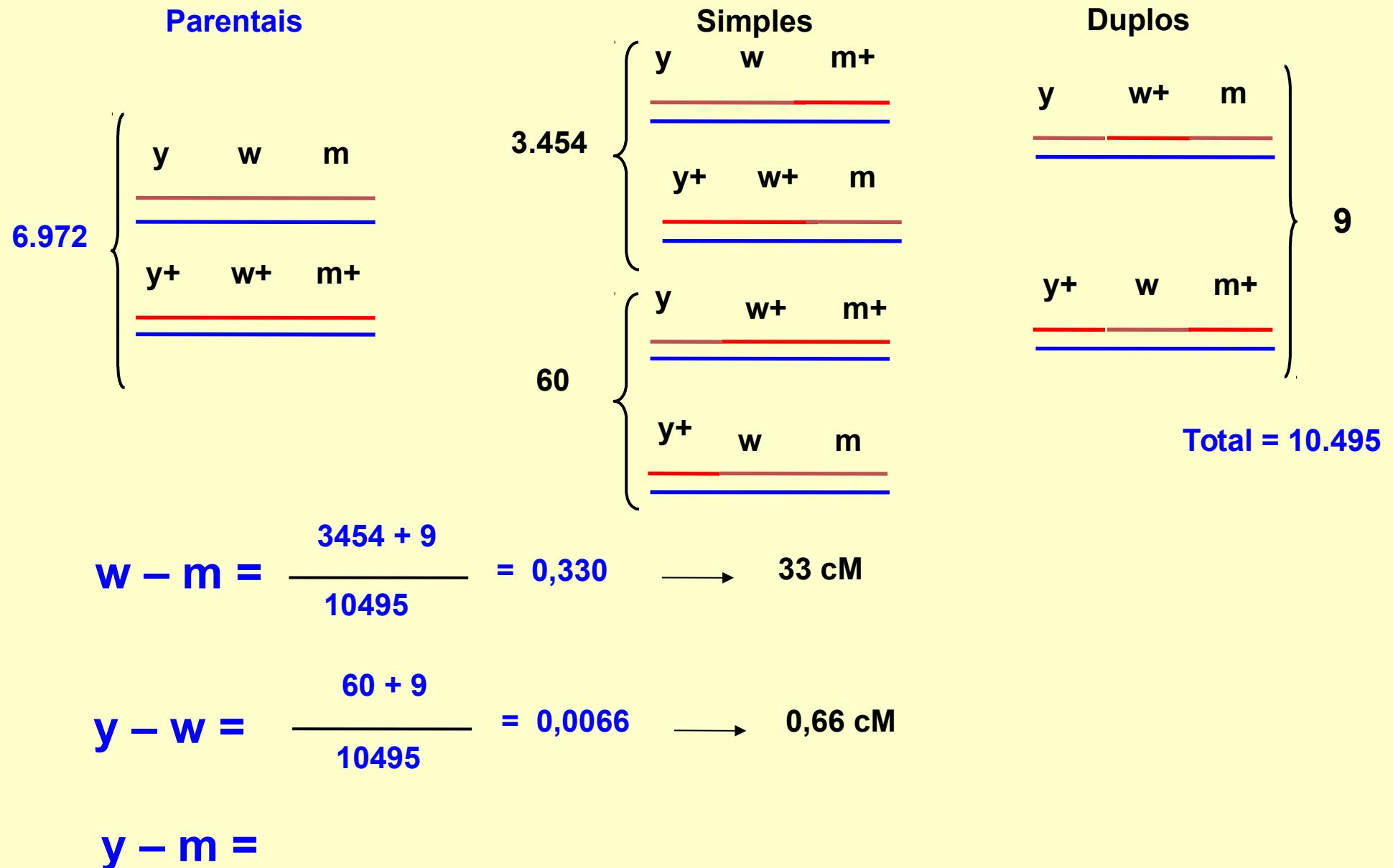


w – m =

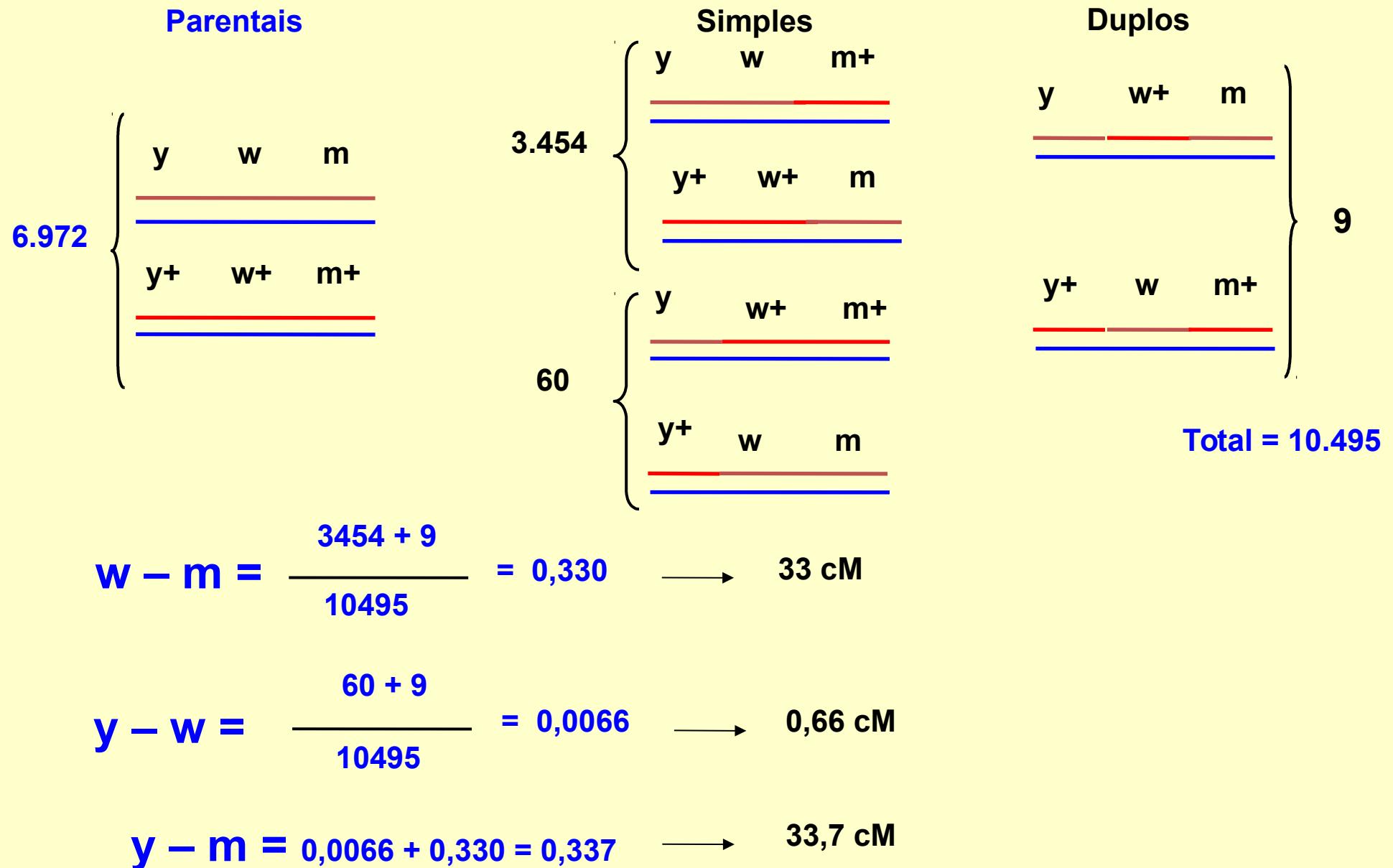
y – w =

y – m =

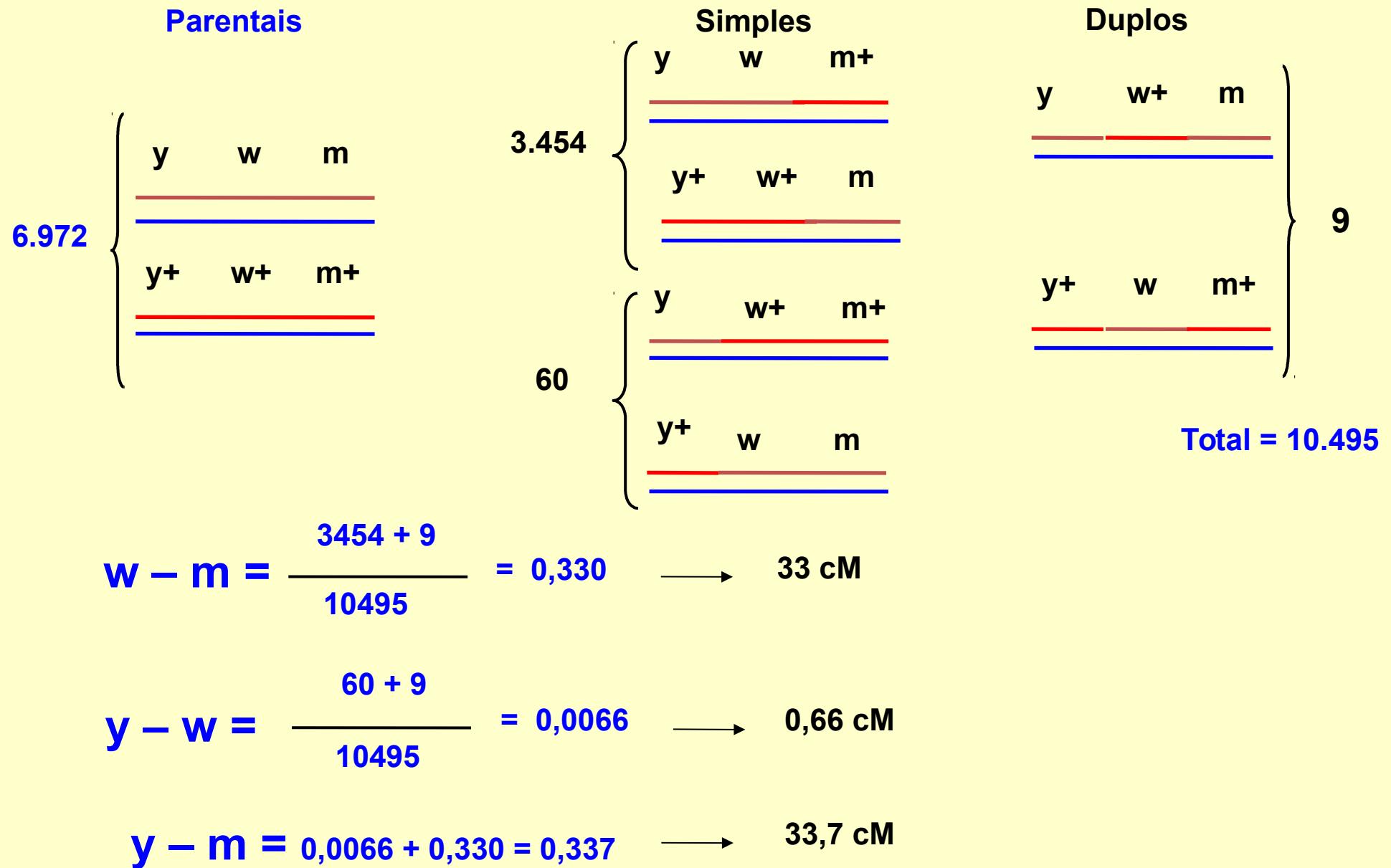
Recombinantes



Recombinantes

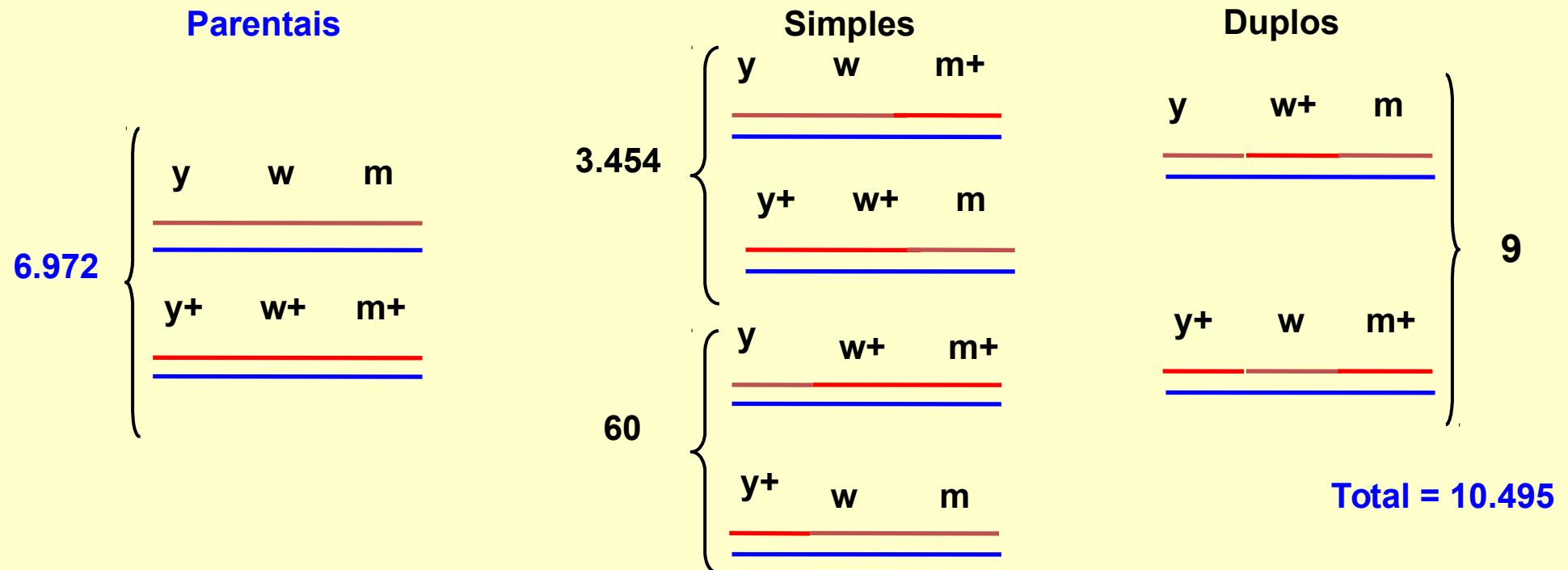


Recombinantes



OU (calculando diretamente a distância entre y e m)

Recombinantes



$$w - m = \frac{3454 + 9}{10495} = 0,330 \longrightarrow 33 \text{ cM}$$

$$y - w = \frac{60 + 9}{10495} = 0,0066 \longrightarrow 0,66 \text{ cM}$$

$$y - m = 0,0066 + 0,330 = 0,337 \longrightarrow 33,7 \text{ cM}$$

OU

$$y - m = \frac{3454 + 60 + 18}{10495} = 0,337 \longrightarrow 33,7 \text{ cM}$$

Coincidência e interferência

(Muller, 1916)

Coeficiente de Coincidência = C. C.

$$C.C. = \frac{\text{Frequência relativa de duplo-recombinantes observada}}{\text{Frequência relativa de duplo-recombinantes esperada}}$$

$$C. C. = \frac{0,00085}{0,0066 \times 0,33} = 0,39 \quad 39\%$$

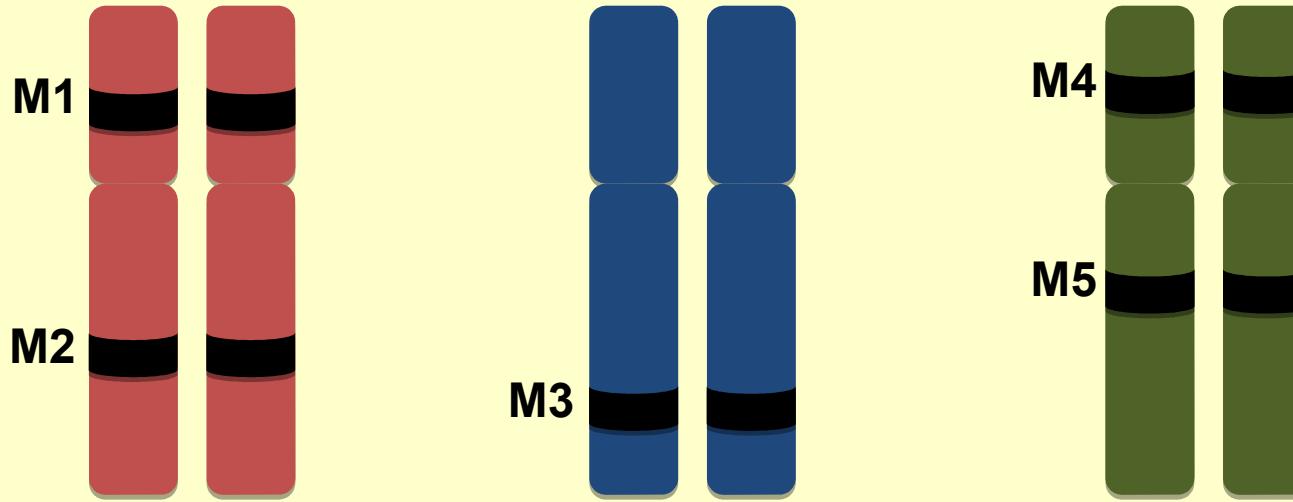
Interferência = I

I = 1 - coeficiente de coincidência

$$I = 1 - C. C. = 1 - 0,39 = 0,61 \quad 61\%$$

DESEQUILÍBRIOS DE LIGAÇÃO

MAPAS DE LIGAÇÃO

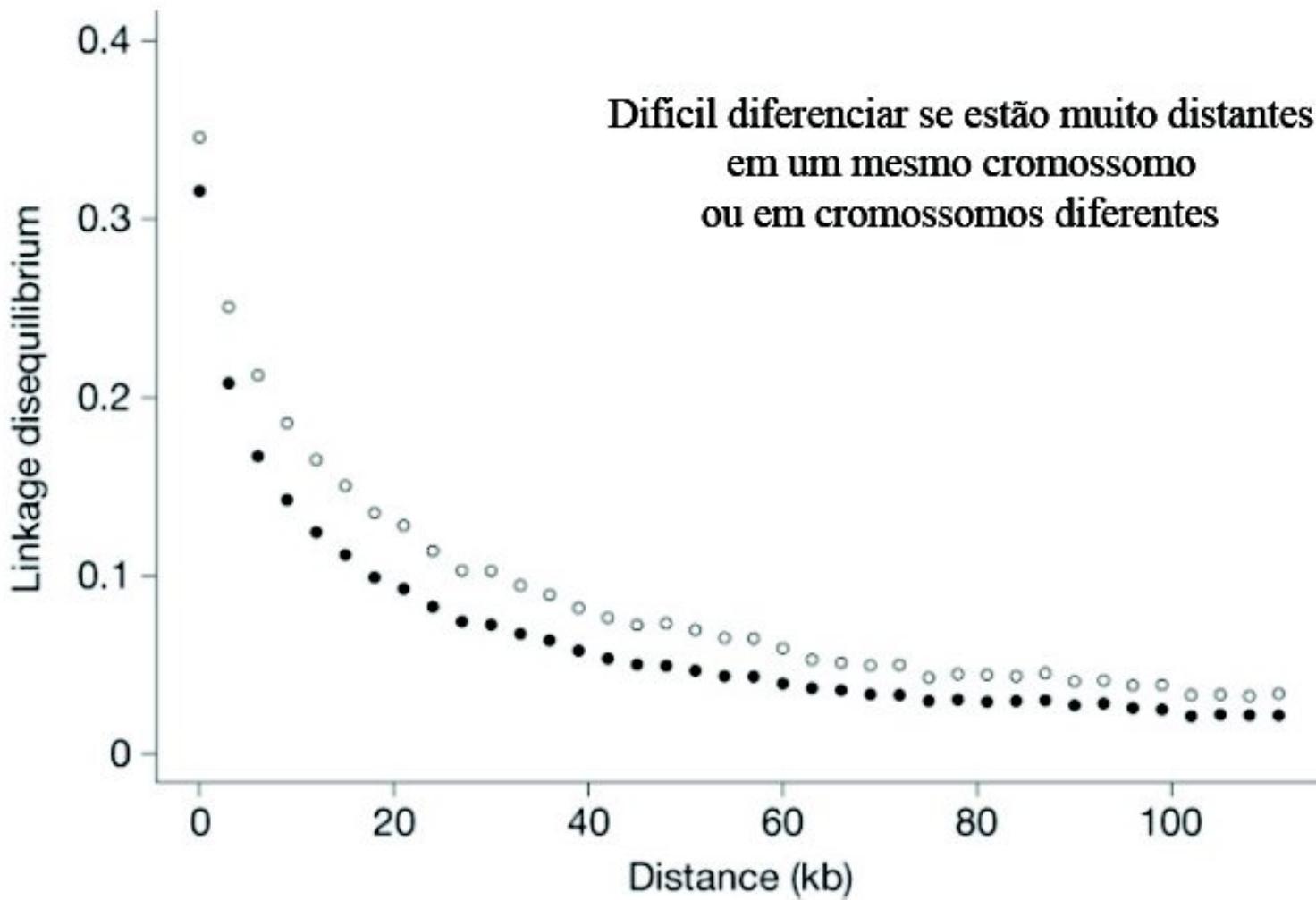


Onde estão os genes que contribuem com as características quantitativas?

VOLTANDO AO MAPEAMENTO DE QTLs

DESEQUILÍBrio DE LIGAÇÃO

MAPAS DE LIGAÇÃO



MAPEAMENTO DE QTLs

EXEMPLO EM CÃES



MAPEAMENTO DE QTLs

EXEMPLO EM CÃES



A Single *IGF1* Allele Is a Major Determinant of Small Size in Dogs

Nathan B. Sutter,¹ Carlos D. Bustamante,² Kevin Chase,³ Melissa M. Gray,⁴ Keyan Zhao,⁵ Lan Zhu,² Badri Padukasahasram,² Eric Karlins,¹ Sean Davis,¹ Paul G. Jones,⁶ Pascale Quignon,¹ Gary S. Johnson,⁷ Heidi G. Parker,¹ Neale Fretwell,⁶ Dana S. Mosher,¹ Dennis F. Lawler,⁸ Ebenezer Satyaraj,⁸ Magnus Nordborg,⁵ K. Gordon Lark,³ Robert K. Wayne,⁴ Elaine A. Ostrander^{1*}

The domestic dog exhibits greater diversity in body size than any other terrestrial vertebrate. We used a strategy that exploits the breed structure of dogs to investigate the genetic basis of size. First, through a genome-wide scan, we identified a major quantitative trait locus (QTL) on chromosome 15 influencing size variation within a single breed. Second, we examined genetic variation in the 15-megabase interval surrounding the QTL in small and giant breeds and found marked evidence for a selective sweep spanning a single gene (*IGF1*), encoding insulin-like growth factor 1. A single *IGF1* single-nucleotide polymorphism haplotype is common to all small breeds and nearly absent from giant breeds, suggesting that the same causal sequence variant is a major contributor to body size in all small dogs.

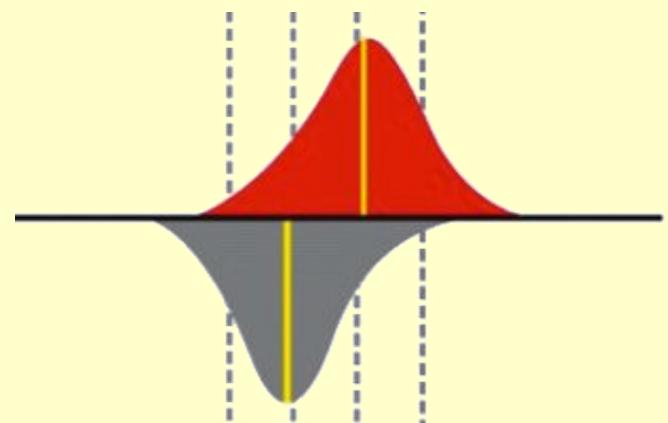
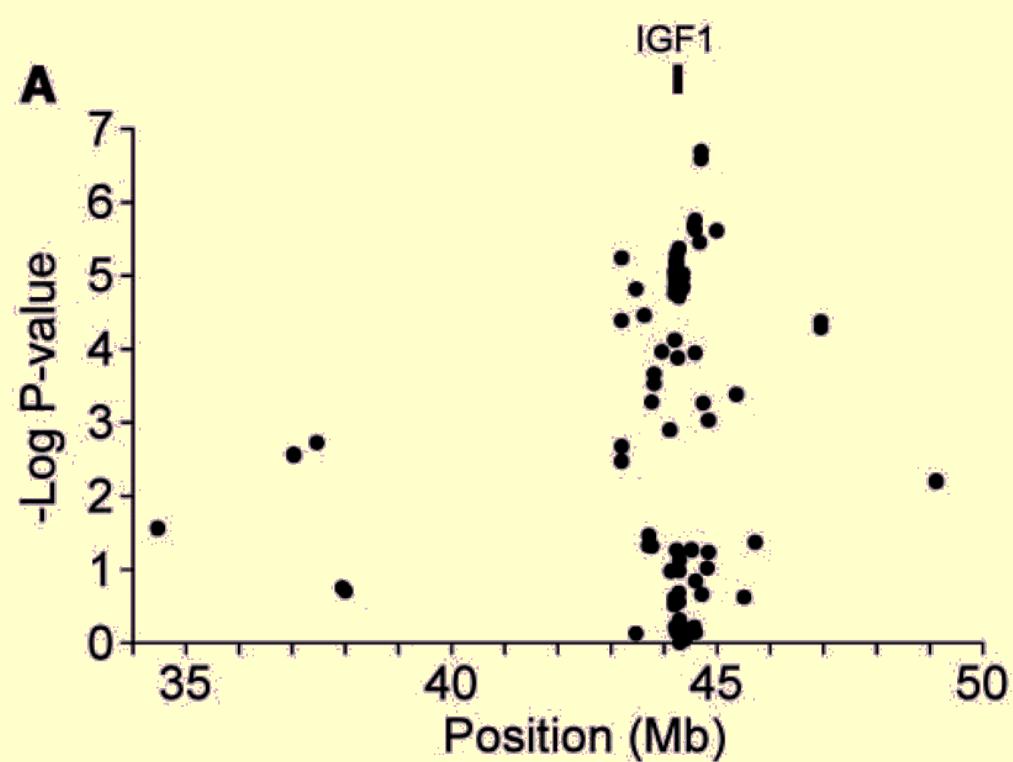
MAPEAMENTO DE QTLs

EXEMPLO EM CÃES



463 cães (cão d'água português)

IGF1 se liga ao receptor transdutor de sinal tirosina quinase, que promove crescimento e longevidade celular



MAPEAMENTO DE QTLs

EXEMPLO EM CÃES



463 cães (cão d'água português)

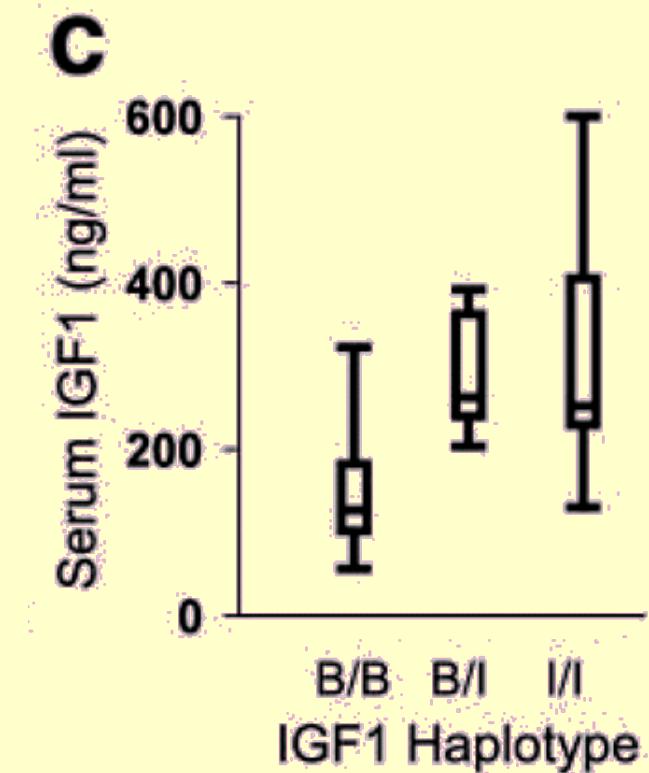
Genótipo B/B = cães menores
Genótipo B/I = cães intermediários
Genótipo I/I = cães maiores

MAPEAMENTO DE QTLs

EXEMPLO EM CÃES



463 cães (cão d'água português)



MAPEAMENTO DE QTLs

EXEMPLO EM CÃES

