

LINKAGE E MAPA DE LIGAÇÃO

Aula 4

LGN0218 – Genética Geral



Thomas Hunt Morgan
Nobel Prize - 1933

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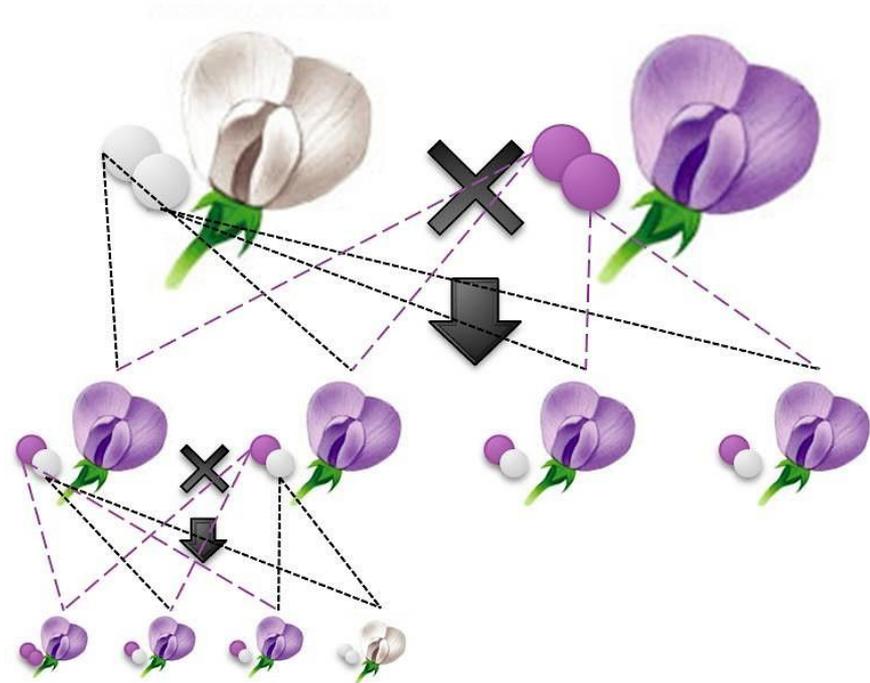


HERANÇA MONOGÊNICA

P_1 Flores brancas \times P_2
Flores púrpuras

F_1 100% Flores púrpuras

F_2 $\frac{3}{4}$ púrpuras : $\frac{1}{4}$ brancas



HERANÇA MENDELIANA PARA 2 OU MAIS CARACTERES (2ª LEI)

Em F₂ tem-se:

$$A_B_ = \frac{3}{4} \times \frac{3}{4} = \frac{9}{16}$$

$$A_bb = \frac{3}{4} \times \frac{1}{4} = \frac{3}{16}$$

$$aaB_ = \frac{1}{4} \times \frac{3}{4} = \frac{3}{16}$$

$$aabb = \frac{1}{4} \times \frac{1}{4} = \frac{1}{16}$$

Seed color



Yellow



Green

Flower color



Purple



White

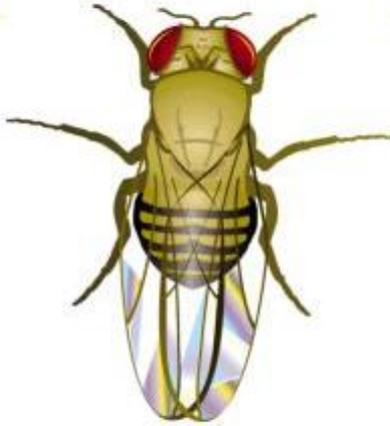
Lei da Segregação Independente!

Mas nem tudo dá certo....

++/++
(Wild type)

X

bb/vgvg
(Black vestigial)



Qual frequência esperada em F1?

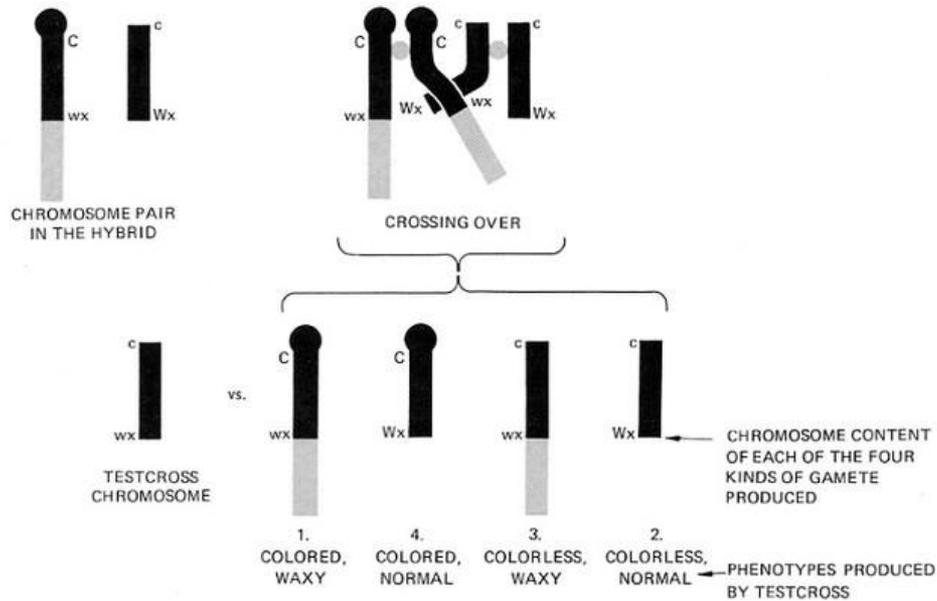
E em um cruzamento di-híbrido teste?

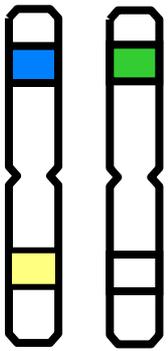
$pr^+/pr \cdot vg^+/vg$ X $pr/pr \cdot vg/vg$

Genótipo	Descendentes
$pr^+ \cdot vg^+$	1339
$pr \cdot vg$	1195
$pr^+ \cdot vg$	151
$pr \cdot vg^+$	154



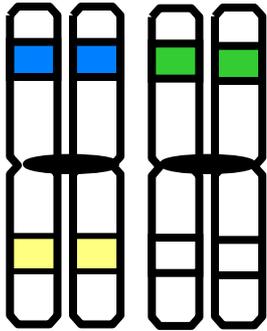
Provas citológicas ...





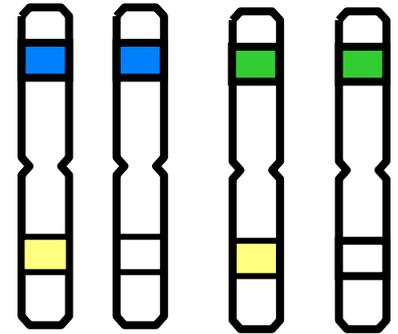
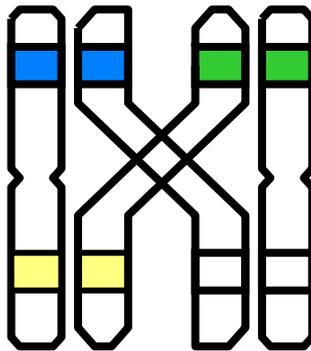
Cada homólogo (ex. "cromossomo 7") se replica para dar origem à duas cromátides irmãs

EMBARALHAMENTO DOS GENES POR *CROSSING-OVER*



Par de homólogos (ex. Cromossomo materno 7 e cromossomo paterno 7)

crossing-over,
recombinação

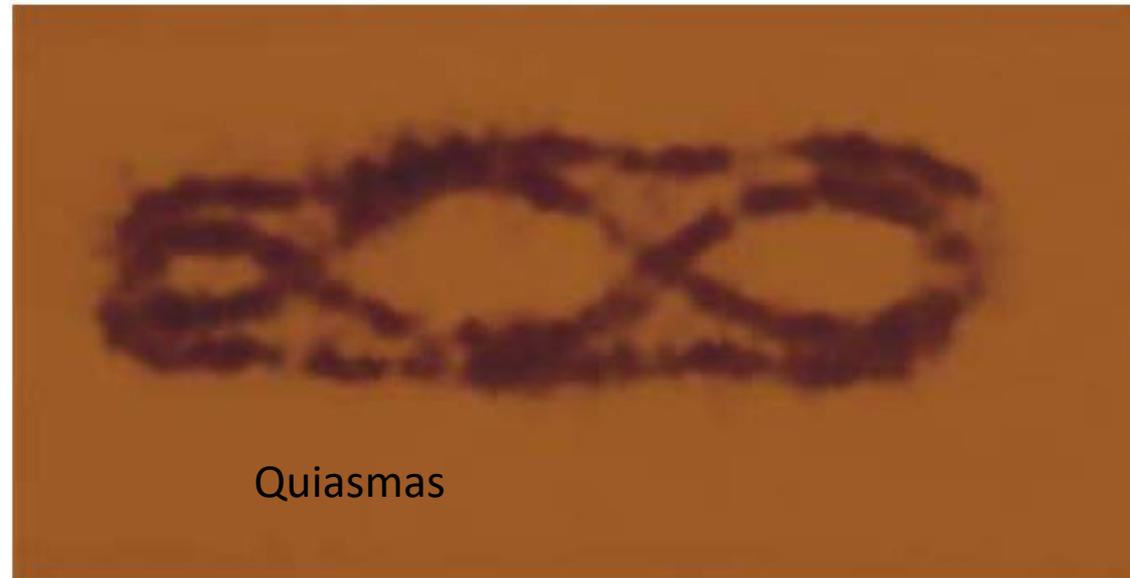
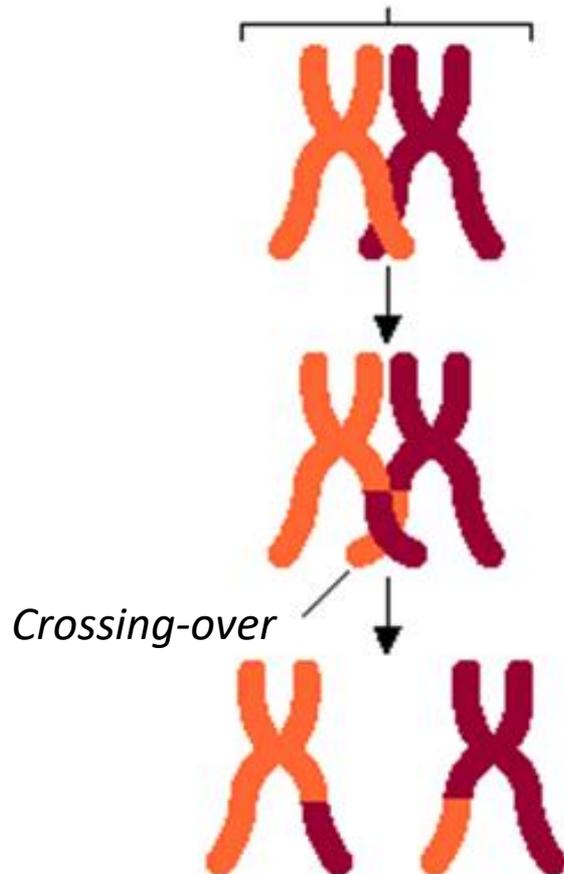


RECOMBINAÇÃO HOMÓLOGA

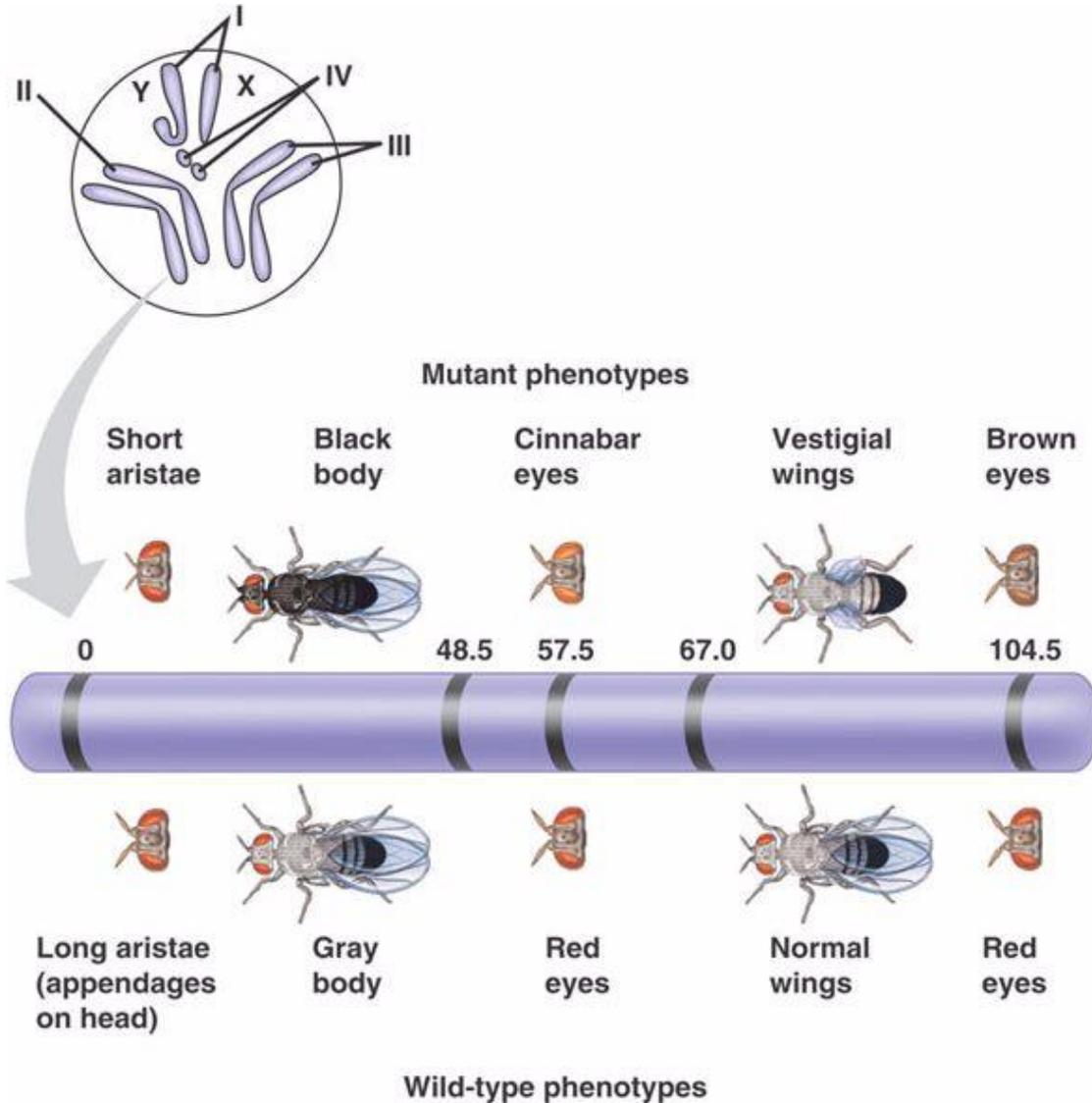
Troca de material genético entre os cromossomos homólogos → *crossing-over* (ocorre na primeira divisão nuclear). Quanto maior a distancia entre os genes mais chances de crossing over. Maior a taxa de recombinantes!!!!

Recombinação homóloga

Pareamento dos cromossomos homólogos



Morgan e colaboradores atribuíram genes aos 4 cromossomos de *Drosophila*



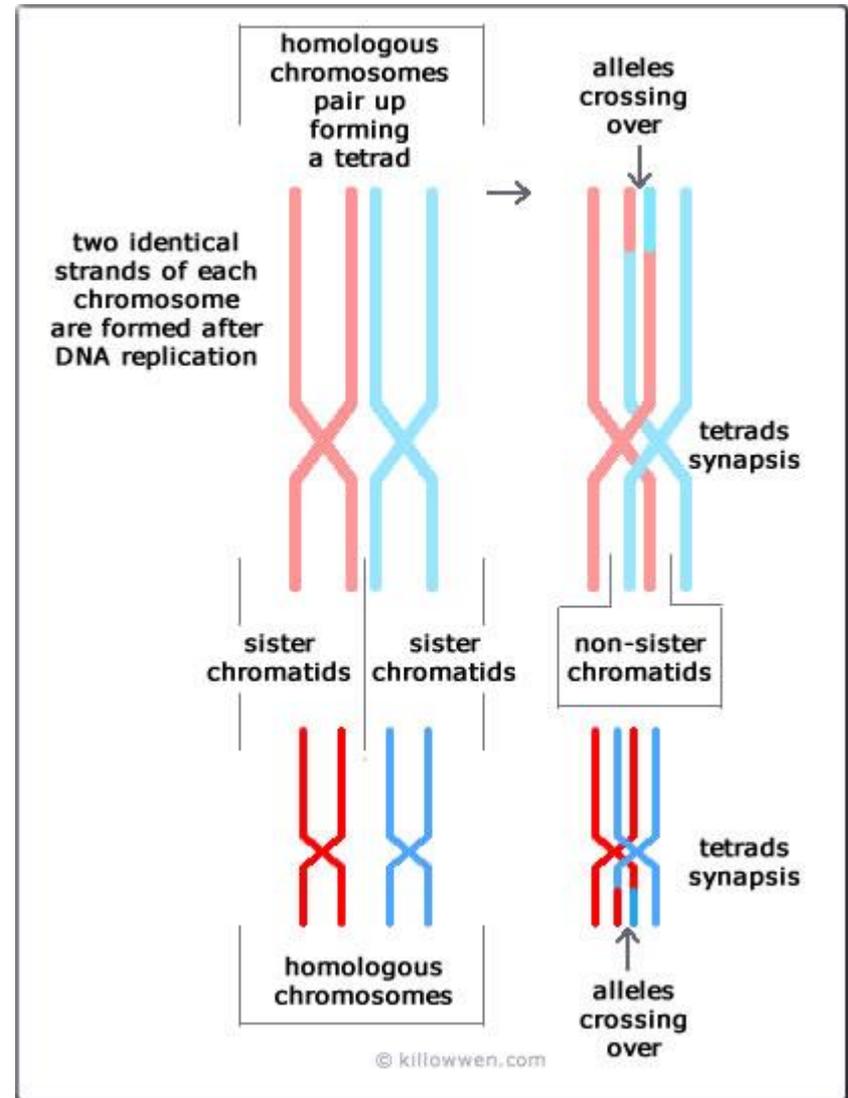
Alfred Sturtevant

Cálculo da *fr*: no Cruzamento-Teste:

$$fr = r = \frac{\sum \text{tipos recombinantes}}{N}$$

A distância entre os genes é função da frequência de recombinação

O crossing-over é o processo pelo qual os dois cromossomos de um par homólogo trocam segmentos iguais entre si. O crossing-over ocorre na Prófase I durante a meiose I. Na interfase, o cromossomo se replicou em duas cadeias - as cromátides irmãs. Os dois cromossomos homólogos de um par sinapse. Enquanto os cromossomos são sinapsados, quebras ocorrem em pontos correspondentes em duas das cromátides não-irmãs. Como resultado, uma nova combinação de alelos é produzida no cromossomo - isso é chamado de recombinação.



Note que há 4 cromátides e só 2 envolvidas no crossing (ou permuta): a frequência de crossing é o dobro da frequência de recombinação

Supor eventos de crossing (meiose)

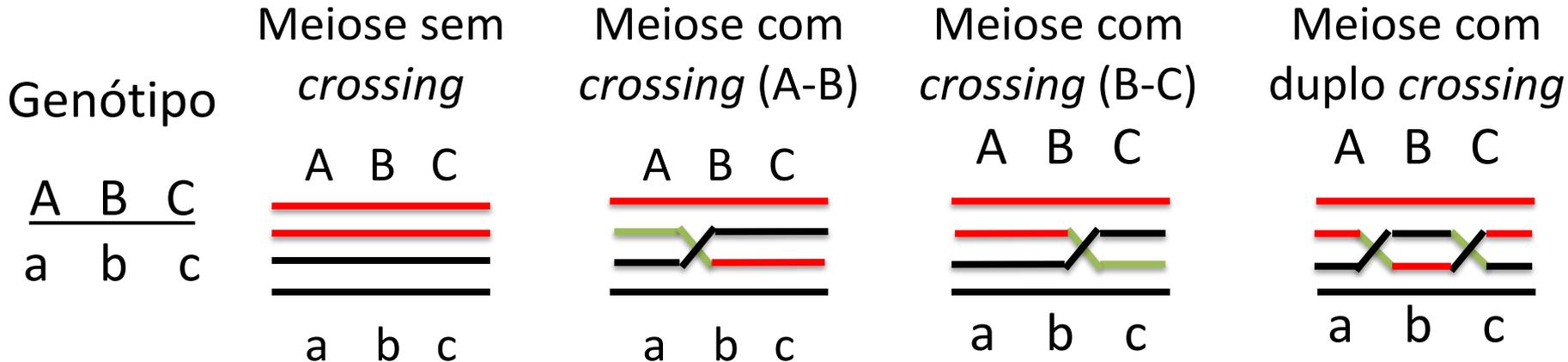
20%



10%



20% × 10% = 2%



Gametas do F₁ (triplamente heterozigótico):

Por diferença:	ABC = 5%	ABC = 2,5%	ABC = 0,5%
ABC = 34%	abc = 5%	abc = 2,5%	abc = 0,5%
abc = 34%	Abc = 5%	ABc = 2,5%	AbC = 0,5%
100 - 32 = 68%	aBC = 5%	abC = 2,5%	aBc = 0,5%

Somando os gametas parentais:

ABC = 34 + 5 + 2,5 + 0,5 = 42%

abc = 34 + 5 + 2,5 + 0,5 = 42%

Total = 42(ABC) + 42(abc) + 5(Abc) + 5(aBC) + 2,5(ABc) + 2,5(aBC) + 0,5(AbC) + 0,5(aBc)
= 84 + 10 + 5 + 1 = 100% ✓

Genótipo

A B C
a b c

**Gametas do F₁
triplamente
heterozigótico:**

ABC	= 42%
abc	= 42%
Abc	= 5%
aBC	= 5%
ABc	= 2,5%
abC	= 2,5%
AbC	= 0,5 %
aBc	= 0,5%
Total	= 100%

Cálculo das distâncias:

Distância entre A e B = $5 + 5 + 0,5 + 0,5 = 11$ cM ou 11%

Distância entre B e C = $2,5 + 2,5 + 0,5 + 0,5 = 6$ cM ou 12%

Distância entre A e C = $11 + 6 = 17$ cM ou 17%

Mapa genético:



Análise a progênie oriunda do cruzamento teste ABC × abc

Determine a distância entre os genes A, B e C:

Progênie	Nº de indivíduos
ABC/abc	410
abc/abc	430
Abc/abc	55
aBC/abc	45
ABc/abc	24
abC/abc	26
AbC/abc	5
aBc/abc	5
Total	1.000

$$\text{Distância entre A-B} = \frac{\sum R}{N} = \frac{55 + 45 + 5 + 5}{1.000} = 11\% \text{ ou } 11 \text{ cM}$$

$$\text{Distância B-C} = \frac{24 + 26 + 5 + 5}{1.000} = 6\% = 6 \text{ cM}$$

$$\text{Distância A-C} = \frac{55 + 45 + 24 + 26}{1.000} = 15\% = 15 \text{ cM}$$

- Note que a distância calculada entre os genes extremos é menor que a real
- Corrigindo: Distância AC = Distância calculada + 2 x Freq DR observada = 15% + 2 x [(5 + 5)/1.000 x 100] = 15% + 2 x [(10/1.000) x 100] = 15% + (2 x 1%) 15% + 2% = 17% ou 17 cM
- Note que é preciso trabalhar sempre com a mesma unidade.

Passo a passo....

Diferentes linhas puras (ou homozigotos), contrastantes, que podem ser cruzadas e dar origem ao F_1 com o mesmo fenótipo, supondo tripla dominância:

$ABC/ABC \times abc/abc \rightarrow F_1 : ABC/abc$

.
. .
. .

Qualquer um desses híbridos F_1 podem ser submetidos ao cruzamento-teste para o cálculo da distância entre os genes

1. Reescrevo a tabela

Progênie do cruz.-teste	No de indivíduos	Progênie do cruz.-teste	No de indivíduos
+++/abc	330	+++/abc	330
abc/abc	320	abc/abc	320
+b+/abc	64	+b+/abc	64
a++/abc	10	a+c/abc	66
a+c/abc	66	++c/abc	100
++c/abc	100	ab+/abc	95
+bc/abc	15	+bc/abc	15
ab+/abc	95	a++/abc	10
Total	1.000	Total	1.000

2. Identifico as classes com maior número de indivíduos (são os parentais)

+++ (330)
abc (320)

3. Identifico as classes com menor número de indivíduos (DRs)

+bc (15)
a++ (10)

Progênie do cruz.-teste	No de indivíduos
+++ /abc	330
abc /abc	320
+b+ / abc	64
a+c / abc	66
++c / abc	100
ab+ / abc	95
+bc / abc	15
a++ / abc	10
Total	1.000

4. Comparo os genótipos (parentais com DRs) e identifico o gene diferente entre as classes. O gene a, portanto, é o gene que está no centro do mapa

➤ A ordem correta é bac ou cab (tanto faz)

5. Construo o genótipo do F₁ = +++/bac

6. Calculo as distâncias entre b — a, a — c, e b — c

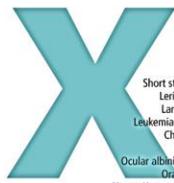
$$b \text{ — } a = 64 + 66 + 15 + 10 = 155/1.000 = 15,5 \text{ cM}$$

$$a \text{ — } c = 100 + 95 + 15 + 10 = 220/ 1.000 = 22 \text{ cM}$$

$$b \text{ — } c = 64 + 66 + 100 + 95 = 325/ 1.000 = 32,5 \text{ cM}$$

$$\text{Corrigindo: } 32,5 + 2 \times \text{FDR obs.} = 32,5 + [2 \times (10+15/1.000)] = 32,5 + 2 \times [(25/1.000) \times 100] = 32,5\% + 2 \times 2,5\% = 37,5 \text{ cM}$$



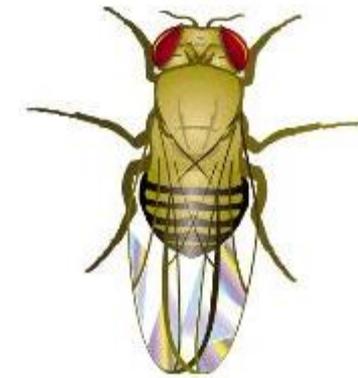
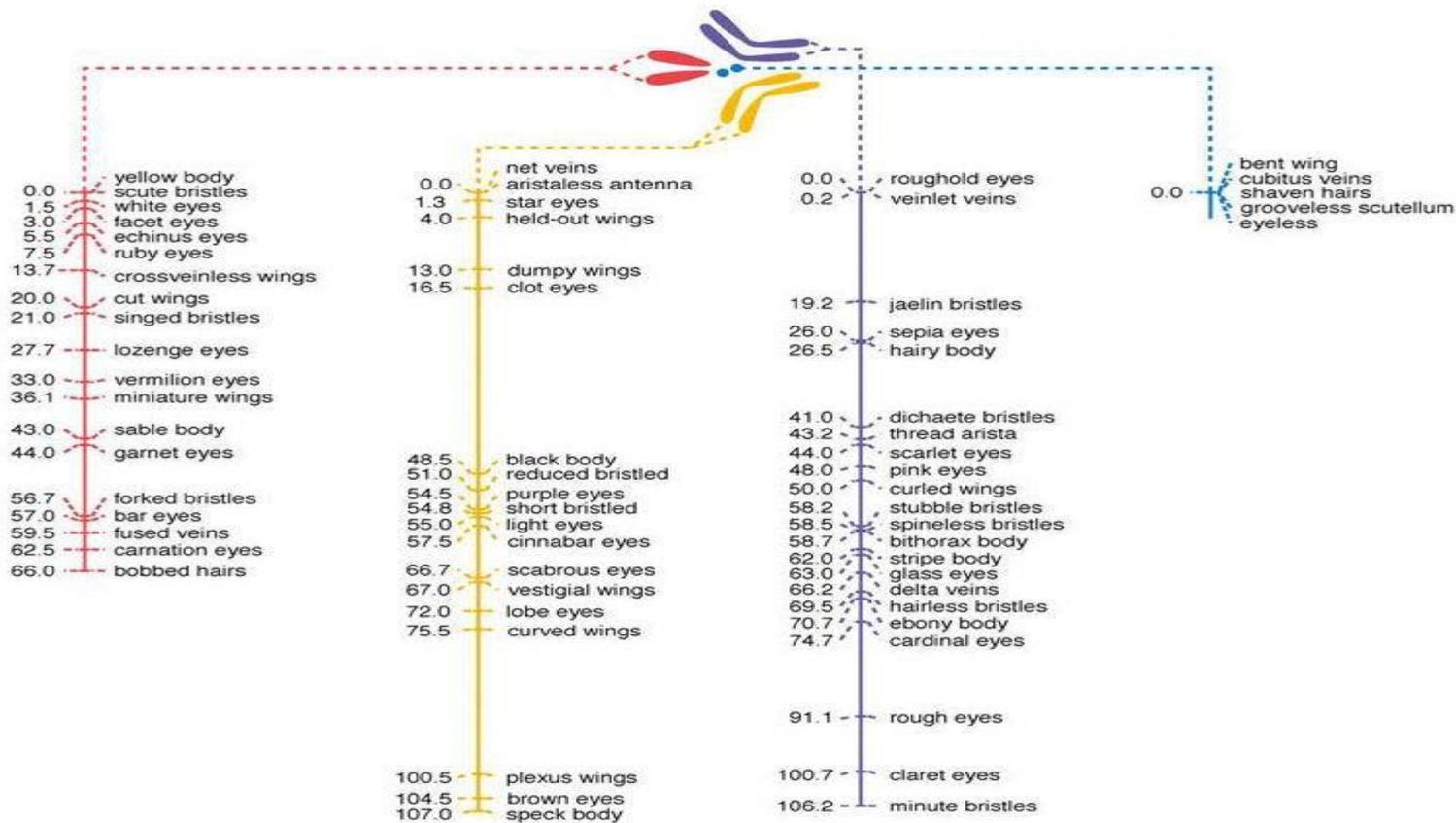


153 million base pairs

- Short stature, idiopathic familial
- Leri-Weill dyschondrosteosis
- Langer mesomelic dysplasia
- Leukemia, acute myeloid, M2 type
- Chondrodysplasia punctata
- Kalman syndrome
- Ocular albinism, Nettleship-Falls type
- Oral-facial-digital syndrome
- Nance-Horan cataract-dental syndrome
- Heterocellular hereditary persistence of fetal hemoglobin
- Pyruvate dehydrogenase deficiency
- Glycogen storage disease
- Coffin-Lowry syndrome
- Mental retardation
- Spondyloepiphyseal dysplasia tarda
- Paroxysmal nocturnal hemoglobinuria
- Infantile spasm syndrome
- Aicardi syndrome
- Deafness, sensorineural
- Simpson-Golabi-Behmel syndrome, type 2
- Adrenal hypoplasia, congenital
- Dosage-sensitive sex reversal
- Deafness, congenital sensorineural
- Retinitis pigmentosa
- Wilson-Turner syndrome
- Cone dystrophy
- Aland island eye disease (ocular albinism)
- Optic atrophy
- Night blindness, congenital stationary, type 1
- Erythroid-potentiating activity
- Arthrogryposis multiplex congenita
- Night blindness, congenital stationary, type 2
- Brunner syndrome
- Wiskott-Aldrich syndrome
- Thrombocytopenia
- Dent disease
- Nephrolithiasis, type I
- Hypophosphatemia, type II
- Proteinuria
- Anemia, sideroblastic/hypochromic
- Cerebellar ataxia
- Renal cell carcinoma, papillary
- Diabetes mellitus, insulin-dependent
- Sutherland-Haas syndrome
- Cognitive function, social
- Mental retardation, nonspecific
- Menkes disease
- Occipital horn syndrome
- Curtis laxa, neonatal
- FG syndrome
- Immunodeficiency, moderate and severe
- Miles-Carpenter syndrome
- Charcot-Marie-Tooth neuropathy, dominant
- Mental retardation
- X-inactivation center
- Premature ovarian failure
- Arts syndrome
- Cleft palate and/or ankyloglossia
- Megalocornea
- Epilepsy (Juberg-Hellman syndrome)
- Peltzæus-Merzbacher disease
- Spastic paraplegia
- Alport syndrome
- Cowchock syndrome
- Hypertrichosis, congenital generalized
- Ptosis, hereditary congenital
- Apoptosis inhibitor
- Panhypopituitarism
- Thoracoabdominal syndrome
- Simpson-Golabi-Behmel syndrome, type 1
- Split hand/foot malformation, type 2
- Hypoparathyroidism
- Mental retardation, Shashi type
- Lesch-Nyhan syndrome
- HPRT-related gout
- Lowe syndrome
- Borjeson-Forsman-Lehmann syndrome
- Testicular germ cell tumor
- Hemophilia B
- Warfarin sensitivity
- Osseous dysplasia (male lethal), digital
- Adrenoleukodystrophy
- Adrenomyeloneuropathy
- Colorblindness, blue monochromatic
- Cardiac valvular dysplasia
- Emery-Dreifuss muscular dystrophy
- Heterotopia, periventricular
- Ferion
- Hemolytic anemia
- Colorblindness, green cone pigment
- Incontinentia pigmenti, type II
- Hydrocephalus
- MASA syndrome
- Spastic paraplegia
- Rett syndrome
- Mature T-cell proliferation
- Myopia (Bornholm eye disease)
- Mental retardation with psychosis
- Endocardial fibroelastosis



- Hodgkin disease susceptibility, pseudoautosomal
- Ichthyosis
- Microphthalmia, dermal aplasia, and sclerocornea
- Episodic muscle weakness
- Mental retardation
- Ocular albinism and sensorineural deafness
- Amelogenesis imperfecta
- Charcot-Marie-Tooth disease, recessive
- Keratosis follicularis spinulosa decalvans
- Hypophosphatemia, hereditary
- Partridge syndrome
- Retinosischisis
- Gonadal dysgenesis, XY female type
- Mental retardation, non-dysmorphic
- Agammaglobulinemia, type 2
- Craniofrontonasal dysplasia
- Opitz G syndrome, type I
- Pigment disorder, reticulate
- Melanoma
- Duchenne muscular dystrophy
- Becker muscular dystrophy
- Cardiomyopathy, dilated
- Chronic granulomatous disease
- Snyder-Robinson mental retardation
- Norrie disease
- Exudative vitreoretinopathy
- Coats disease
- Reepening syndrome
- Retinitis pigmentosa, recessive
- Mental retardation, nonspecific and syndromic
- Dyserythropoietic anemia with thrombocytopenia
- Chondrodysplasia punctata, dominant
- Autoimmunity-immunodeficiency syndrome
- Renal cell carcinoma, papillary
- Facio-genital dysplasia (Aarskog-Scott syndrome)
- Chorioathetosis with mental retardation
- Sarcoma, synovial
- Prieto syndrome
- Spinal muscular atrophy, lethal infantile
- Migraine, familial typical
- Androgen insensitivity
- Spinal and bulbar muscular atrophy
- Prostate cancer
- Perineal hypospadias
- Breast cancer, male, with Reifenstein syndrome
- Ectodermal dysplasia, anhidrotic
- Alpha-thalassemia/mental retardation
- Juberg-Marsidi syndrome
- Sutherland-Haas syndrome
- Smith-Fineman-Myers syndrome
- Hemolytic anemia
- Myoglobinuria/hemolysis
- Wieacker-Wolff syndrome
- Torsion dystonia-parkinsonism, Filipino type
- Leukemia, myeloid/lymphoid or mixed-lineage
- Anemia, sideroblastic, with ataxia
- Allan-Henderson syndrome
- Deafness
- Choroideremia
- Agammaglobulinemia
- Fabry disease
- Mohr-Tranebjærg syndrom
- Jensen syndrome
- Lissencephaly
- Bazex syndrome
- Mental retardation with growth hormone deficiency
- Mental retardation, South African type
- Lymphoproliferative syndrome
- X inactivation, familial skewed
- Pettigrew syndrome
- Gustavson mental retardation syndrome
- Immunodeficiency, with hyper-IgM
- Retinitis pigmentosa
- Wood neuroimmunologic syndrome
- Heterotaxy, visceral
- Albinism-deafness syndrome
- Cone dystrophy, progressive
- Prostate cancer susceptibility
- Fragile X mental retardation
- Epidermolysis bullosa, macular type
- Diabetes insipidus, nephrogenic
- Cancer/testis antigen
- Dyskeratosis
- Hemophilia A
- Hunter syndrome
- Mucopolysaccharidosis
- Intestinal pseudoobstruction, neuronal
- Melanoma antigens
- Mental retardation-skeletal dysplasia
- Myotubular myopathy
- Otopalatodigital syndrome, type I
- Colorblindness, red cone pigment
- Goemien TKCR syndrome
- Waisman parkinsonism-mental retardation
- Barth syndrome
- Cardiomyopathy, dilated
- Noncompaction of left ventricular myocardium
- Von Hippel-Lindau binding protein



Exercício: Observe o mapa do cromossomo II de *Drosophila*.

Calcule o quanto se espera de cada classe fenotípica na progênie de um cruzamento-teste entre moscas com corpo cinza (+), olhos vermelhos (+) e asas normais (+) e moscas com corpo negro (*b*), olhos cinnabar (*c*) e asas vestigiais (*vg*).

Importante: suponha que apenas 50% dos DR esperados ocorreram (ou seja, houve uma interferência de 50% na probabilidade teórica de ocorrência de duplo crossing-over).

Genetic Map Based on Recombination Frequencies in <i>Drosophila</i>		
MUTANT		WILD TYPE
Short aristae	0	Long aristae
Black body	48.5	Gray body
Cinnabar eyes	57.5	Red eyes
Vestigial wings	65.5	Normal wings
Brown eyes	104.5	Red eyes
Values in centimorgan (cM) map units; recombination frequency of 0.01 = 1 cM		

LISTA DE EXERCÍCIOS...

