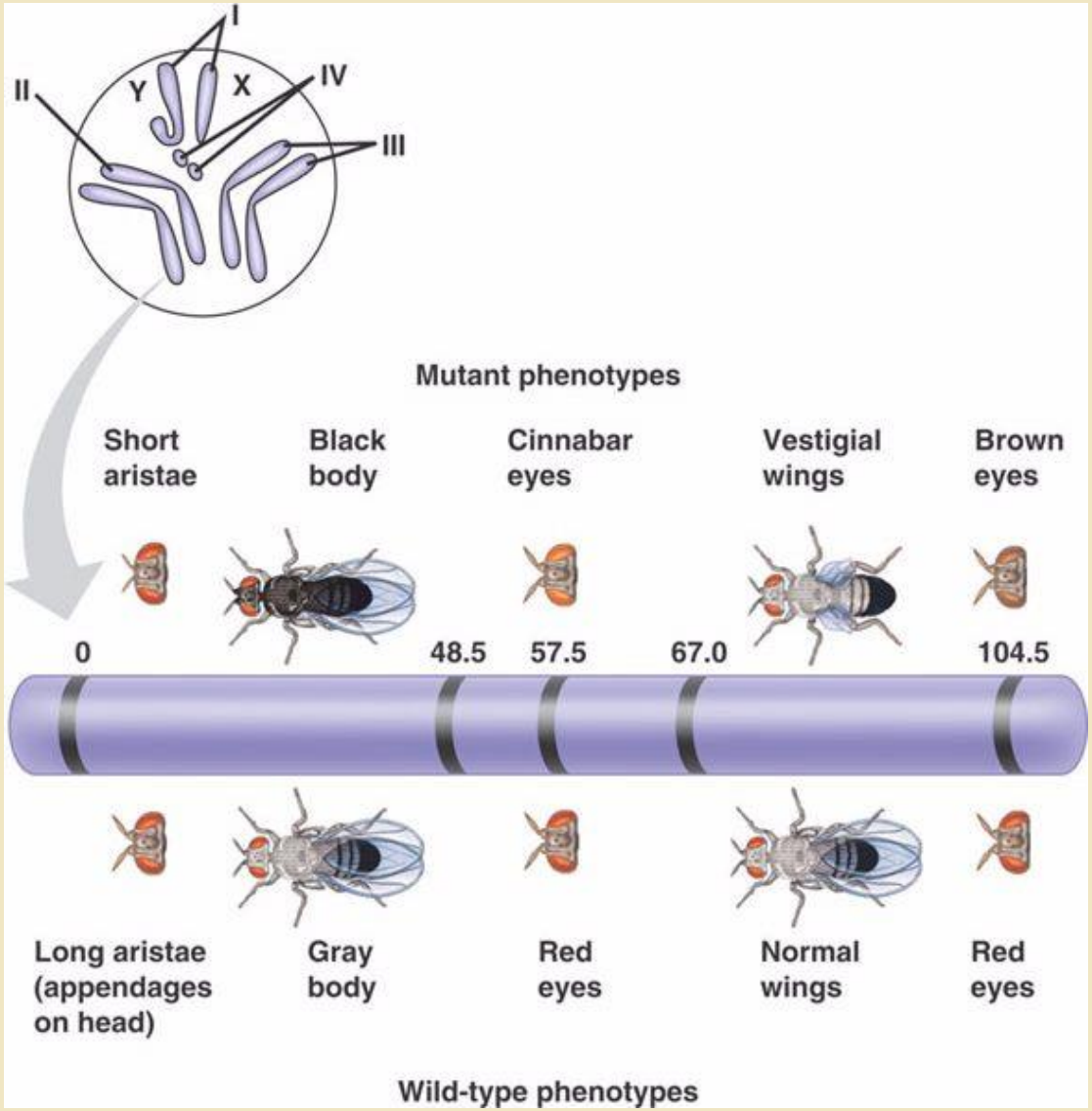
4a semana LGN 0218
Ligação e mapa genético
Material Didático, Departamento de Genética, ESALQ/ USP

Thomas Hunt Morgan was awarded the Nobel Prize in 1933)

Professora Maria Lucia Carneiro Vieira

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

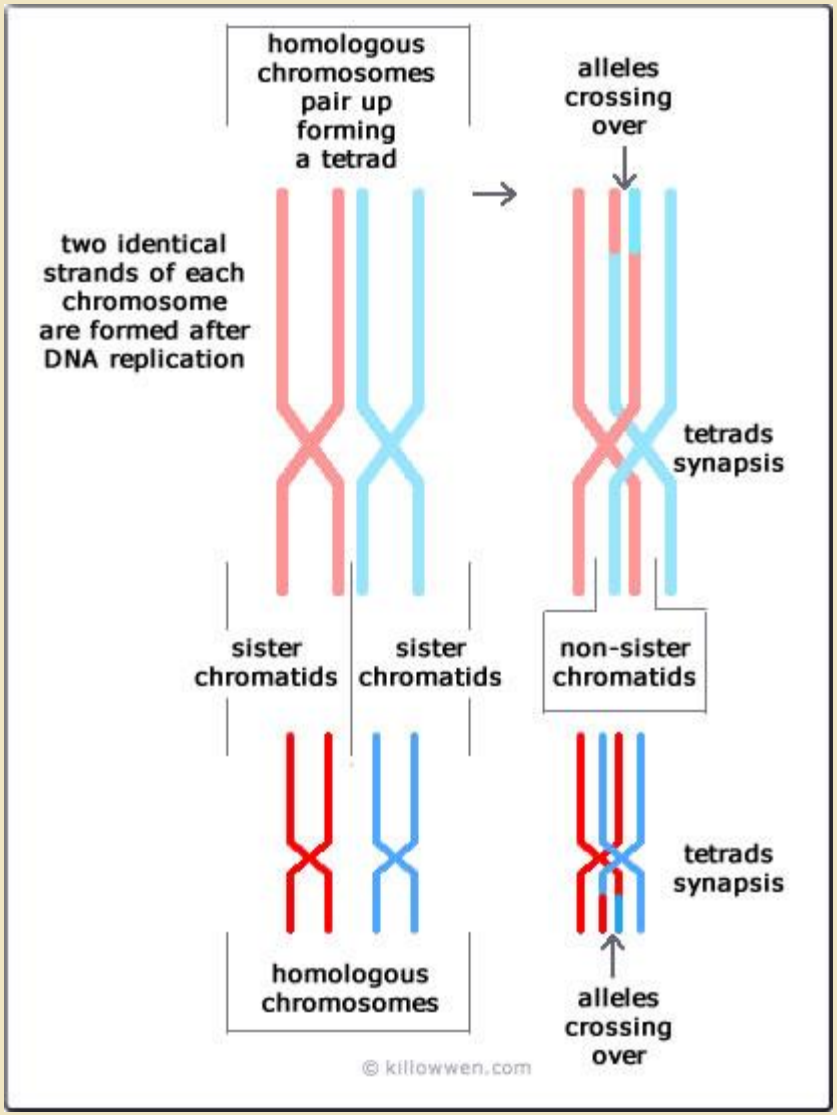


Cálculo da *fr*: no Cruzamento-Teste:

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

A distância entre os genes é função da frequência de recombinação

Crossing over is the process by which the two chromosomes of a homologous pair exchange equal segments with each other. Crossing over occurs in Prophase I during meiosis I. At interphase, chromosome has replicated into two strands - the sister chromatids.
The two homologous chromosomes of a pair synapse. While the chromosomes are synapsed, breaks occur at corresponding points in two of the **non-sister** chromatids. As a result, a new combination of alleles is produced on the chromosome - this is called **recombination**.

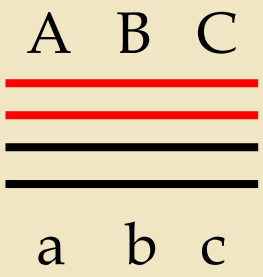


Supor eventos de crossing (meiose) 20% ↓ 10% ↓ 20% × 10% = 2% ↓

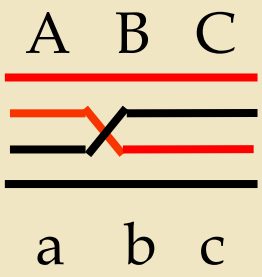
Genótipo

A B C
a b c

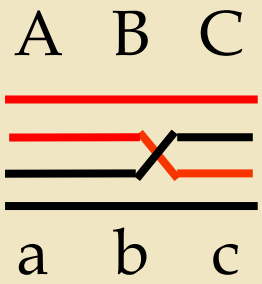
Meiose sem crossing



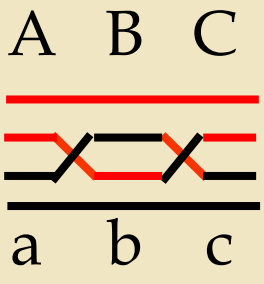
Meiose com crossing (A-B)



Meiose com crossing (B-C)



Meiose com duplo crossing



Gametas do F1 (triplamente heterozigótico):

Por diferença:
ABC = 34%
abc = 34%
100 – 32 = 68%

ABC= 5%
abc = 5%
Abc = 5%
aBC = 5%

ABC = 2,5%
abc = 2,5%
ABc = 2,5%
abC = 2,5%

ABC = 0,5%
abc = 0,5%
AbC = 0,5%
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% ✓

Analise a progênie oriunda do cruzamento teste $\frac{ABC}{abc} \times \frac{abc}{abc}$

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

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

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

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

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 x abc/ abc → F_1 : ABC/abc

AbC/ AbC x aBc /aBc → F_1 : AbC/aBc

Abc/Abc x aBC/aBC → F_1 : Abc/aBC

aBC/ aBC x Abc/Abc → F_1 : aBC/Abc

abC/ abC x ABc/ ABc → F_1 : abC/ABc

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

Exercício: **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

https://www.youtube.com/watch?v=D3fPuqJ_Fls

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 b**a**c ou c**a**b (tanto faz)

5. Construo o genótipo do F_1 = +++/bac

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

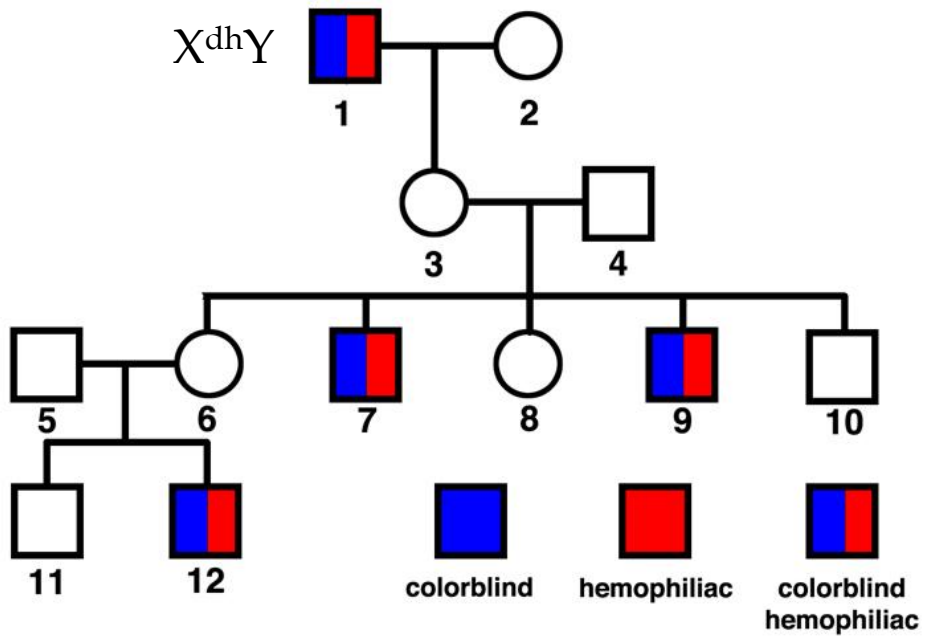
b — a = 64 + 66 + 15 + 10 = 155/1.000 = 15,5 cM

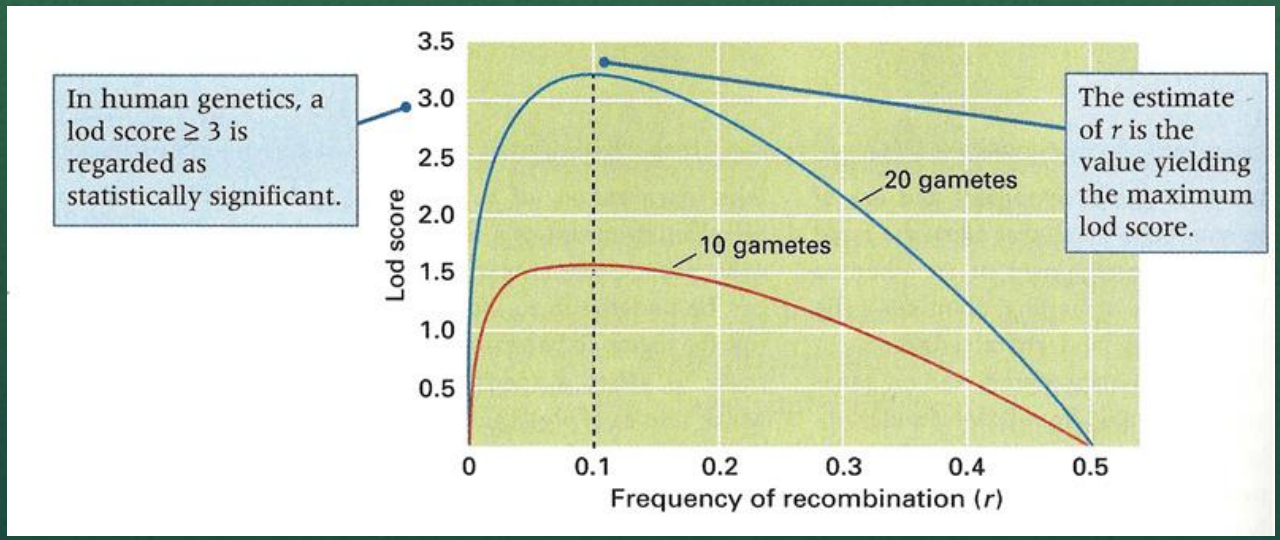
a — c = 100 + 95 + 15 + 10 = 220/ 1.000 = 22 cM

b — c = 64 + 66 + 100 + 95 = 325/ 1.000 = 32,5 cM

Corrigindo: 32,5 + 2 x FDR obs. = 32,5 + [2 x (10+15/1.000)] = 32,5 + 2 x [(25/1.000) x 100)] = 32,5% + 2 x 2,5% = 37,5 cM

Hemophilia and color blindness





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136 million base pairs

Sex-reversal, autosomal
Hyperglycinemia, nonketotic
Suppression of tumorigenicity, pancreas
Diaphyseal medullary stenosis
Melanoma
Trichoepithelioma, multiple familial
Immotile cilia syndrome
Cartilage-hair hypoplasia
X-ray repair
Fanconi anemia, complementation group G
Sialuria
Hyperoxaluria, primary, type II
Cardiomyopathy
Deafness, autosomal recessive
Choreoacanthocytosis
Prostate-specific gene
Bamforth-Lazarus syndrome
Tyrosine kinase-like orphan receptor
Brachydactyly, type B1
Nephronophthisis (infantile)
Neuropathy, sensory and autonomic, type 1
Fructose intolerance
Basal cell carcinoma, sporadic
Muscular dystrophy, Fukuyama congenital
Basal cell nevus syndrome
Dysautonomia (Riley-Day syndrome)
Esophageal cancer
Endotoxin hyporesponsiveness
Amyotrophic lateral sclerosis, juvenile dominant
Berardinelli-Seip congenital lipodystrophy
Dystonia, torsion, autosomal dominant
Lethal congenital contracture syndrome
Leukemia, acute undifferentiated
Tuberous sclerosis
Hemolytic anemia
Telangiectasia, hereditary hemorrhagic
Ehlers-Danlos syndrome, types I and II
Joubert syndrome
Leukemia, T-cell acute lymphoblastic

Ovarian cancer
Albinism, brown and rufous
Interferon, alpha, deficiency
Leukemia
Cyclin-dependent kinase inhibitor
Venous malformations, multiple cutaneous and mucosal
Arthrogryposis multiplex congenita, distal, type 1
Galactosemia
Acromesomelic dysplasia, Maroteaux type
Myopathy, inclusion body, autosomal recessive
Hypomagnesemia with secondary hypocalcemia
Friedreich ataxia
Geniospasm
Bleeding diathesis
Hemophagocytic lymphohistiocytosis, familial
Chondrosarcoma, extraskeletal myxoid
Pseudohermaphroditism, male, with gynecomastia
Tangier disease
HDL deficiency, familial
Fanconi anemia, type C
Xeroderma pigmentosum
Epithelioma, self-healing, squamous
Leukemia, T-cell acute lymphoblastic
Muscular dystrophy, limb-girdle, type 2H
Bladder cancer
Sex reversal, XY, with adrenal failure
Leukemia transcription factor, pre-B-cell
Porphyria, acute hepatic
Lead poisoning, susceptibility to
Citrullinemia
Dopamine-beta-hydroxylase deficiency
Amyloidosis, Finnish type
Microcephaly, primary autosomal recessive
Leigh syndrome
Leukemia
Nail-patella syndrome
Prostaglandin D2 synthase (brain)
Pituitary hormone deficiency

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).