Bio 97

Linked genes

Mendel's Laws & the Chromosome Theory - I

- **Homologous pairs of chromosomes contain the same genes (excptn: X and Y)**
- **Information is often non-identical = <u>alleles</u>**
- **Homologous chromosomes <u>segregate</u> at meiosis I**

--> The two alleles of a given gene " " " "

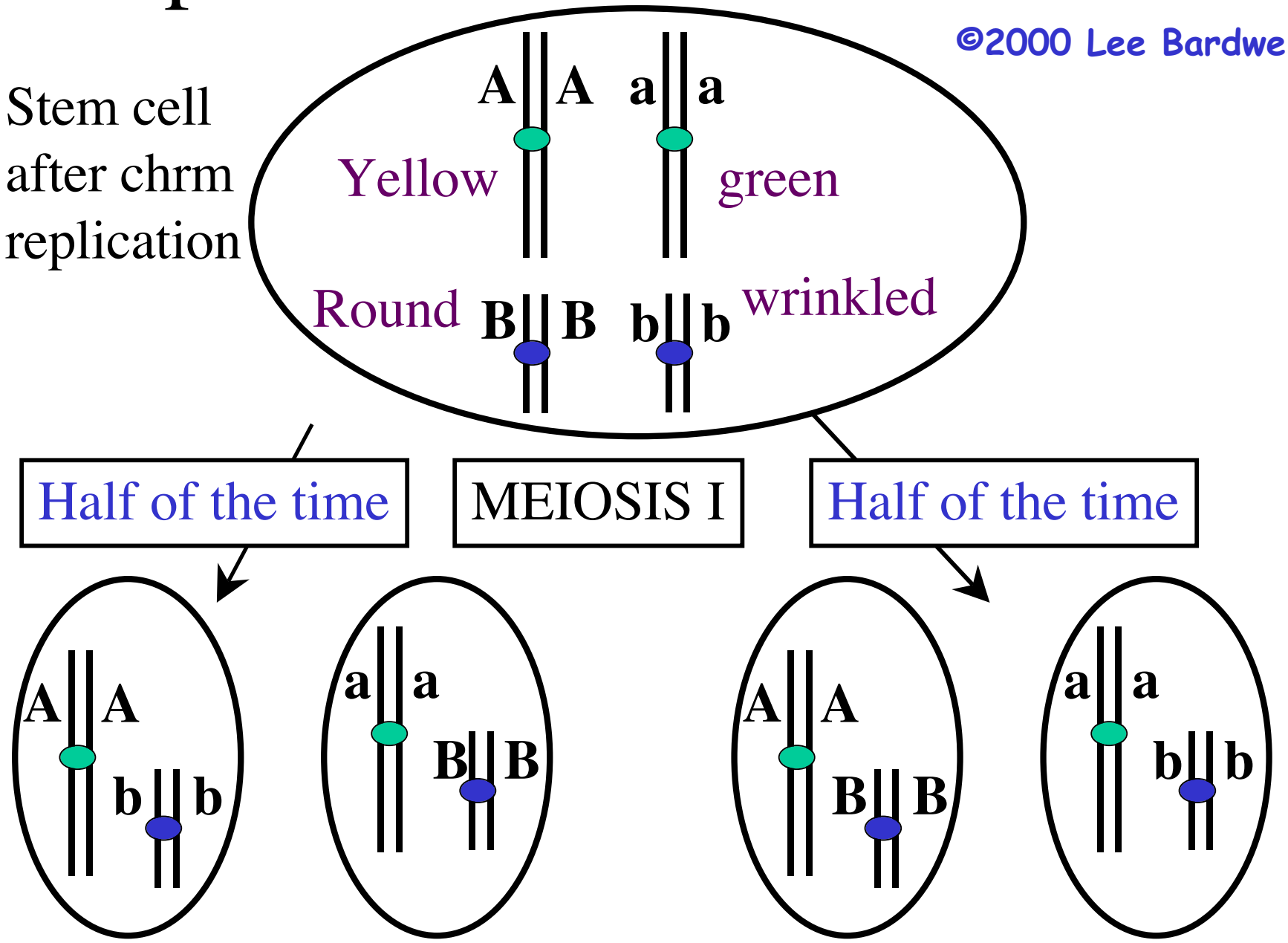
Mendel's Laws & the Chromosome Theory - II

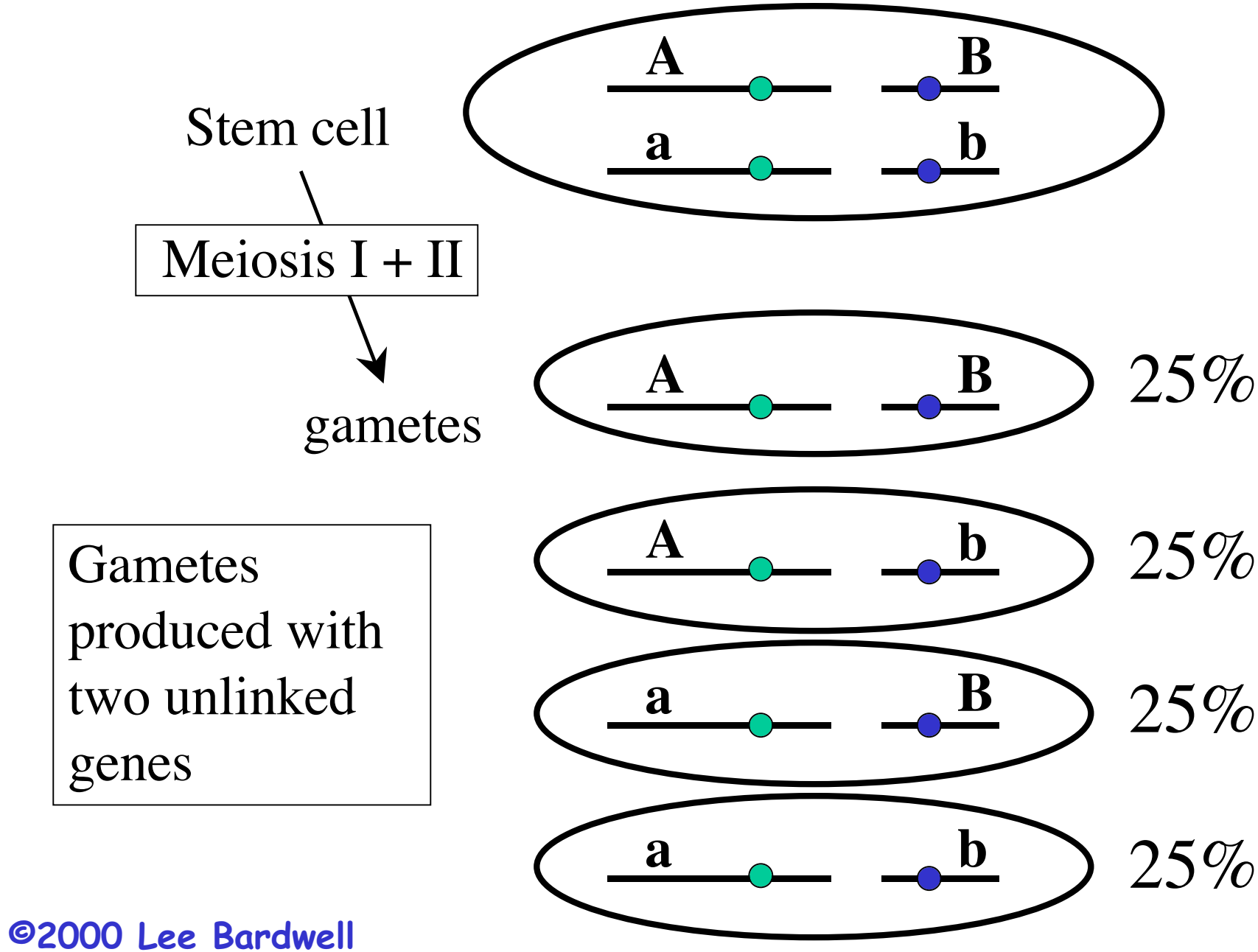
- **Homologous pairs of chromosomes line up randomly (with respect to other pairs of homologs) at Meiosis I.**

--> Alleles of genes on different chromosomes <u>assort independently</u>

Show movie

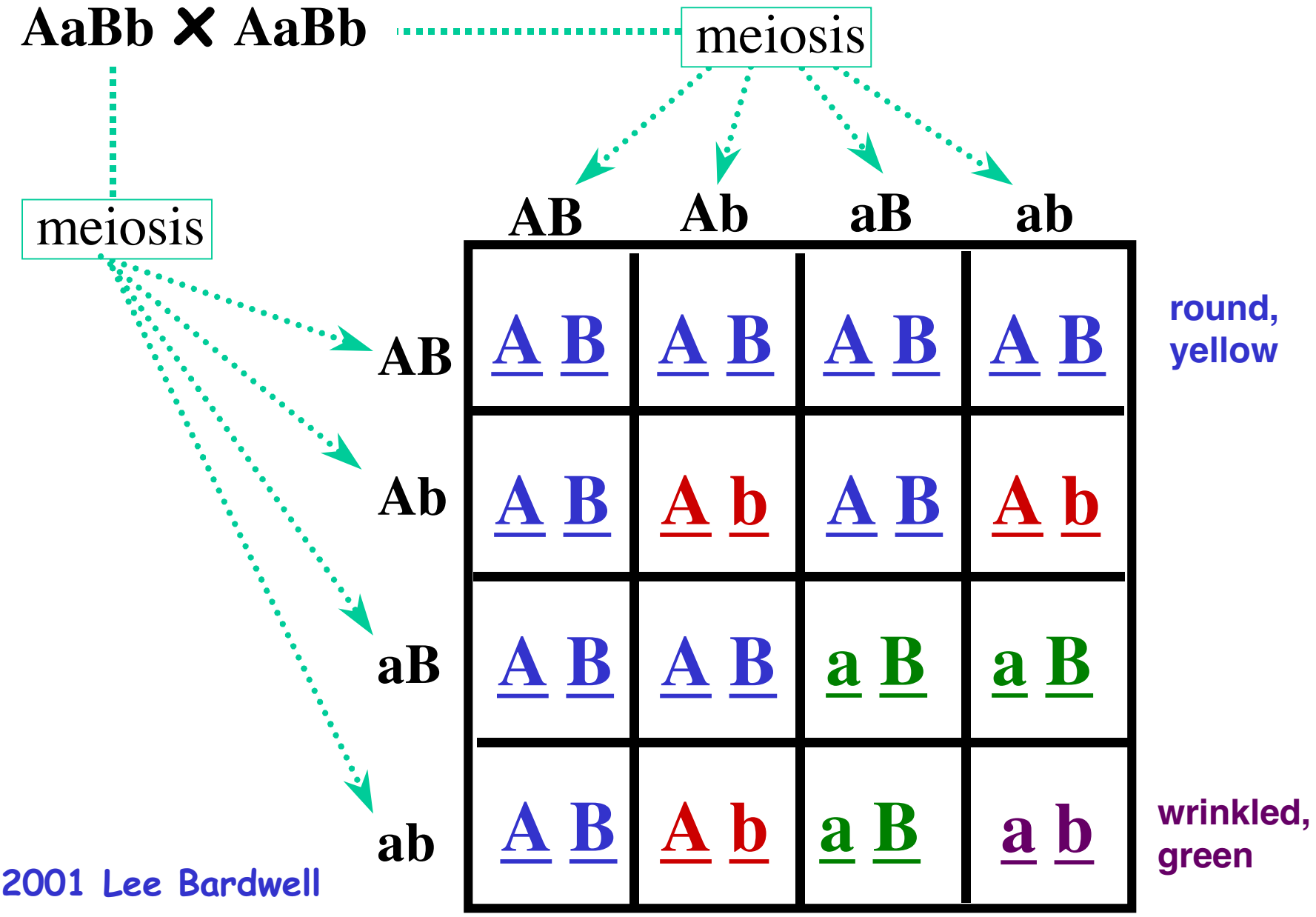
Independent Assortment of Chrms



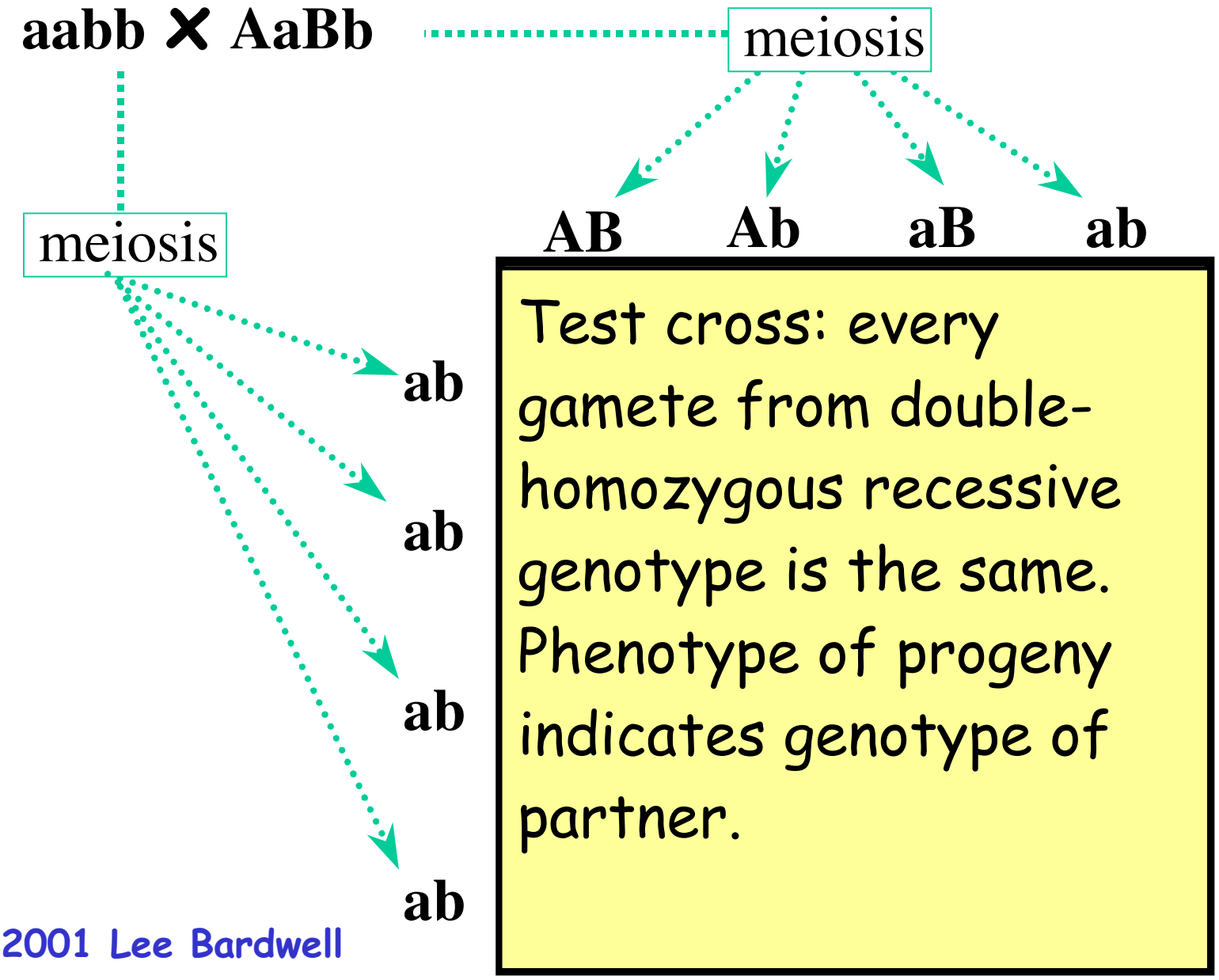


Gametes produced with two unlinked genes

Independent assortment F1 x F1

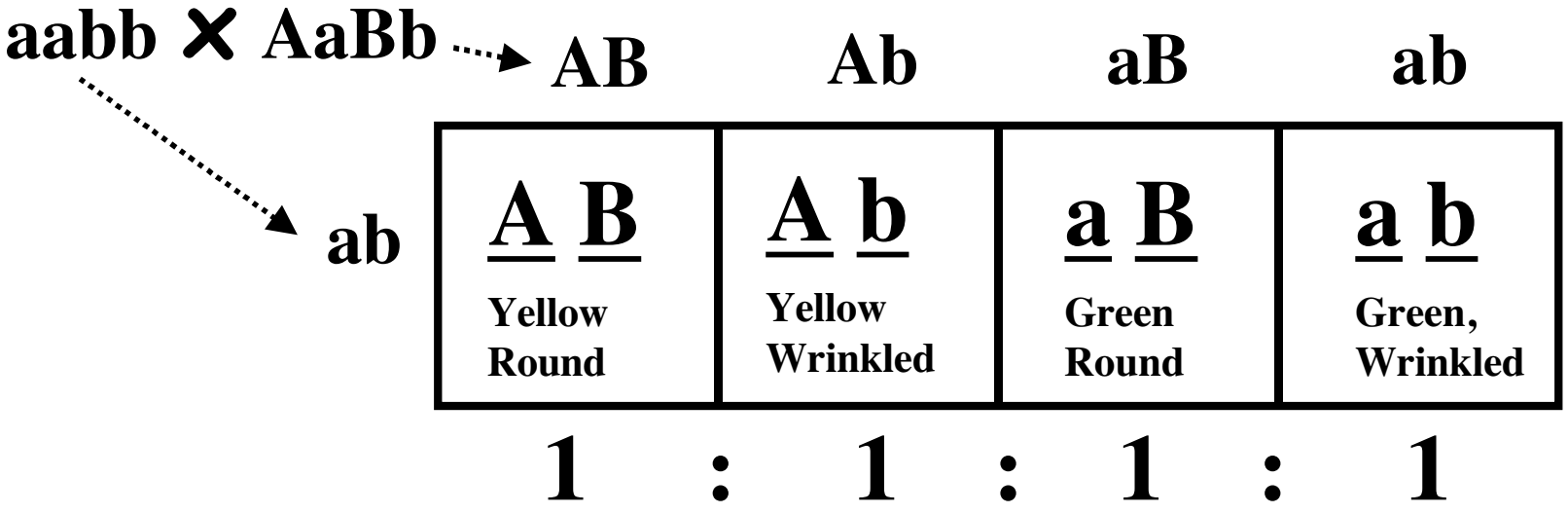


Indep. Assort. in a Test Cross



Test cross: every gamete from double-homozygous recessive genotype is the same. Phenotype of progeny indicates genotype of partner.

Test cross: dihybrid heterozygote
- genes are unlinked



CAPITALS = dominant
small = recessive
Underline = phenotype
Not underlined = genotype

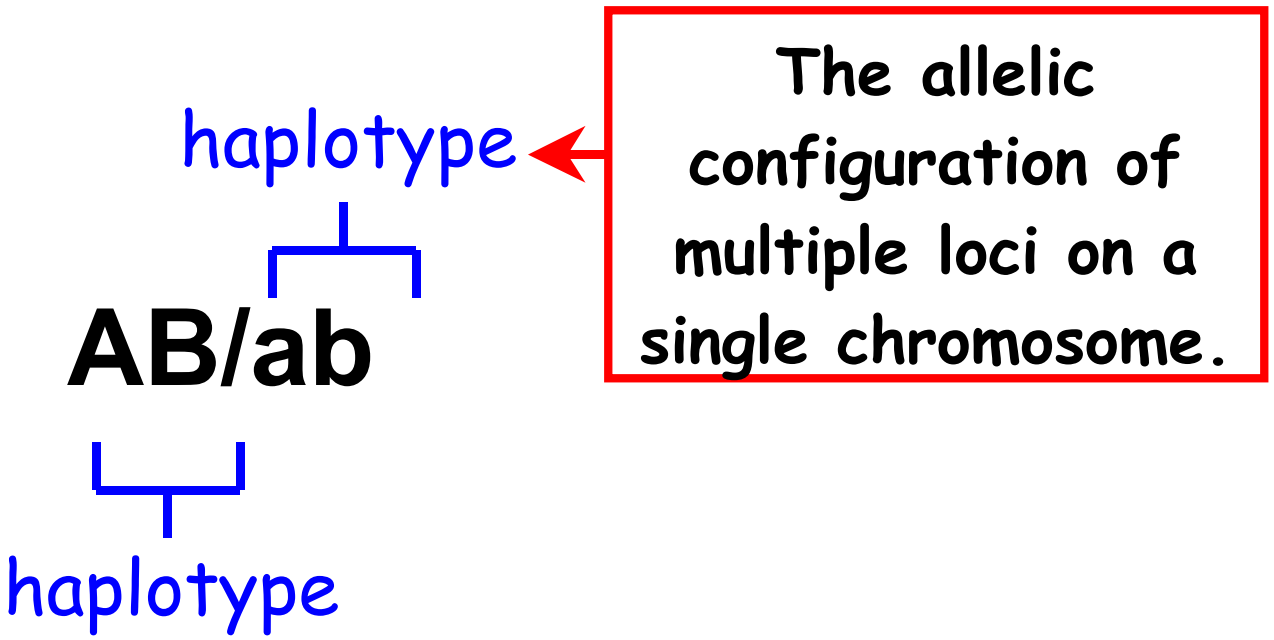
Here A and a are two alleles of a gene controlling seed color
B and b are two alleles of a gene controlling seed shape

But wait…

If we have 30,000 genes, and only 23 chrms (haploid set), then all our genes can't segregate independently

T.H. Morgan, in 1910, sets out to test the hypothesis that some genes should show a segregation pattern indicating they are linked

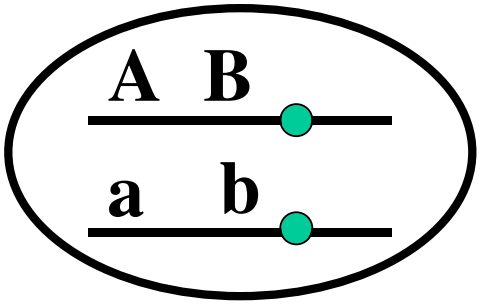
(= on same chrm)



haplotype

AB/ab

haplotype



Yellow, Round diploid cell

Recessive alleles are cis

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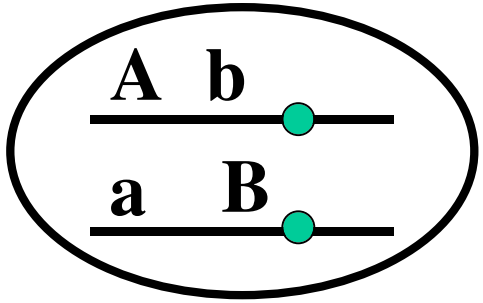
haplotype

Ab/aB

haplotype



Yellow, Round diploid cell

Recessive alleles are in trans

Three test crosses:

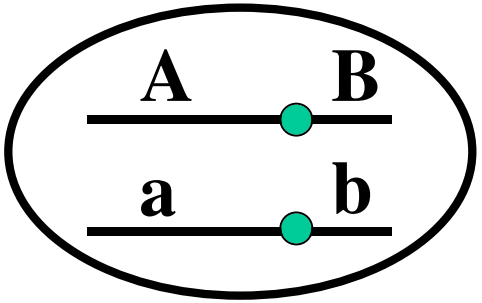
of green wrinkled to Yellow Round

1. aabb X AaBb (no linkage)

green wrinkled **Yellow Round**

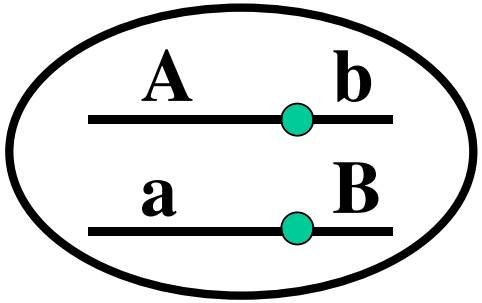
2. ab/ab X AB/ab (linked)

Recessive alleles are cis

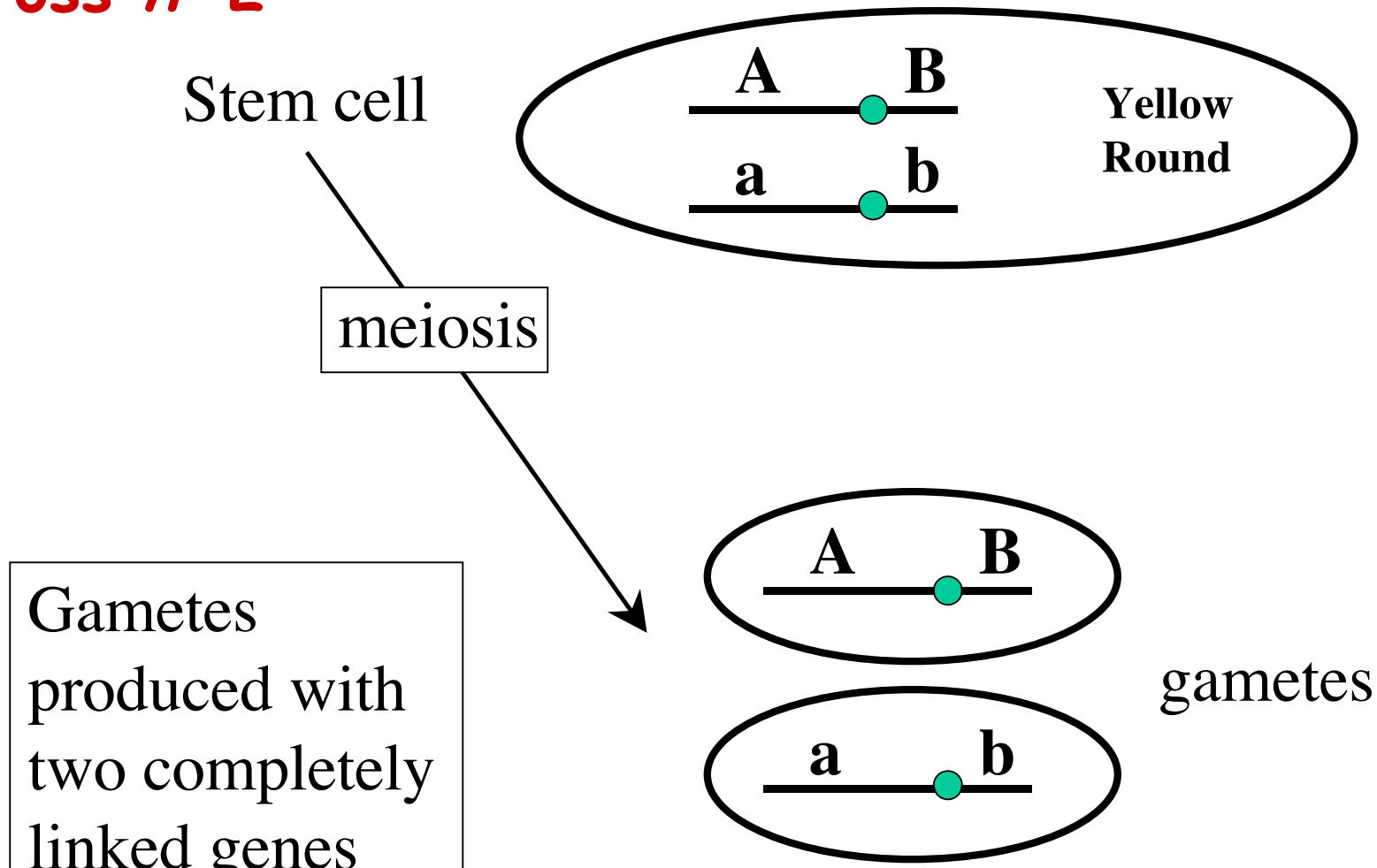


3. ab/ab X Ab/aB (linked)

Recessive alleles are in trans

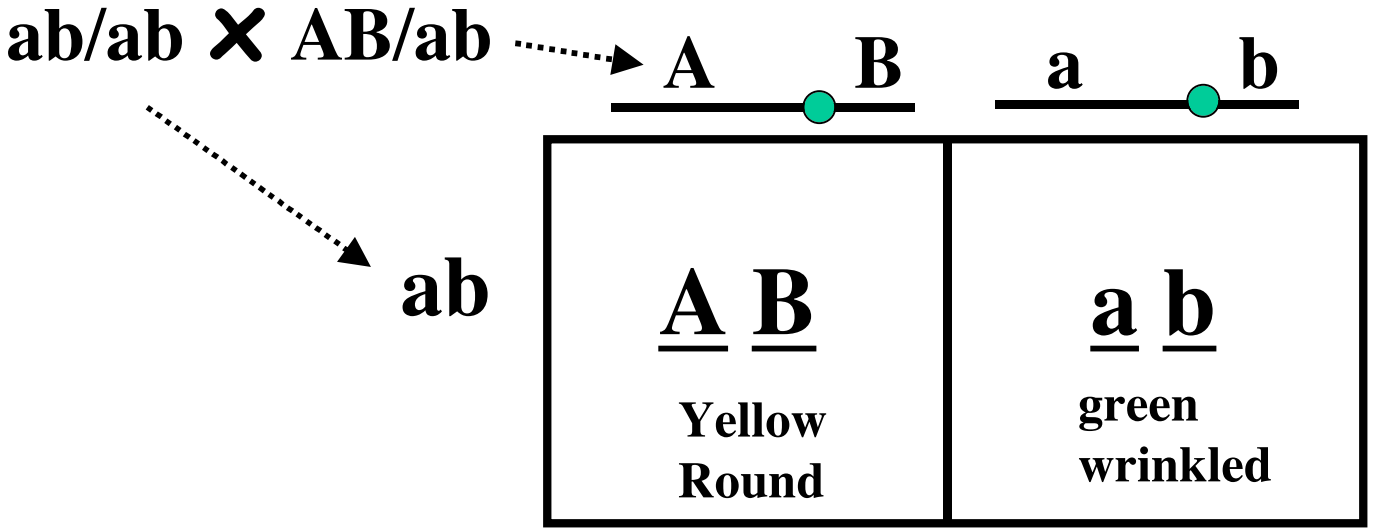


Cross # 2



Test cross: dihybrid heterozygote

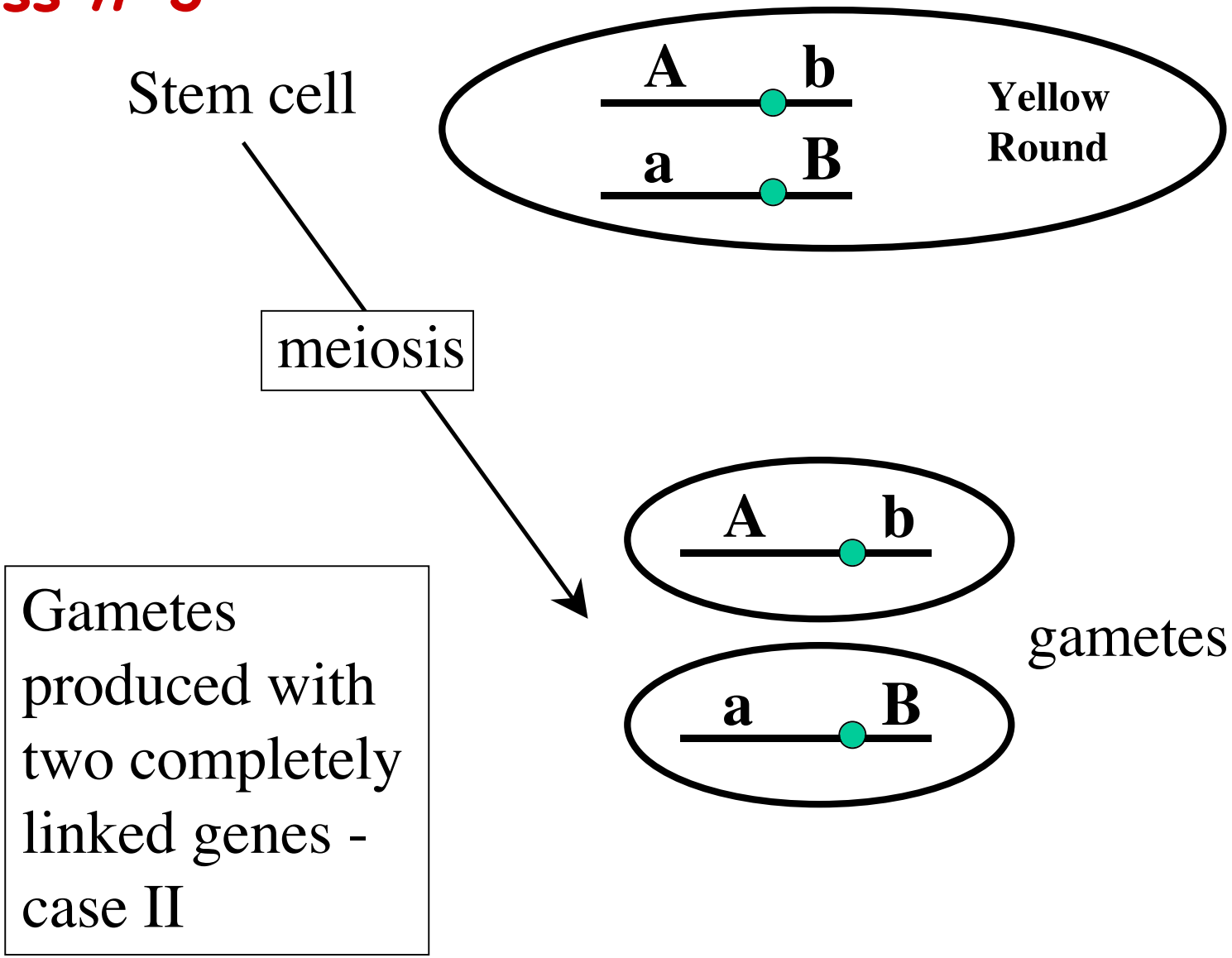
- genes are completely linked



1 : 1

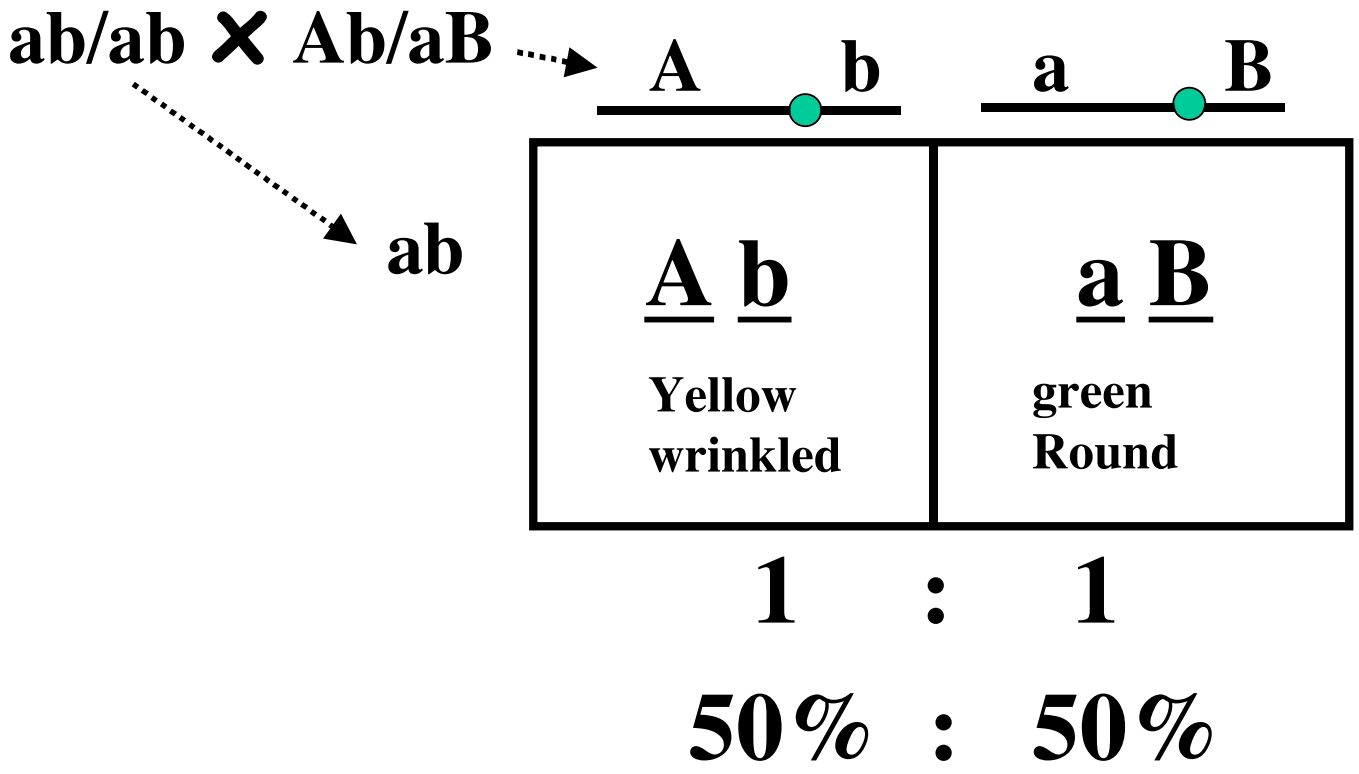
50% : 50%

Cross # 3

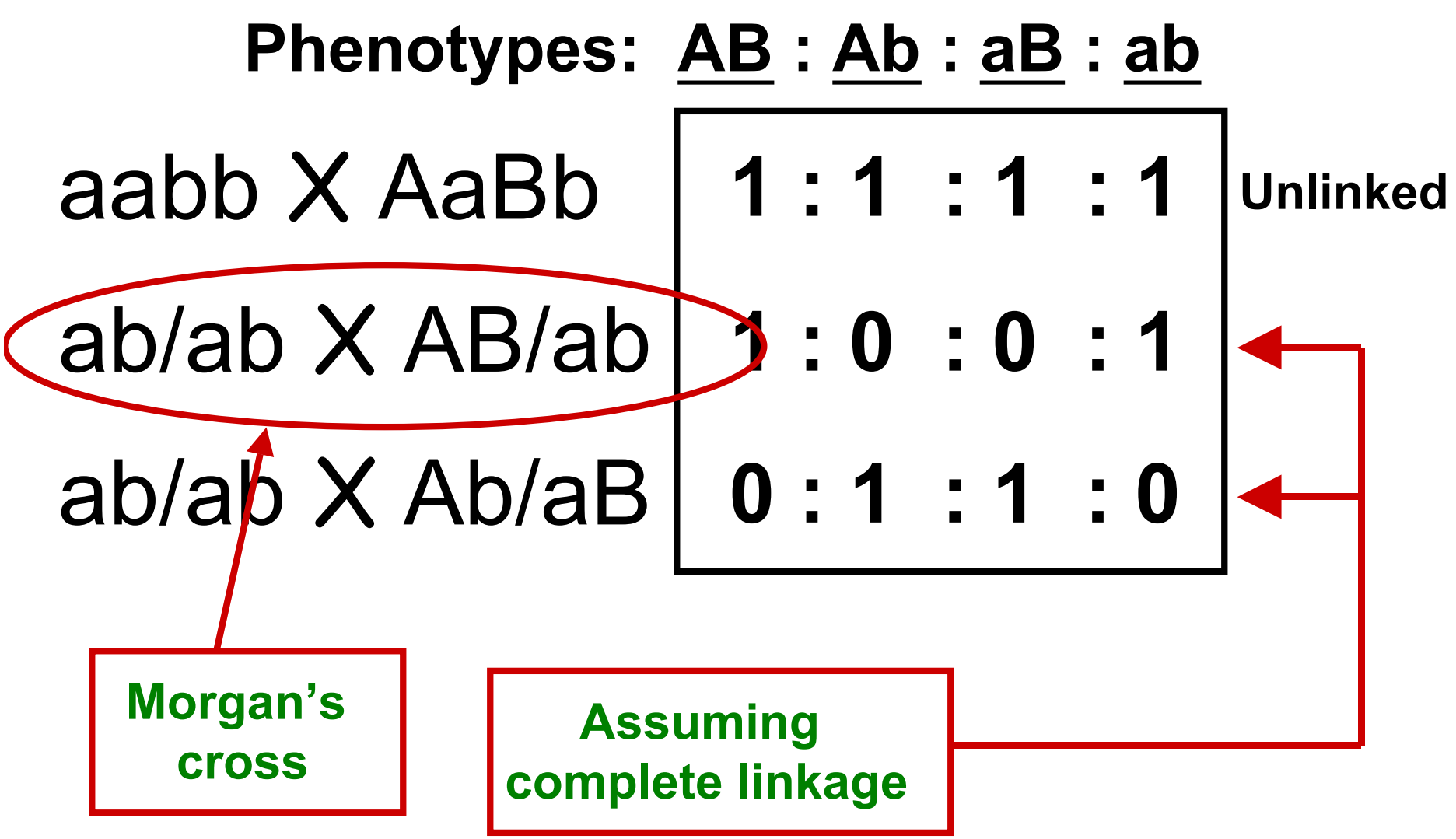


Test cross: dihybrid heterozygote

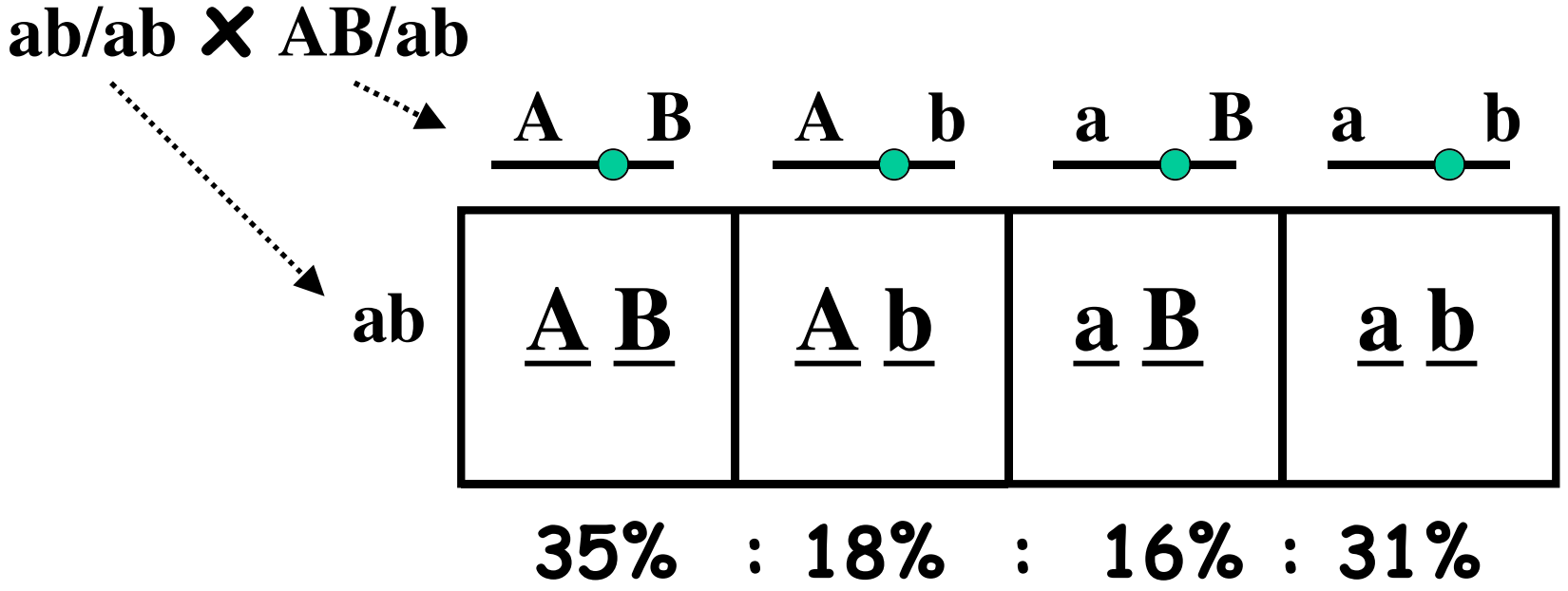
- genes are completely linked



The expectation

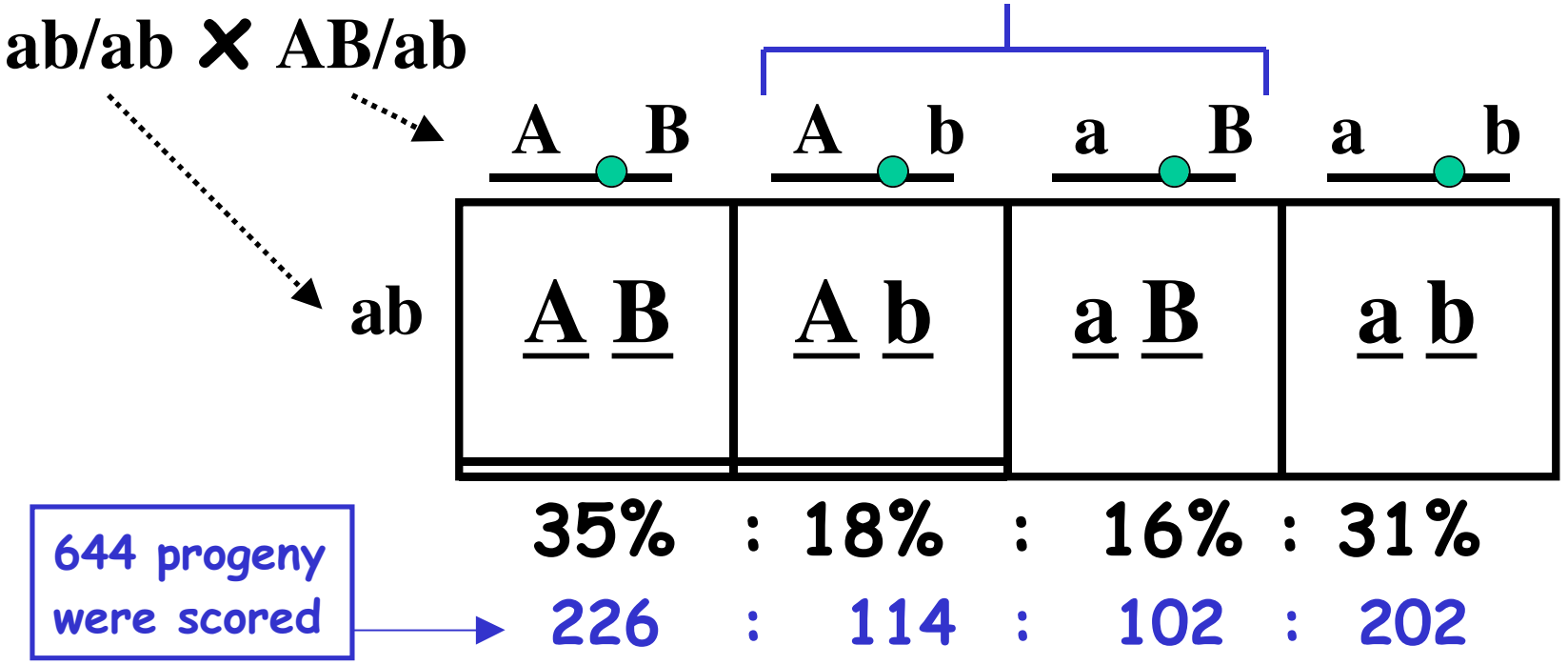


The Result



- Inconsistent with independent assortment
- Inconsistent with complete linkage
- What's going on?

Non-parental chrms



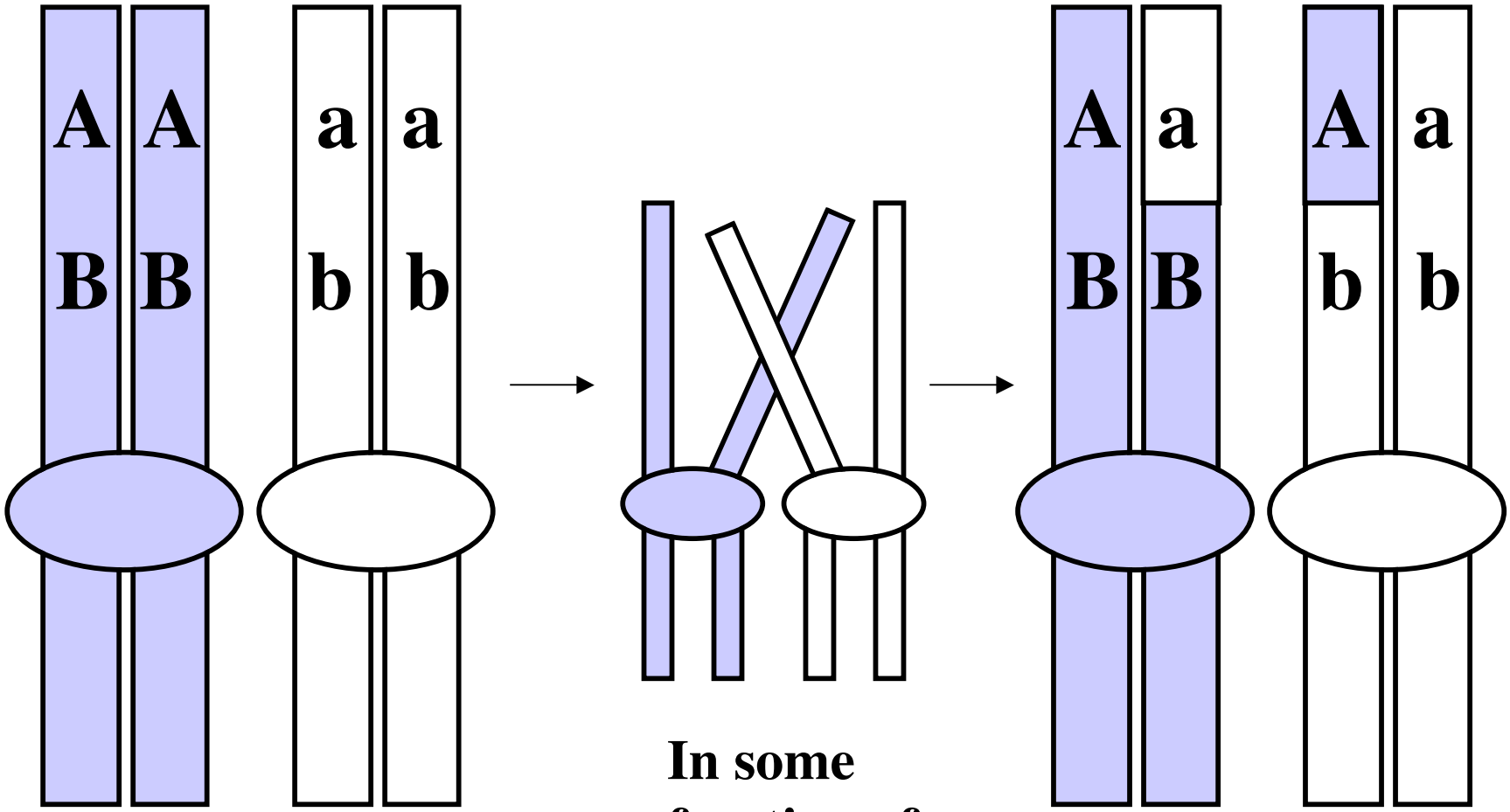
Somehow, chromosomes got into the progeny that didn't come from either parent.

Where did these chrms come from ?!?

Infidelity? NO Aliens? NO

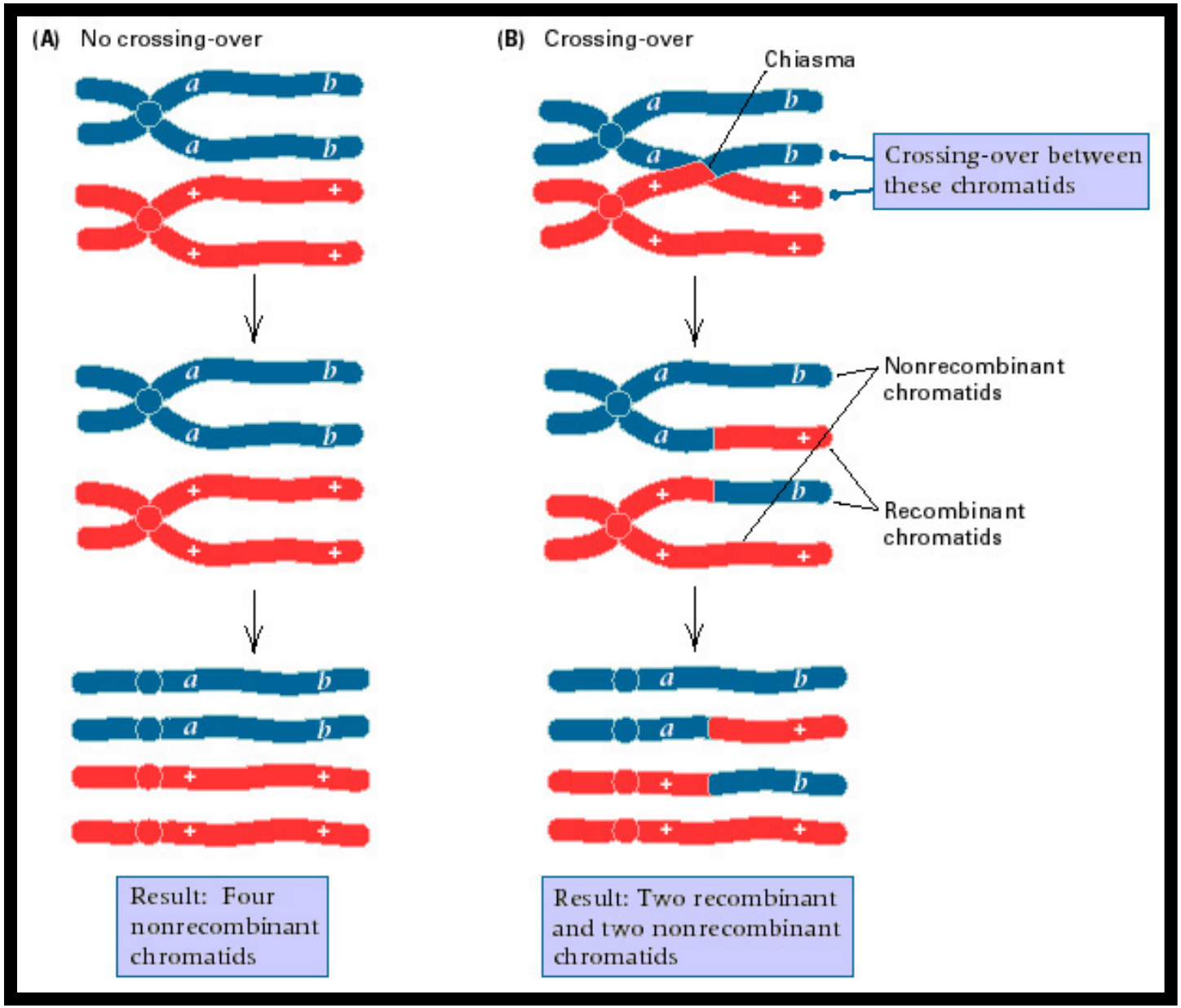
Statistical fluctuation? NO

Non-parental haplotypes in progeny --> meiotic recombination (crossing-over)



Paired homologous chrms in prophase of meiosis I

In some fraction of meioses


(A) No crossing-over
(B) Crossing-over
Chiasma
Crossing-over between these chromatids
Nonrecombinant chromatids
Recombinant chromatids
Result: Four nonrecombinant chromatids
Result: Two recombinant and two nonrecombinant chromatids

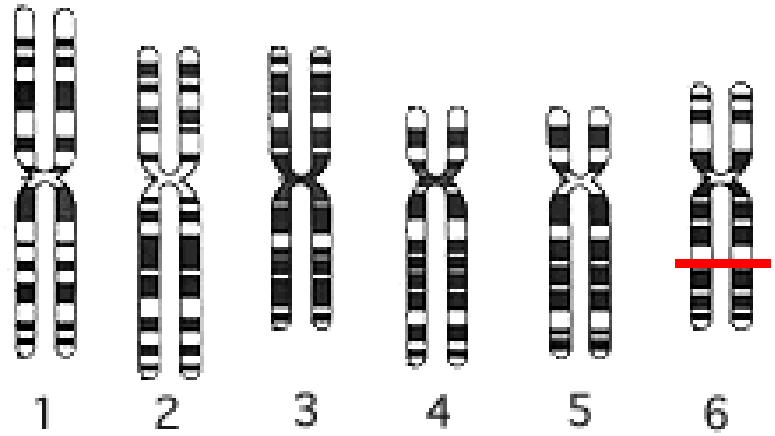
H&J Fig 4.4

Recombination = Crossing-over

- Non-parental chromosomes (or haplotypes) are result of recombination = crossing-over = physical exchange of segments between homologous chrms
- Occurs ~ 1-3 times/chrm, on average
- Occurs during synapsis of meiotic prophase I
- chiasma = cross-shaped configuration caused by breakage and rejoining of chromatids
- Catalyzed by enzymes (= proteins = "the recombination machinery")
- Greatly increases the number of possible genotypes in progeny
- Enables genetic mapping

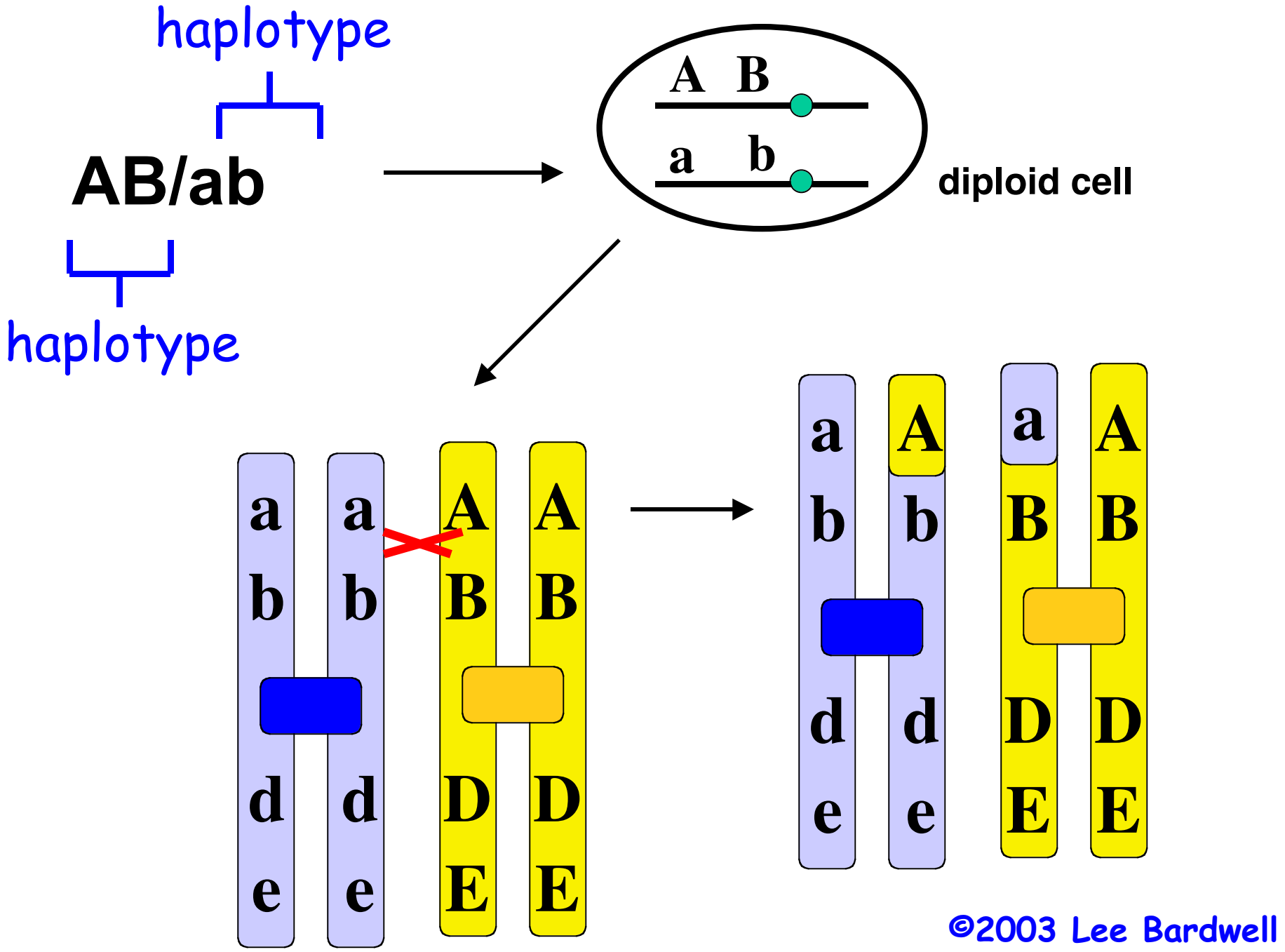
Bio 97 2004 Lecture 5b

Gene Mapping

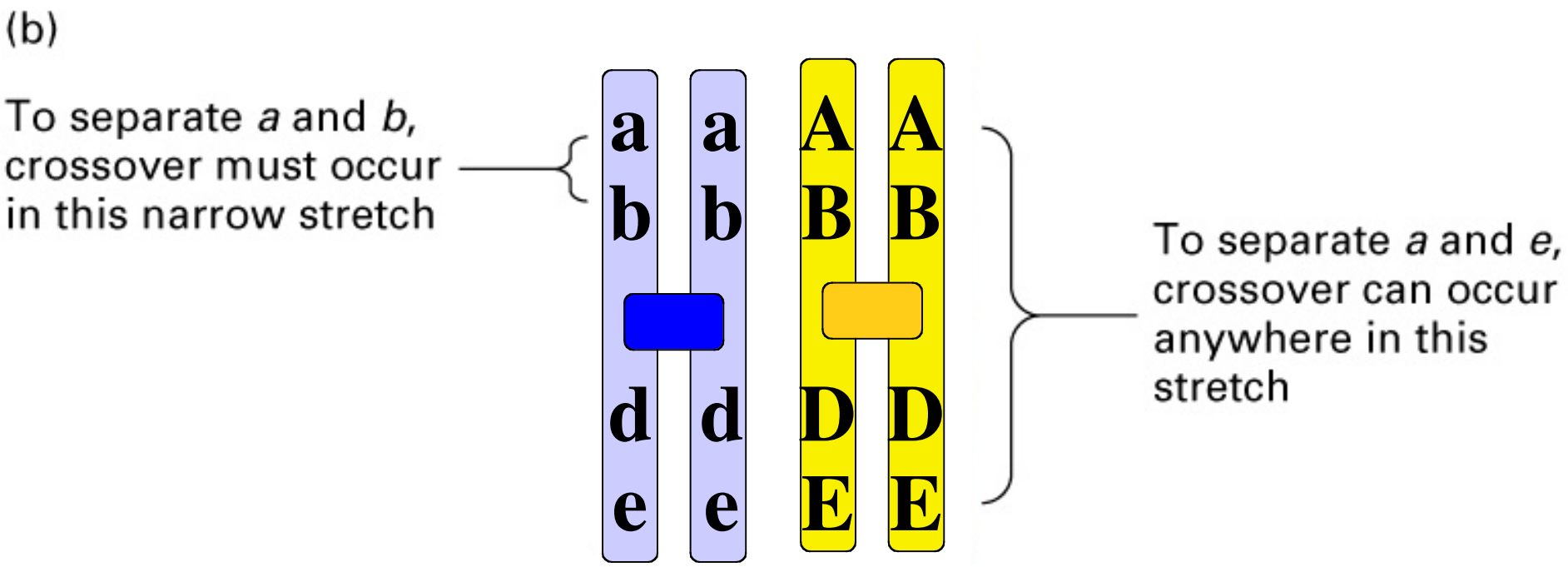


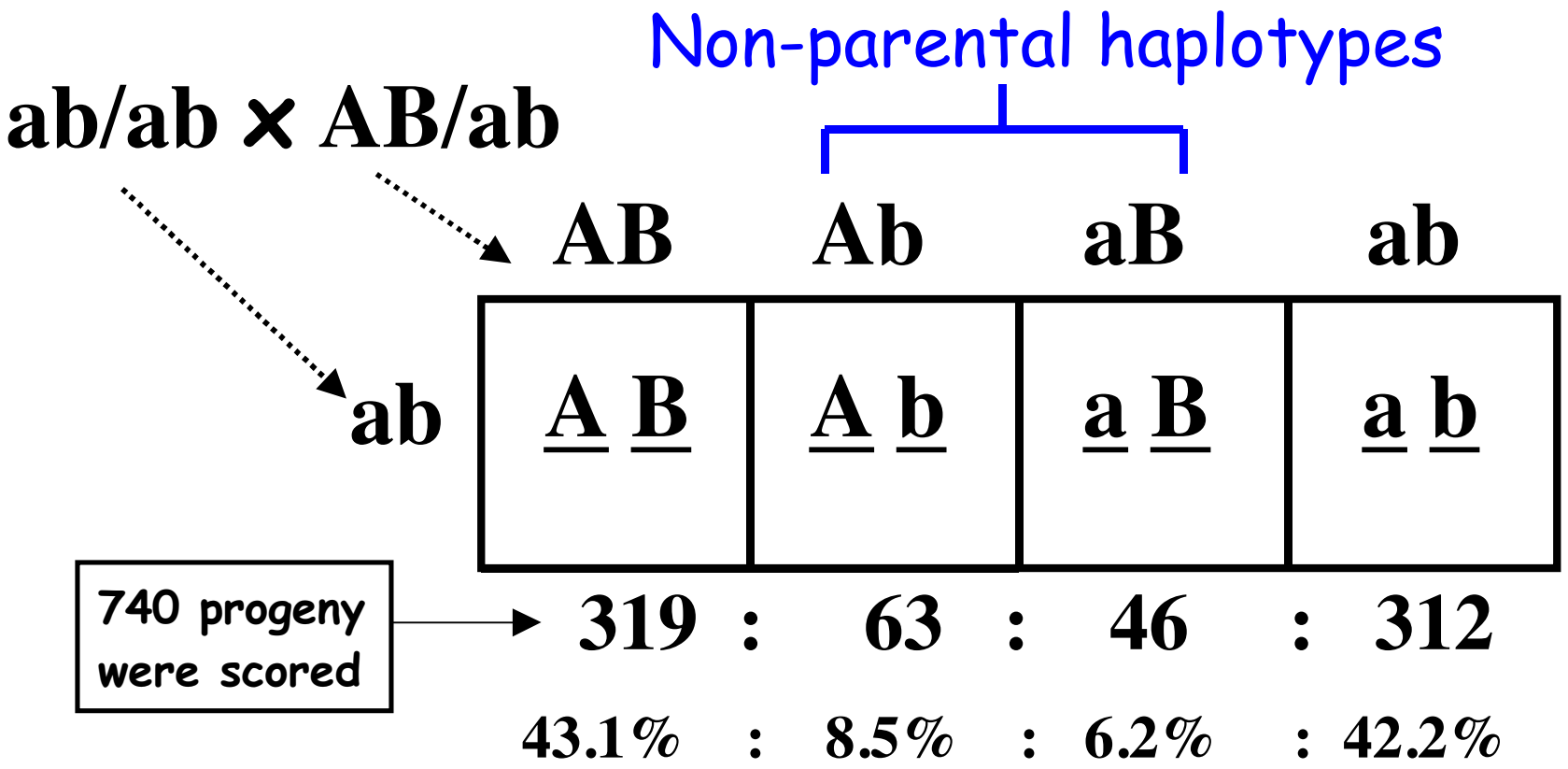
Each gene occurs at a specific site, or locus, on a chromosome.

The probability of crossing over between two genes (or loci) is roughly proportional to their distance apart on the chromosome.


haplotype
AB/ab
haplotype
A B
a b
diploid cell
a b d e
a b d e
A B D E
A B D E
a b d e
A B D E
a b d e
A B D E
©2003 Lee Bardwell

(b)


To separate *a* and *b*, crossover must occur in this narrow stretch
a
b
d
e
a
b
d
e
A
B
D
E
A
B
D
E
To separate *a* and *e*, crossover can occur anywhere in this stretch



14.7% recombination

1% recombination

=

1 centiMorgan (cM)

=

1 map unit

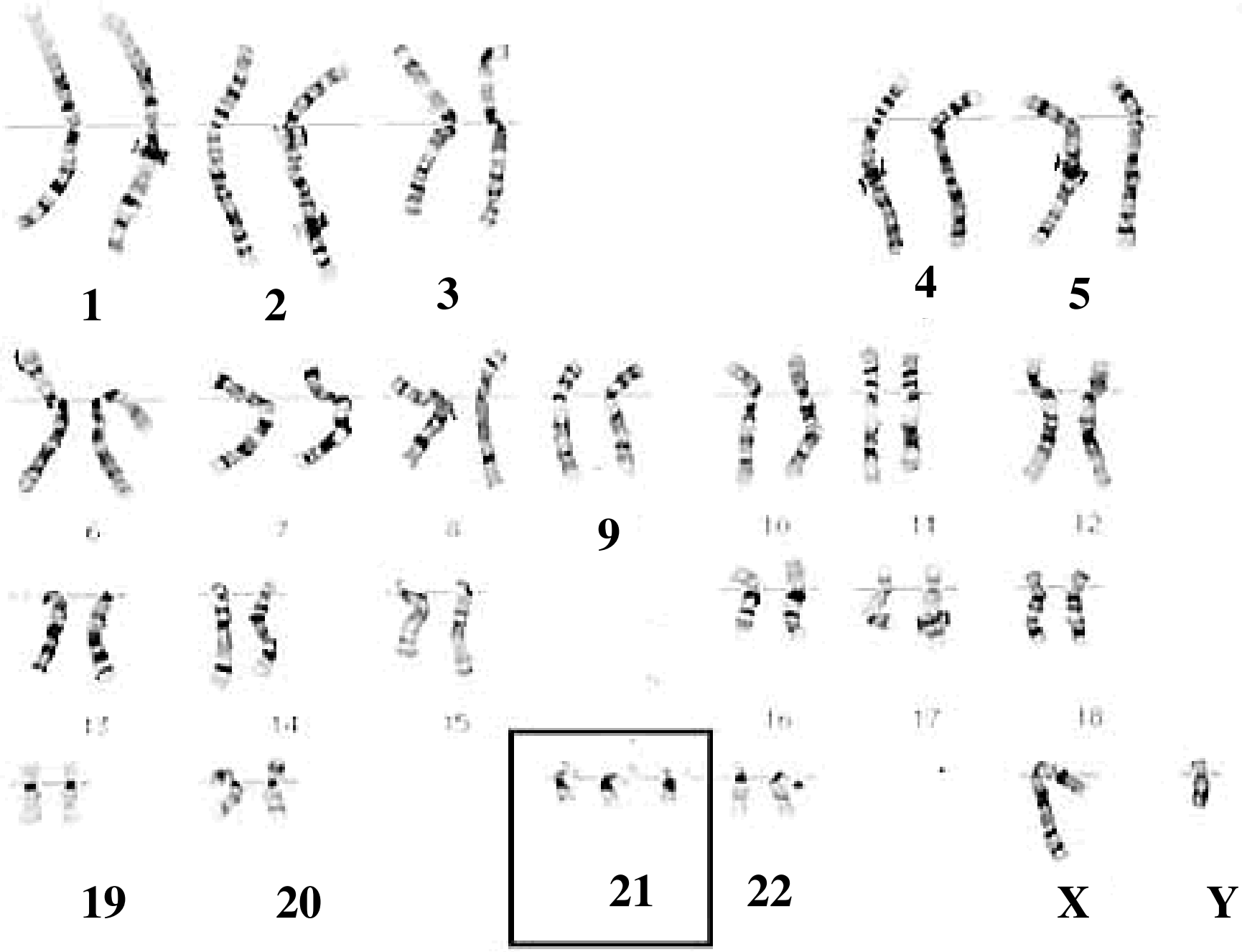
~

1 million base pairs

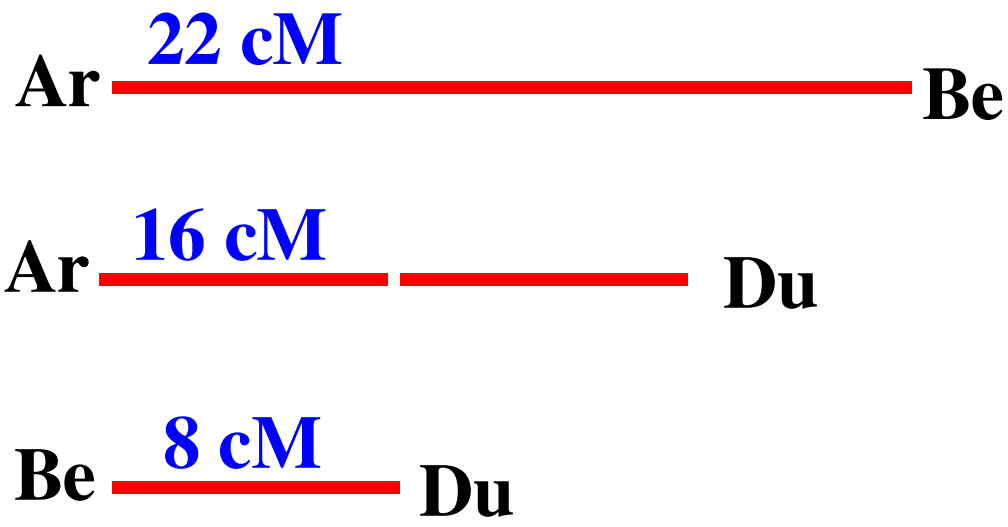
Definition of linkage

Linked genes exhibit less than 50% recombination (that is, they are less than 50 cM apart)

(Human Chrm 9 is ~ 200 cM)


1
2
3
4
5
9
19
20
21
22
X
Y

ab/ab × AB/ab:	39% AB	11% Ab	11% aB	39% ab
ad/ad × AD/ad:	42% AD	8% Ad	8% aD	42% ad
bd/bd × BD/bd:	41% BD	4% Bd	4% bD	41% bd

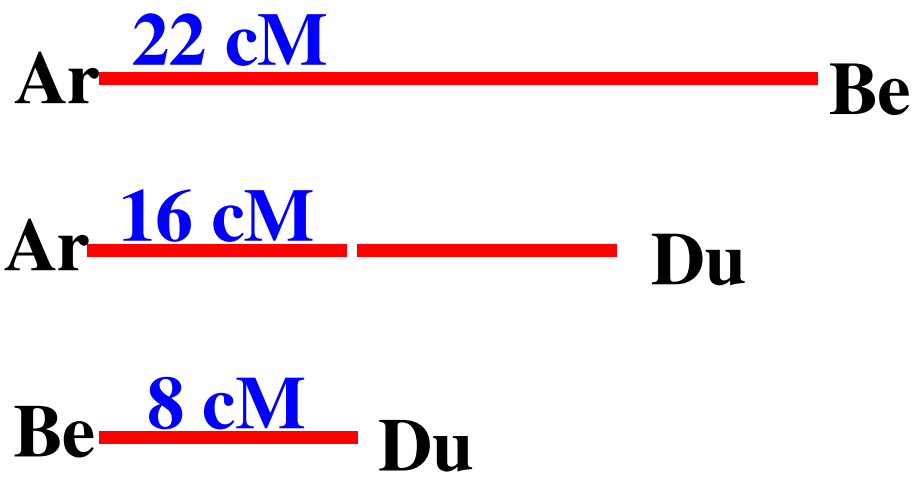


Map: which gene is in the middle?

Be —— Ar — Du = Du — Ar —— Be

Be —— Du — Ar = Ar — Du —— Be

Ar —— Be — Du = Du — Be —— Ar



Alfred H. Sturtevant

"The linear arrangement of sex-linked factors in Drosophila, as shown by their mode of association"

J. Exp. Zool., 1913

Work done while he was an undergraduate In T.H. Morgan's lab

Be —8 cM— **Du** —16 cM— **Ar**

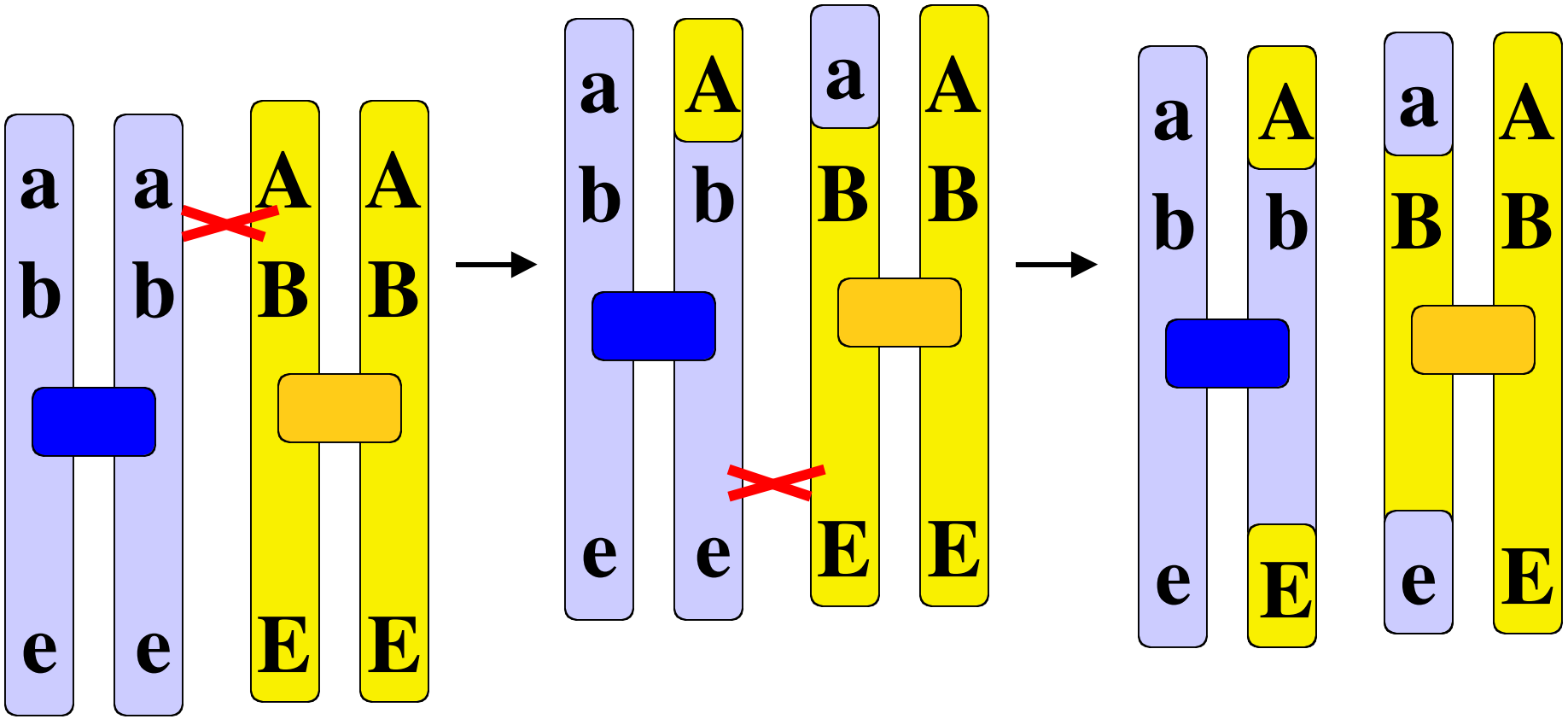
=

Ar —16 cM— **Du** —8 cM— **Be**

Be —22 cM— **Ar** **?**

Why don't the numbers add up?

Double-crossovers cause an under-estimation of the distance between two loci.



0 crossover result: 2 ae gametes, 2 AE gametes

2 crossover result: 2 ae gametes, 2 AE gametes