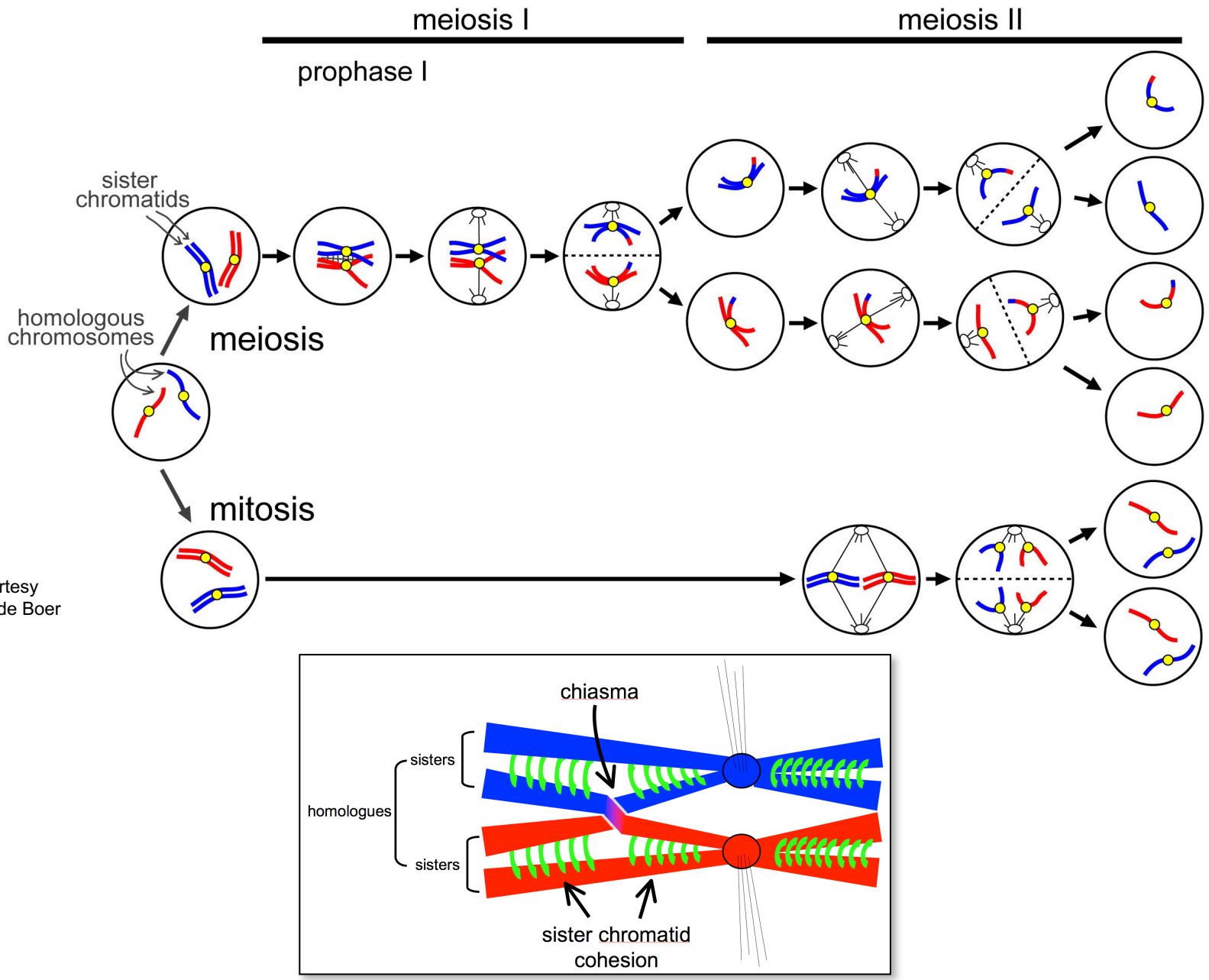
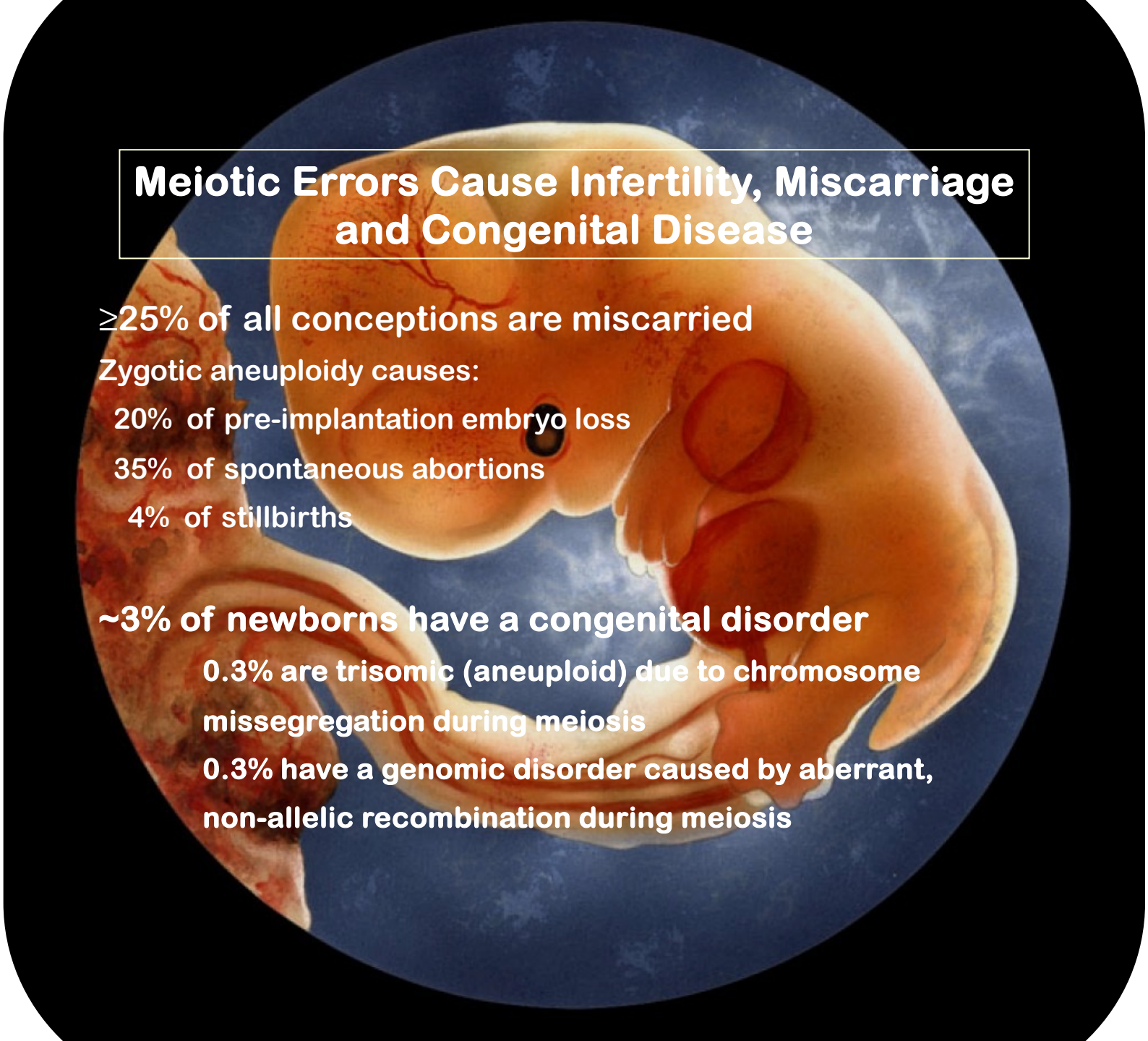


figure courtesy of Esther de Boer

Crossovers (chiasmata) plus sister chromatid cohesion hold homologous chromosomes together until the first meiotic division



Meiotic Errors Cause Infertility, Miscarriage and Congenital Disease

≥25% of all conceptions are miscarried

Zygotic aneuploidy causes:

20% of pre-implantation embryo loss

35% of spontaneous abortions

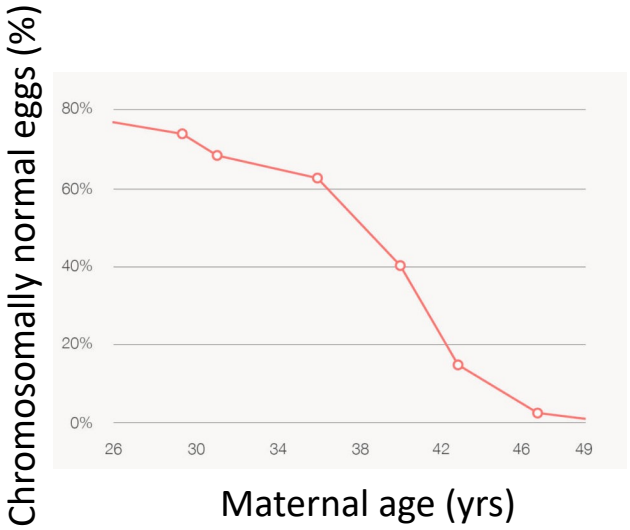
4% of stillbirths

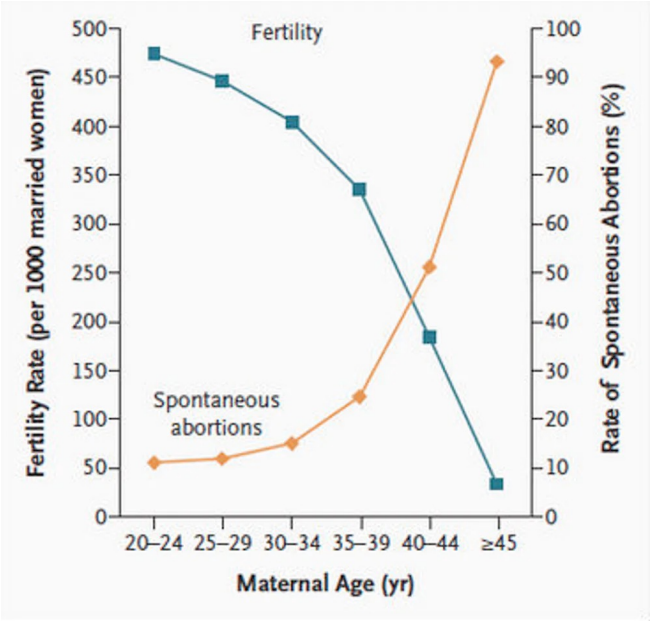
~3% of newborns have a congenital disorder

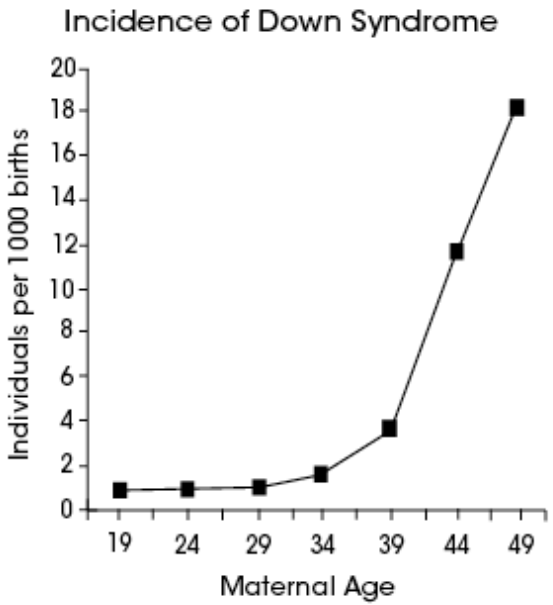
0.3% are trisomic (aneuploid) due to chromosome missegregation during meiosis

0.3% have a genomic disorder caused by aberrant, non-allelic recombination during meiosis

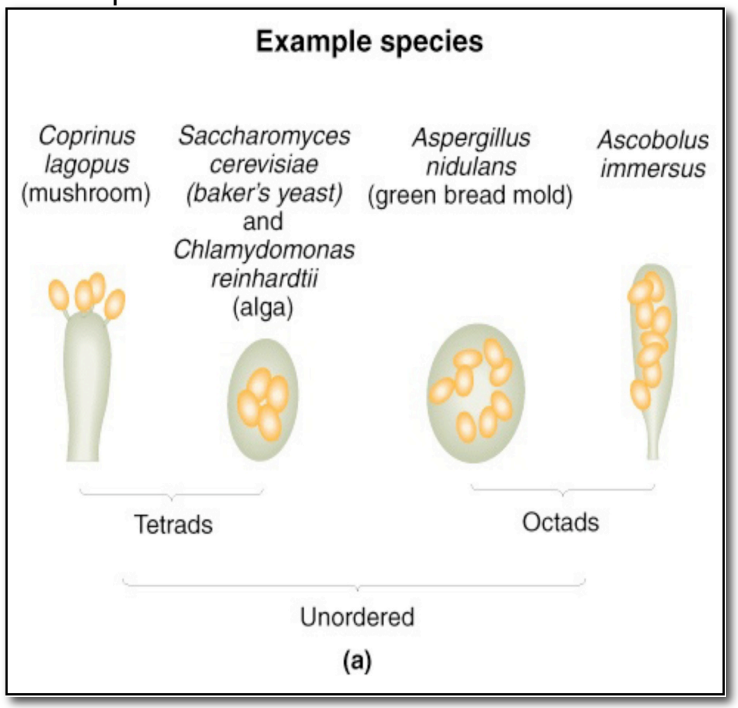
Oocyte QUALITY Declines Dramatically With Age: the maternal age effect



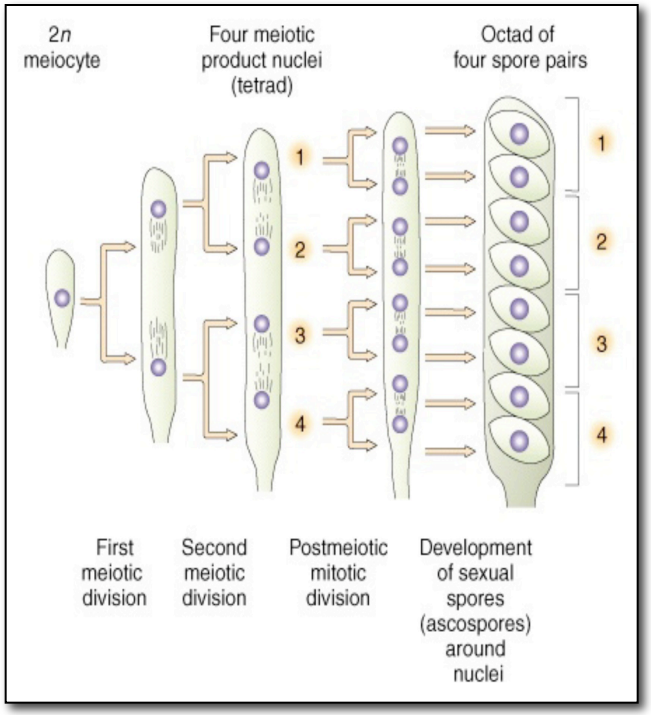


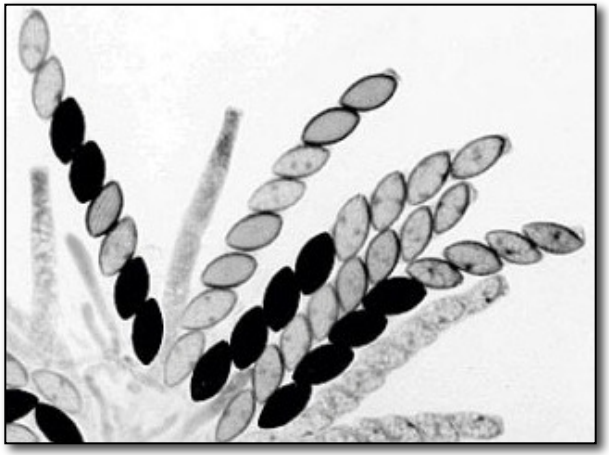


Examples of unordered asci:



Ordered octads: *Neurospora crassa*

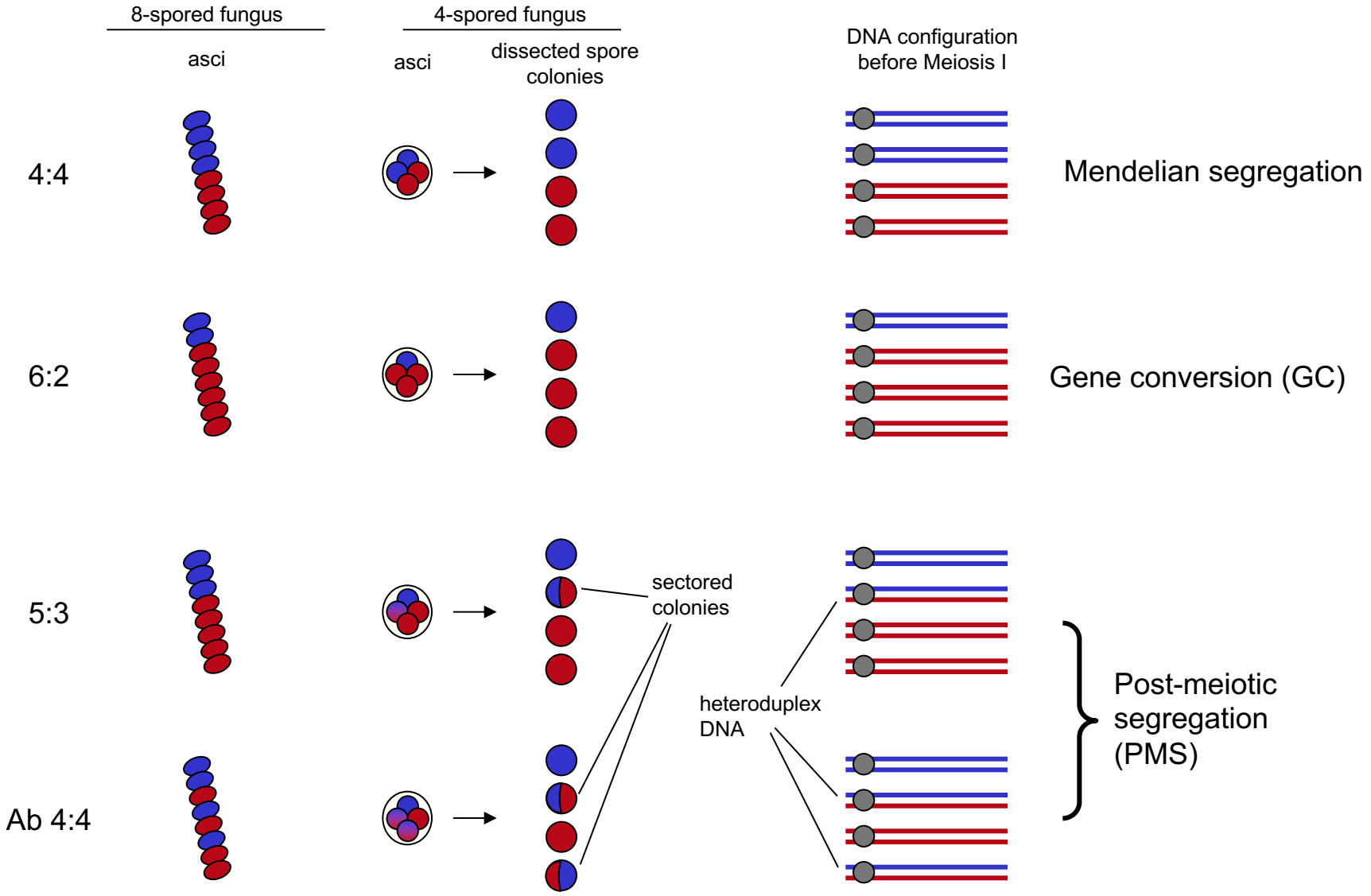




Neurospora asci from a cross between a wild-type strain (black spores) and a spore color mutant (tan spores)

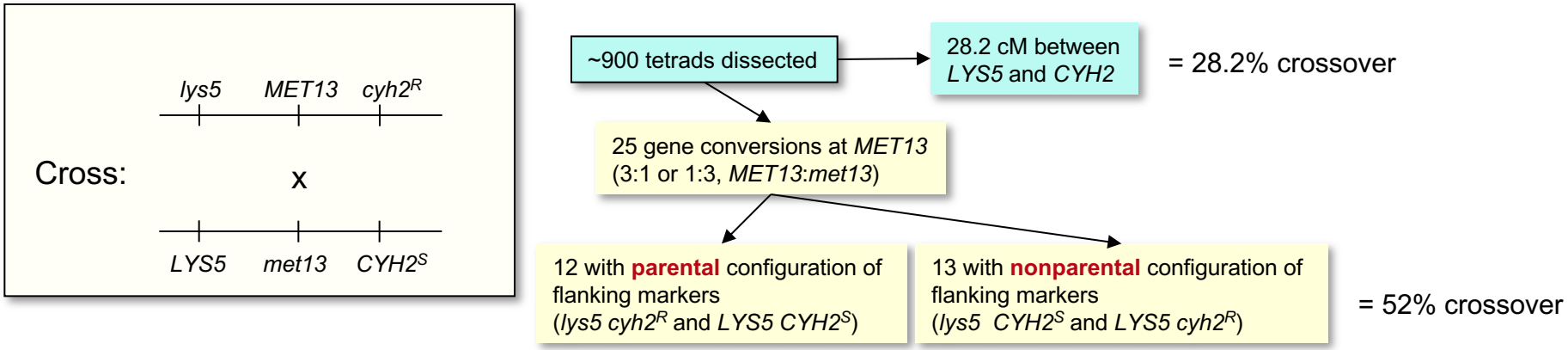
Griffiths et al., 6th Ed.

Non-Mendelian segregation patterns



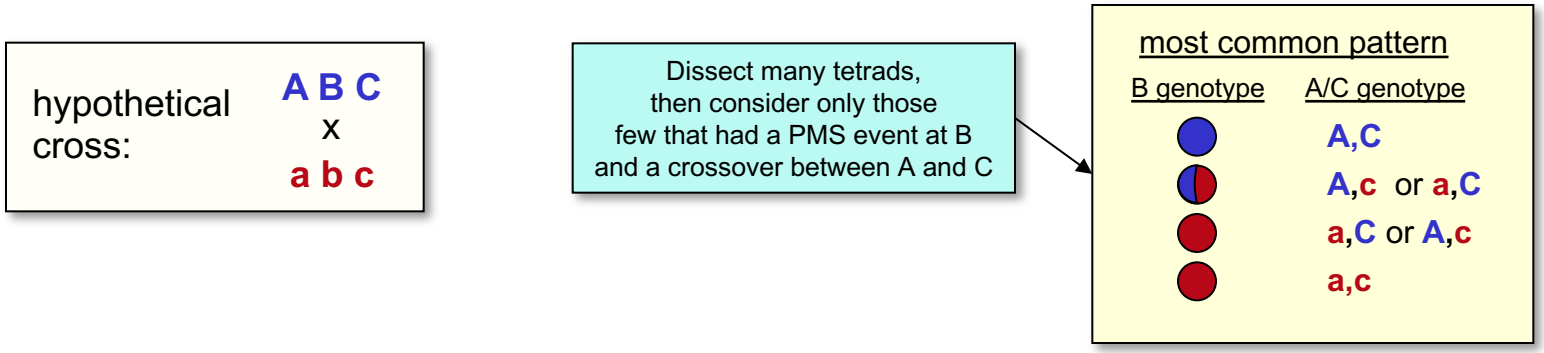
Properties of nonMendelian segregation events

1. Gene conversions and postmeiotic segregation events are often associated with crossing over of flanking markers



source: Martini et al., 2006, *Cell* **126**: 285, and unpublished data

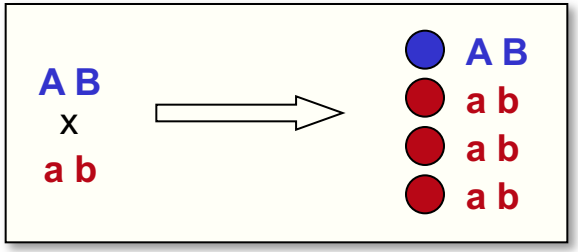
2. In tetrads where there is a nonMendelian segregation accompanied by crossing over of flanking markers, the same chromatid is involved in both.



Properties 1 and 2 imply that there is some sort of mechanistic connection between the formation of heteroduplex DNA and the act of forming a crossover.

Properties of nonMendelian segregation events

3. Closely spaced markers can often be seen to convert simultaneously in the same tetrad = “coconversion tracts”



4. For some loci, nonMendelian segregation is more frequent in some positions in the gene, and decreases as a function of position away from the most frequent position = “polarity gradient”

ARG4

	Nsph	Acc	RV	Bcl	Dra	Aha	Bgl
Mutation(bp)	G→C	+2	- 2	+4	- 3	+2	+4
Position(bp)	+3	131	260	345	601	830	1,274
3+:1−	21	22	31	13	11	1	0
1+:3−	17	20	31	7	10	6	3
p.m.s.	10	0	0	0	0	0	0
Total tetrads	530	674	838	584	742	480	676
Conversion frequency (%)	9.1	6.2	7.4	3.4	2.8	1.5	0.4

Nicolas et al., 1989, *Nature* **338**, 35

Properties 3 and 4 suggest that there can be preferred sites for initiation of recombination and that heteroduplex DNA can “spread” out from the initiation site.

Properties of nonMendelian segregation events

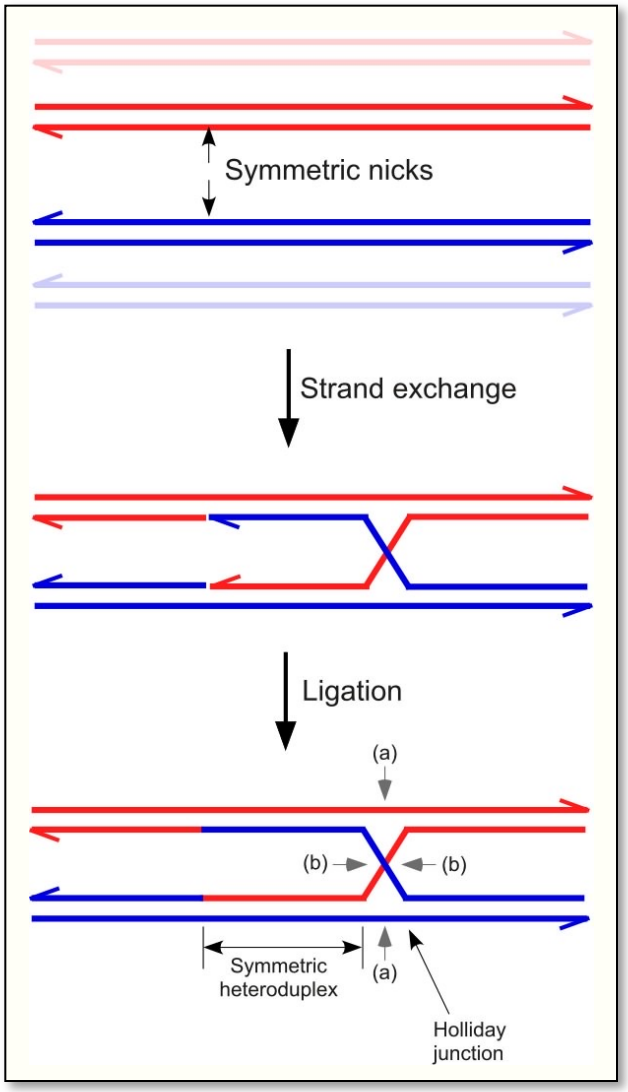
5. The initiator of recombination is the recipient of genetic information.

Most alleles at most loci show "parity", but sometimes "disparity" is observed, in which case the "hot" allele is most likely converted to the "cold" allele.

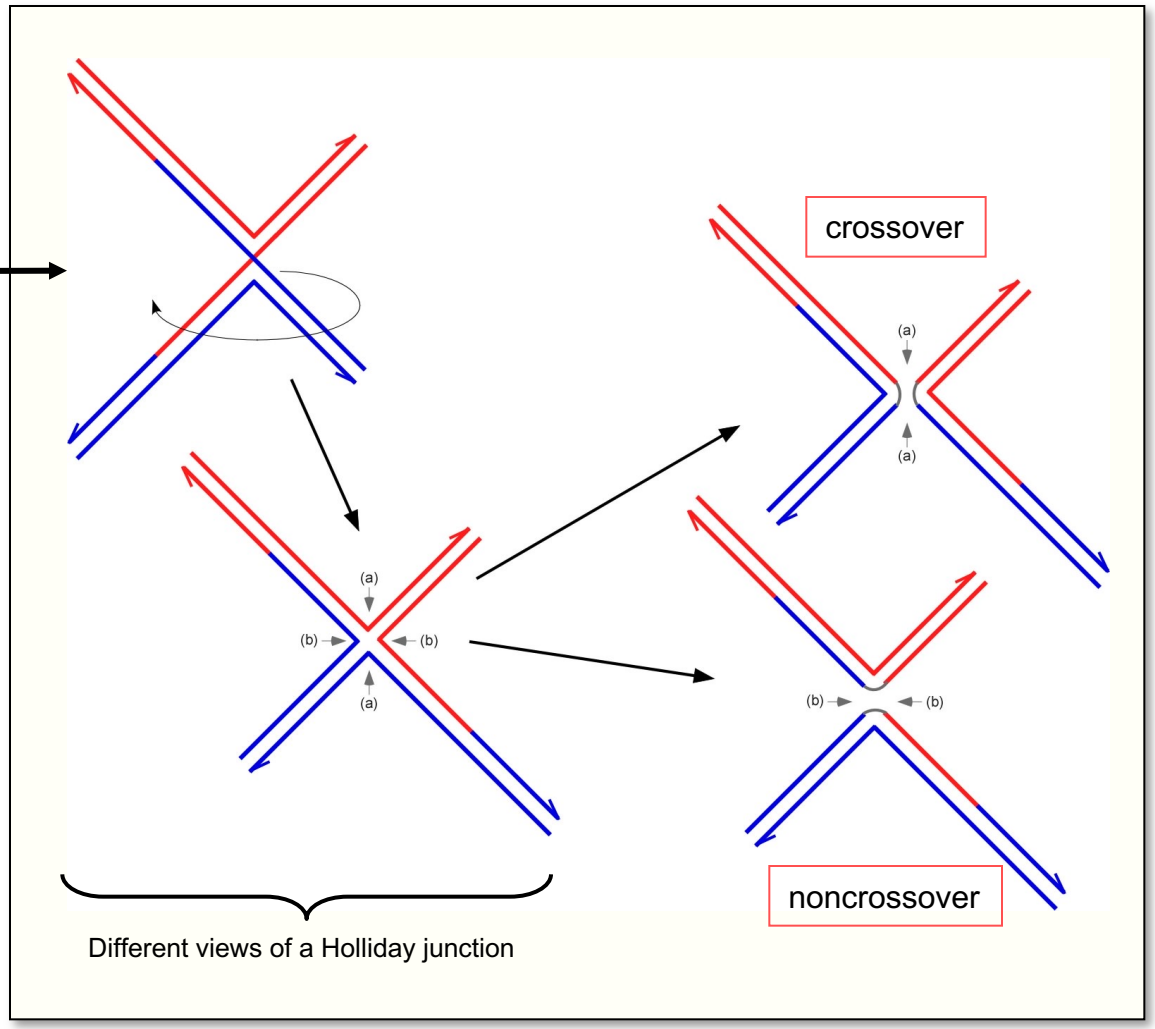
S. pombe cross	Number of tetrads: Total	3:1	1:3
ade6^{+} x *ade6-M26*	1018	46 (4.5%)	6 (0.59%)
ade6^{+} x *ade6-M216*	1593	4 (0.25%)	3 (0.19%)
ade6-M26 x *ade6-M216*	1032	3 (0.29%)	29 (2.8%)

Gutz, 1971, *Genetics* **69**, 317-337

Holliday Model

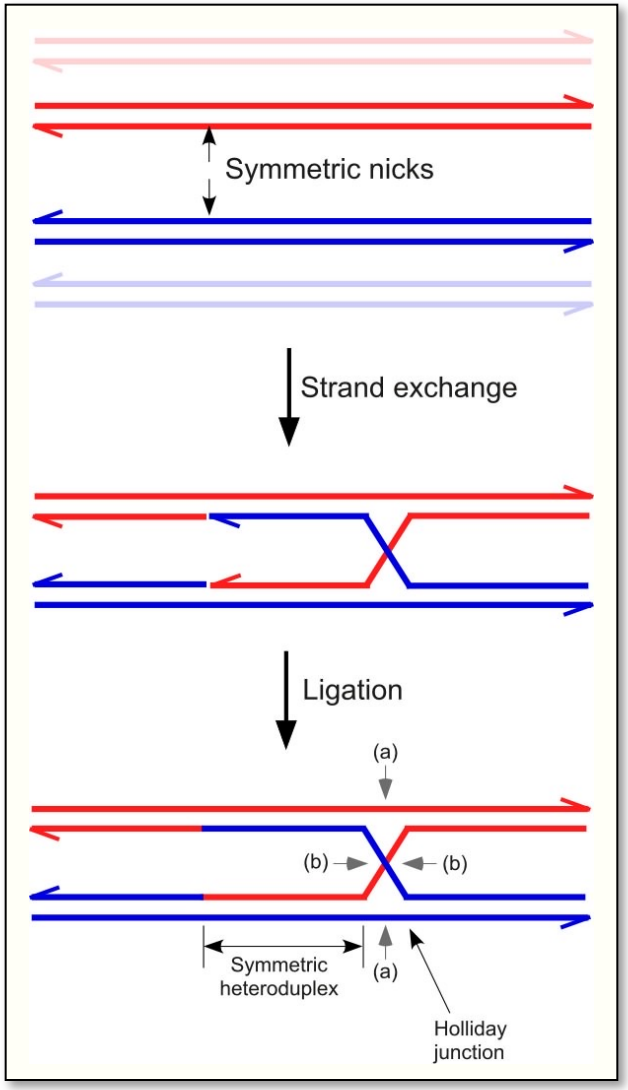


Holliday Junction Resolution

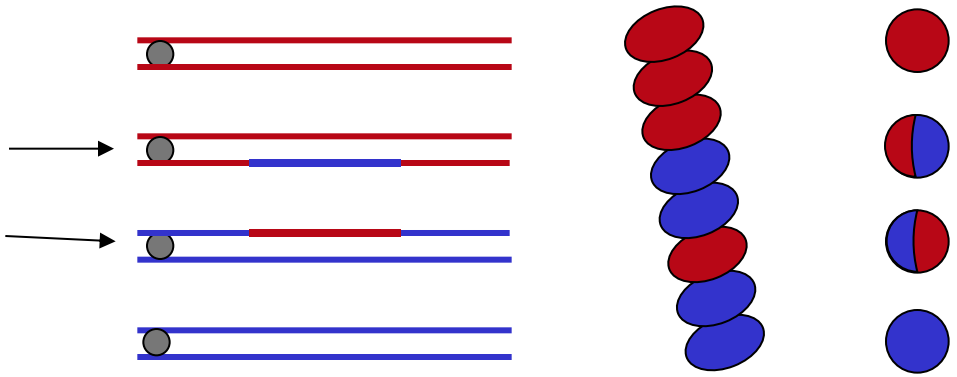


Holliday, R. (1964). A mechanism for gene conversion in fungi. *Genet. Res.* **5**: 282-304.

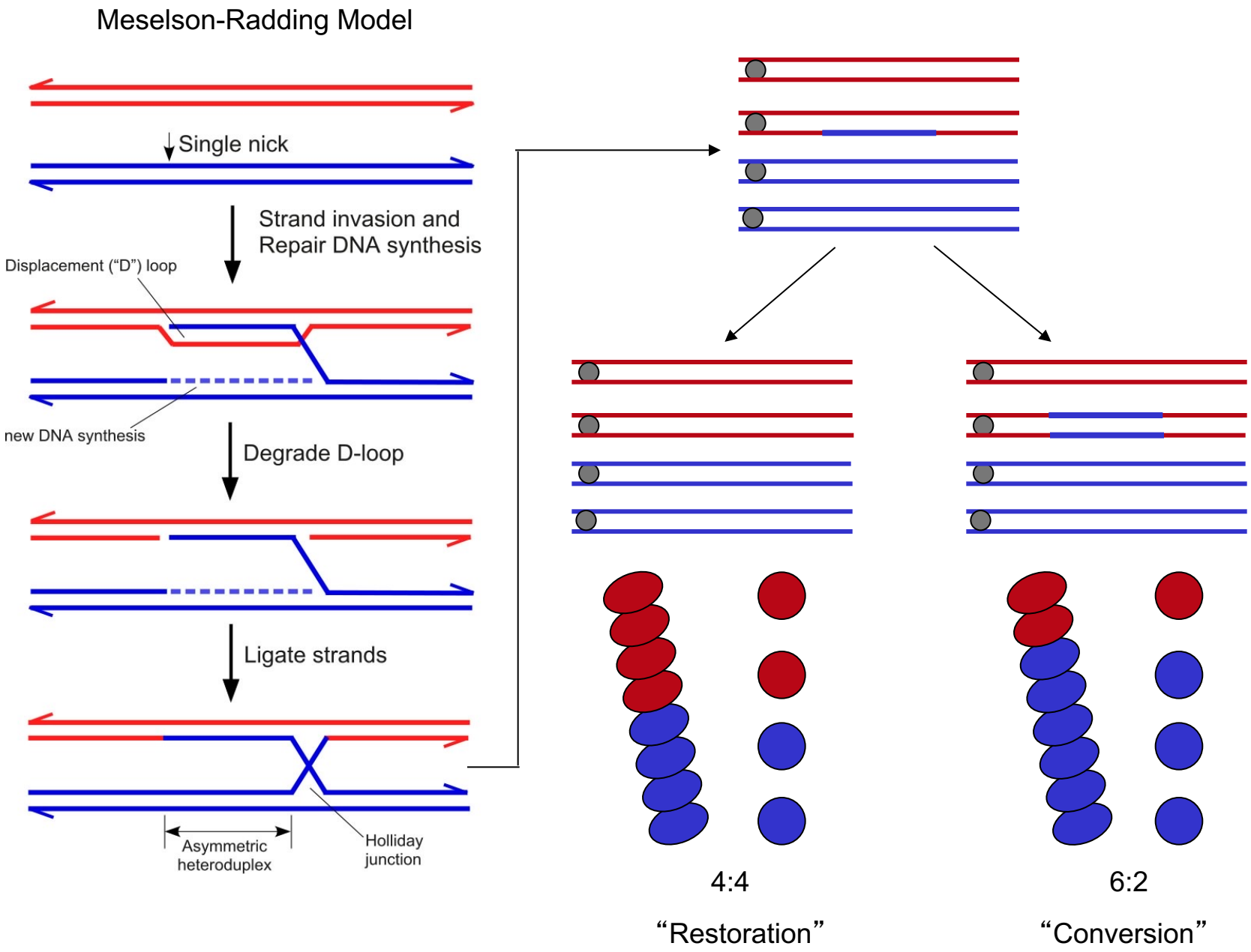
Holliday Model



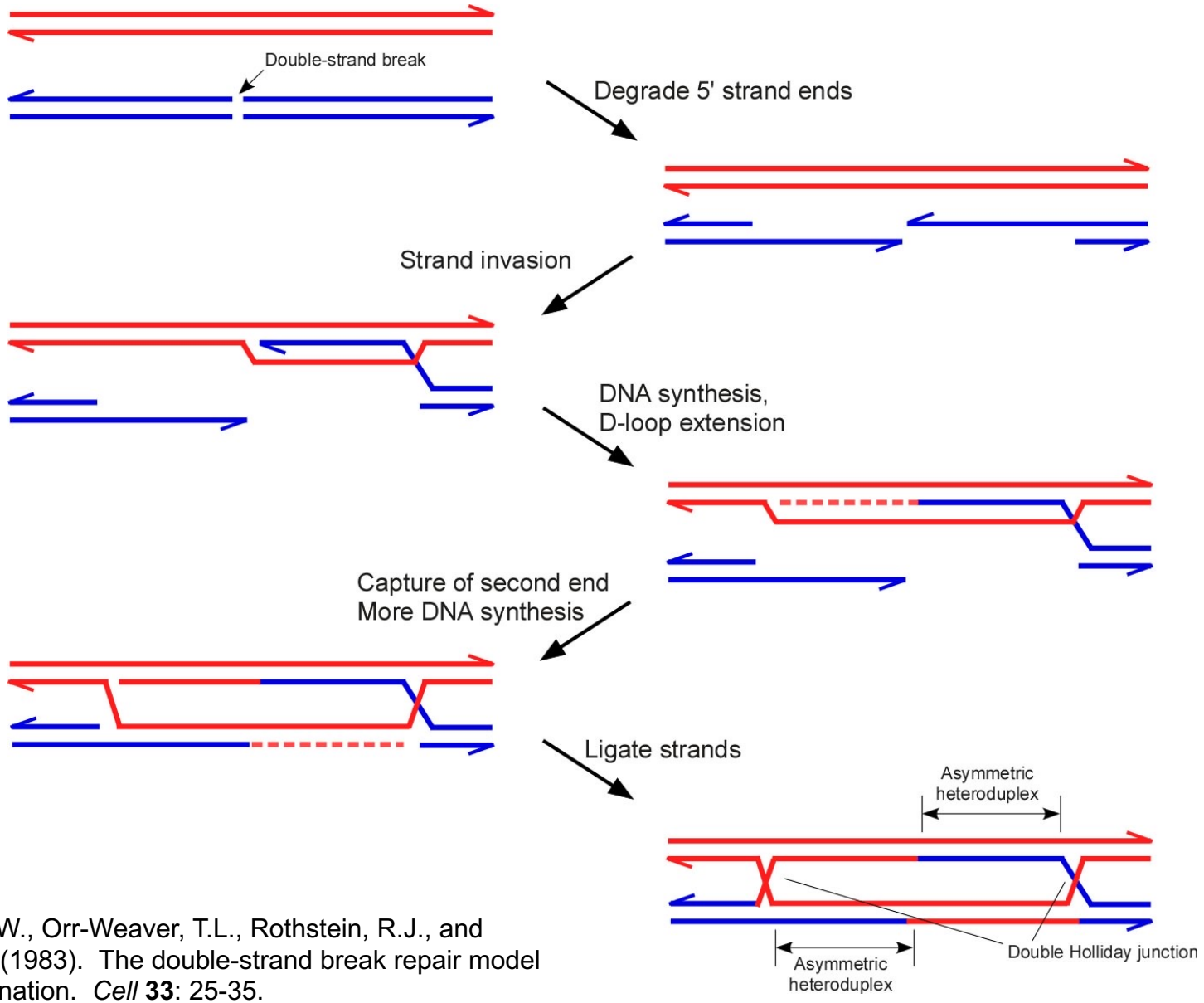
Prediction: alleles that show frequent PMS should also show frequent Ab 4:4 segregation



Ab 4:4

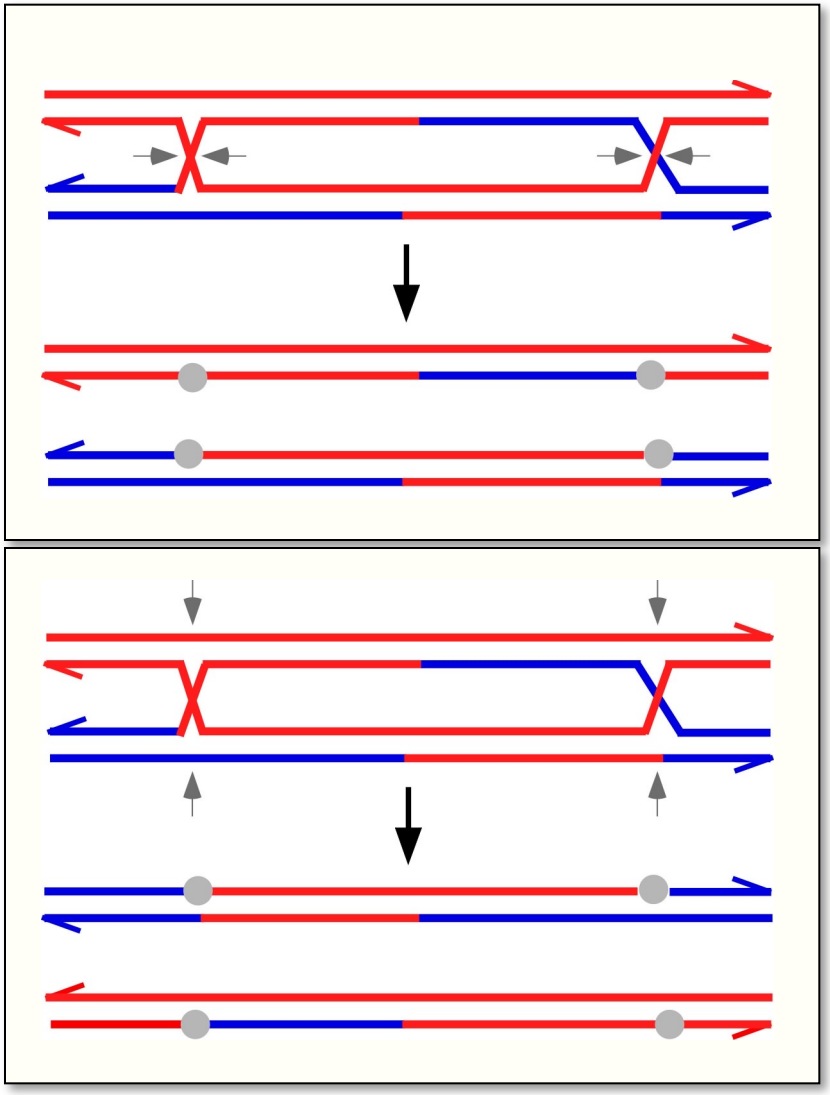

Meselson-Radding Model
Single nick
Strand invasion and
Repair DNA synthesis
Displacement (“D”) loop
new DNA synthesis
Degrade D-loop
Ligate strands
Asymmetric
heteroduplex
Holliday
junction
4:4
“Restoration”
6:2
“Conversion”

Double-strand break repair model

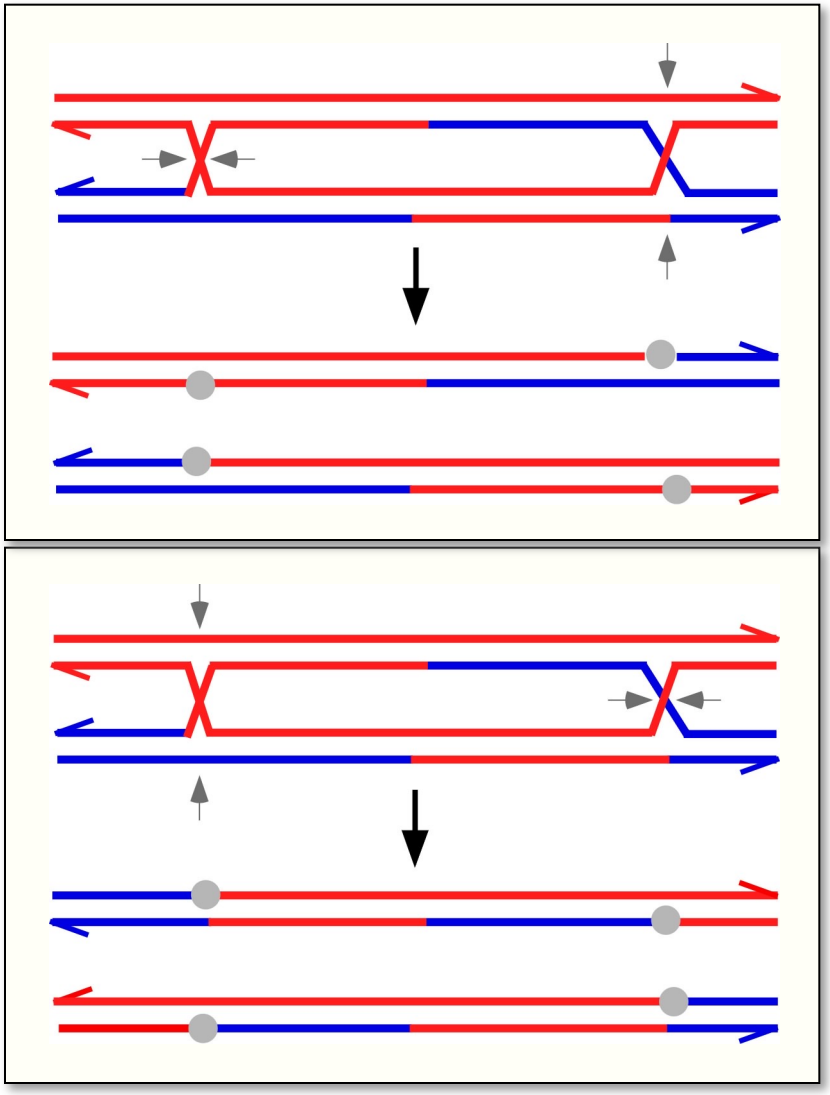


Szostak, J.W., Orr-Weaver, T.L., Rothstein, R.J., and Stahl, F.W. (1983). The double-strand break repair model for recombination. *Cell* **33**: 25-35.

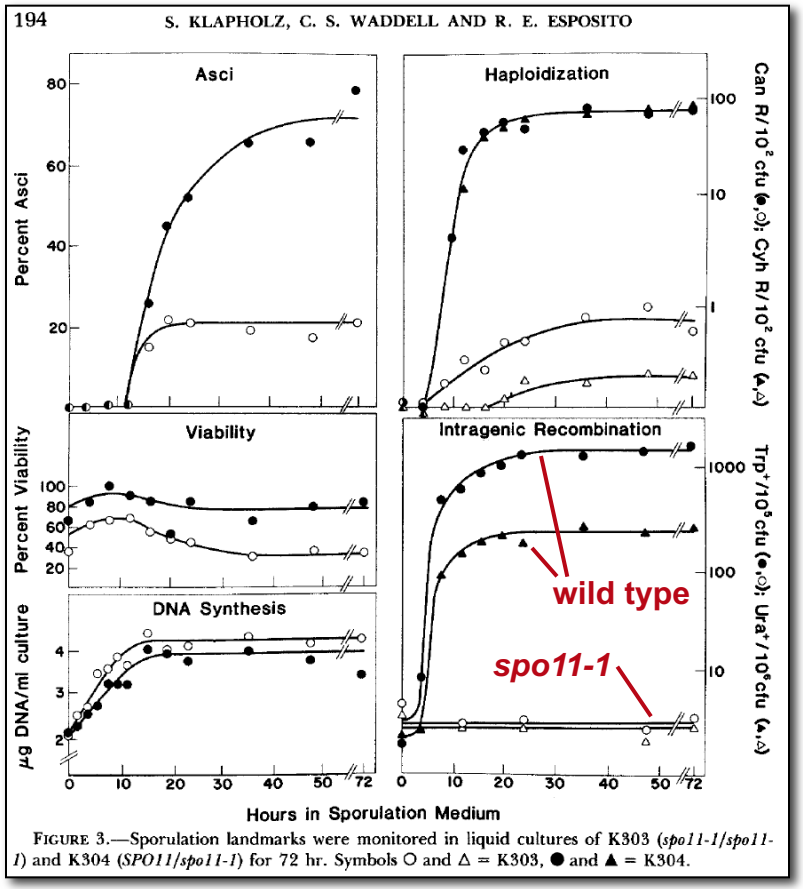
Alternative modes of double Holliday junction resolution



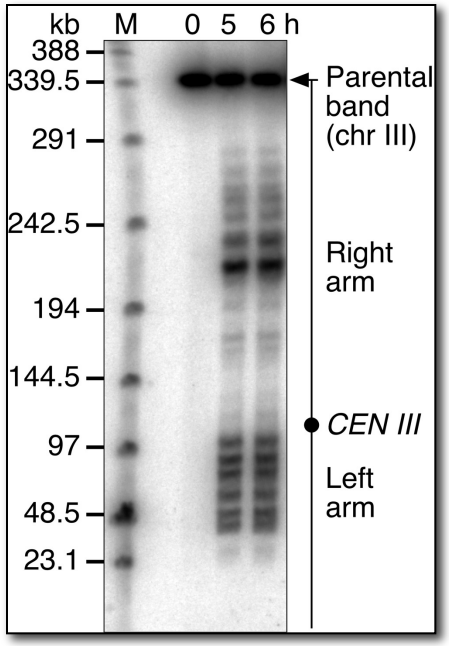
Non-crossover = resolve both junctions in **same** orientation



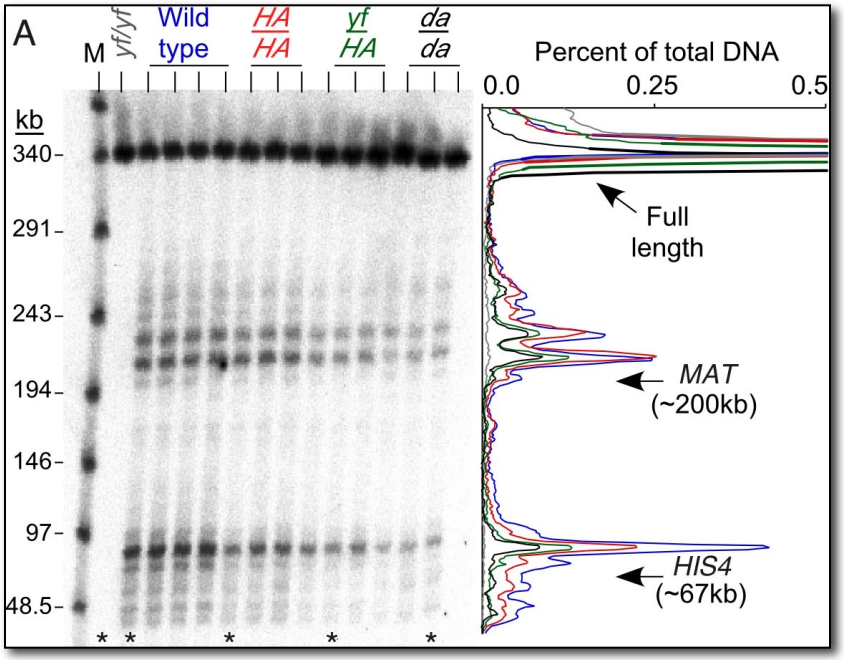
Crossover = resolve junctions in **opposite** orientation



Klapholz et al. (1985) *Genetics* **110**, 187-216



Murakami et al., 2009
Methods Mol Biol **557**



Martini et al., 2006, *Cell* **126**: 285