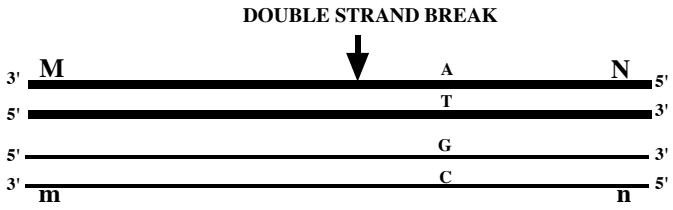
Model for crossing over and gene conversion

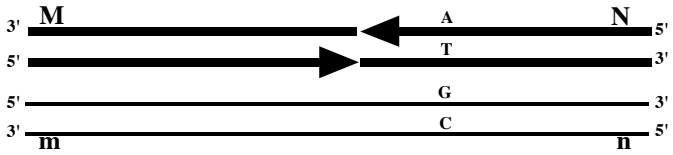
Only two of the four chromatids (each as a double helix) are shown. These are two non sister chromatids; a two strand break will occur at the arrow; note the marker genes M and n and N and n at the ends of the chromatids; it is a double heterozygote in the cis configuration. Also note the AT bases on the heavy chromatid and the GC bases on the light chromatid

1



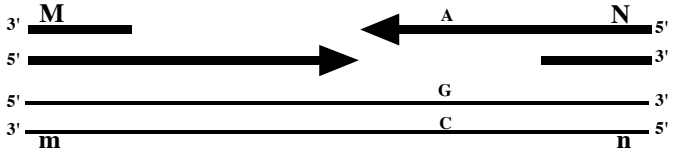
There is a two strand break within one double helix; the arrow heads are the 3' broken ends

2



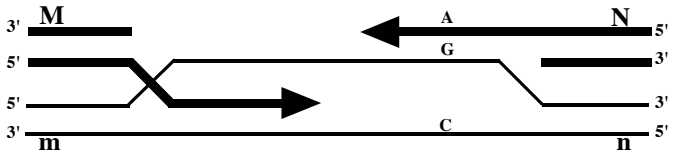
Enzymatic degredation of the 5' ends; note the gaps in the upper and lower strands.

3



There is invasion of the left hand 3' ledge into the bottom chromatid; the bottom chromatid throws up a D-loop into the upper chromatid. Now note the gaps at the upper and lower strands. The arrow heads are 3' ends, ready for DNA synthesis

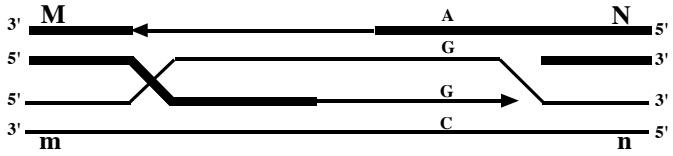
4



DNA synthesis from the arrow heads in a 5' to 3' direction (thin lines); then ligation at the left upper arrow head to make a complete DNA strand.

The right hand lower arrow head then completes the second half chromatid exchange (seen below), giving two pre-Holliday junctions: the x on the left and the x to be made on the right as seen in figure 6

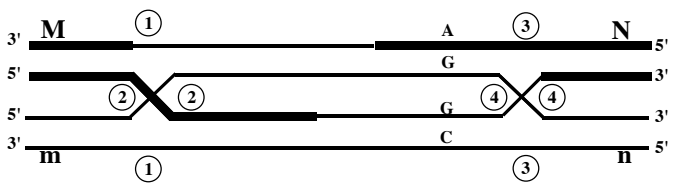
5



The gaps are filled in; there are two half chromated exchanges. Note possible break points at the circles; breaks at these points will complete the exchanges.

Model completed on other side.

6

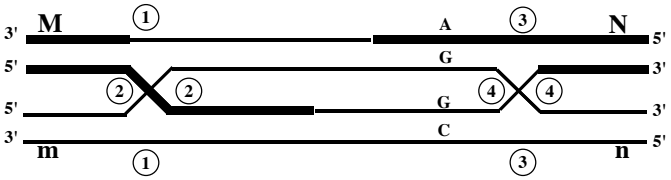


This is a repeat of picture 6.

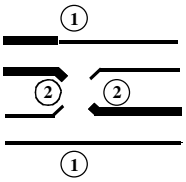
The circled numbers show the location of possible breaks to resolve the Holliday junctions into a crossover or a non-crossover

The Holliday junctions are at the intersection of the two strands at circles 2 and circles 4; the two "X" figures.

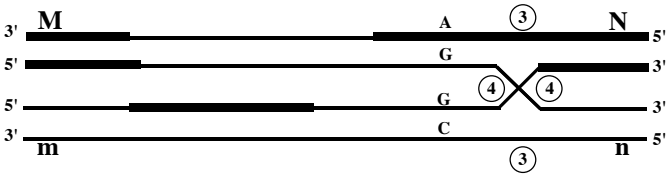
6



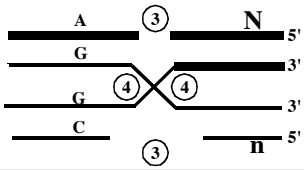
There is now a double break at circles 2 and then a horizontal fusion of heavy and light lines at circles 2.
The left hand x is thus resolved into a non cross over



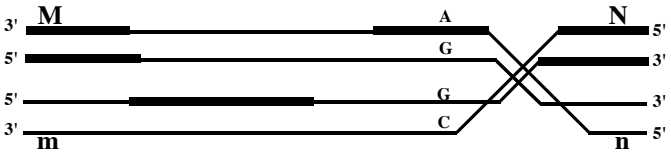
7



On the right there are breaks at circles 3 and vertical fusions as indicated; this gives a trans arrangement for M and N



8

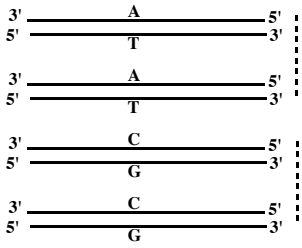


Now both the left and right Holliday junctions have been resolved (corrected).

The left junction to a non crossover and the right junction to a crossover.

A correction must now be made to the base mis-match on the top double helix; to either an AT or a GC.

9

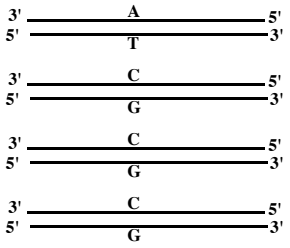


cromatids

cromatids

For a correction to AT we get the four chromatids shown at the left. Note that this will give a 1:1 ratio of AT's and GCs.

For the GC correction we get a 1:3 ratio of ATs and GCs shown at the right. This is gene conversion



cromatids

cromatids

This model fits the double strand breakage and gene conversion data. The main points are:
Crossing over involves a double strand break in one double helix; strand invasion, etc. will lead to a D-loop, to heteroduplexes.and to the Holliday junctions; the Holliday junctions may be resolved into either a crossover or a non crossover; the heteroduplexes may contain a mismatch of bases which may be corrected to a change in the base sequence, a gene conversion.

The model is from: Szostak, J. W., T. L. Orr-Weaver, et al. (1983). "The double-strand-break repair model for recombination." Cell 33(1): 25-35.

A recent review: Petes, T. D. (2001). "Meiotic recombination hot spots and cold spots." Nat Rev Genet 2(5): 360-9.