# RELATED AND UNRELATED CHANGES IN CONVERSION AND RECOMBINATION FREQUENCIES WITH TEMPERATURE IN *SORDARIA FIMICOLA*, AND THEIR RELEVANCE TO HYBRID-DNA MODELS OF RECOMBINATION[1]

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IN current models (e.g., WHITEHOUSE 1963; HOLLIDAY 1964); recombination and gene conversion are postulated to have some processes in common, such as the formation of hybrid-DNA: factors influencing these particular processes should therefore have related effects on recombination and conversion frequencies. Processes not in common might be affected differently, so some treatments should cause recombination and conversion frequencies to change in related ways, while others might change them in unrelated ways. Factors such as temperature and ultraviolet light have been tried: for example, MITCHELL (1957) found that heat shock of conidia used in fertilization increased conversion but not recombination frequency in Neurospora. In Ascobolus, LISSOUBA (1960) found steady increases in conversion and recombination frequencies with temperature, but with $Q_{10}$s of 5 and 2, respectively, while STADLER (1959) found no marked differences in conversion or recombination frequencies in a Neurospora cross at 18° compared with 25°. UV light strongly stimulated non-reciprocal inter-allelic recombination in yeast but not outside-marker recombination (ROMAN and JACOB 1958). These results are consistent with conversion and recombination being independent processes, but data such as those of CASE and GILES (1958a and b) and KITANI, OLIVE and EL-ANI (1962) strongly suggest that they are not independent. This question has been reinvestigated here by studying changes in conversion and recombination frequencies from crosses of *Sordaria fimicola* incubated at different temperatures.

Temperature effects have frequently been used to study recombination (see MCNELLY-INGLE, LAMB and FROST 1966) but few parallel studies on conversion have been made, and then using only a small range of temperatures. *Sordaria fimicola* is suitable for studies of recombination and conversion (OLIVE 1956, 1959) and is fertile over a wide range of temperatures. To test the prediction outlined above, crosses were incubated at different temperatures over the widest range possible, 10° to 30°C, using successive 2.5°C intervals for detailed coverage.

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Recombination was studied using second division segregation frequencies of the ascospore-pigmentation markers *gray* and *hyaline* in ordered asci from crosses of these mutants with their respective wild types (the abbreviations "MI" and "MII" will be used for first and second division segregation, respectively). Conversion was scored, in the same crosses, from asci with segregation ratios other than 4 mutant (*m*):4 wild type (+); post-meiotic segregation in 4*m*:4+ asci was not distinguishable from spindle overlap at the third division in the ascus and was not estimated.

## MATERIALS AND METHODS

The stocks and crossing methods used have been described previously (LAMB 1966a). For the segregation counts, asci were mounted in a 2M sucrose solution and the various precautions concerning scoring biases and ascal maturation outlined earlier (LAMB 1966a, 1967; LAMB, MCNELLY-INGLE and FROST 1967) were taken. Tests for phenocopies as a cause of apparent conversion were made and proved negative (LAMB 1968). Each cross was made in duplicate at each temperature and each set of crosses was repeated at least twice at each temperature: maximum temperature variation observed in any incubator was ± 0.3°C but was usually ± 0.1°C.

## RESULTS

The second division segregation (MII) frequencies of *gray* and *hyaline* showed both rises and decreases with increasing temperature over different temperature

TABLE 1

*Effect of temperature on second division segregation frequency*

| Locus: Cross: Temperature °C | Total asci | *hyaline* C7×C7*h* 2nd division segregation (percent) | $\chi^2$ 2×2 df=1 | Total asci | *gray* $g^+ \times g$ 2nd division segregation (percent) | $\chi^2$ 2×2 df=1 |
|---|---|---|---|---|---|---|
| 31 | 3532 | 63.3 | | 1782 | 57.7 | |
| | | | 0.6 | | | 8.7** |
| 30 | 3545 | 62.4 | | 3446 | 61.9 | |
| | | | 0.2 | | | 1.5 |
| 27.5 | 3566 | 61.9 | | 3829 | 63.3 | |
| | | | 8.9** | | | 0.0 |
| 25 | 4826 | 58.7 | | 3147 | 63.5 | |
| | | | 16.6** | | | 11.3** |
| 22.5 | 3712 | 54.3 | | 4857 | 67.0 | |
| | | | 65.1** | | | 0.1 |
| 20 | 6141 | 45.9 | | 3957 | 66.7 | |
| | | | 2.1 | | | 0.1 |
| 17.5 | 2971 | 47.5 | | 5449 | 67.0 | |
| | | | 0.7 | | | 2.6 |
| 15 | 2655 | 46.4 | | 3708 | 65.3 | |
| | | | 32.9** | | | 2.8 |
| 12.5 | 4354 | 53.4 | | 3379 | 63.4 | |
| | | | 13.6** | | | 1.5 |
| 10 | 5364 | 57.2 | | 4490 | 62.1 | |

** Significant at P = 0.01.

ranges: there was a marked difference between the loci in their responses (Table 1 and Figure 1). The MII frequencies of *hyaline* show a U-shaped curve when plotted against temperature, with a minimum frequency over the range 15 to 20°C. In contrast, those of *gray* give an inverted U-curve with a maximum frequency over the range 17.5 to 22.5°. Changes in MII frequency with temperature of incubation can be expressed in terms of the temperature coefficient, $Q_{10}$, using a negative sign where decreases are observed with increasing temperature (these $Q_{10}$s differ from Van't Hoff coefficients in being calculated from frequencies, not rates of reaction). The $Q_{10}$s for MII frequencies of *gray* and *hyaline* are given in Table 2.

No significant differences between replicate crosses or repeat experiments at the same temperature were found but differences between MII frequencies at

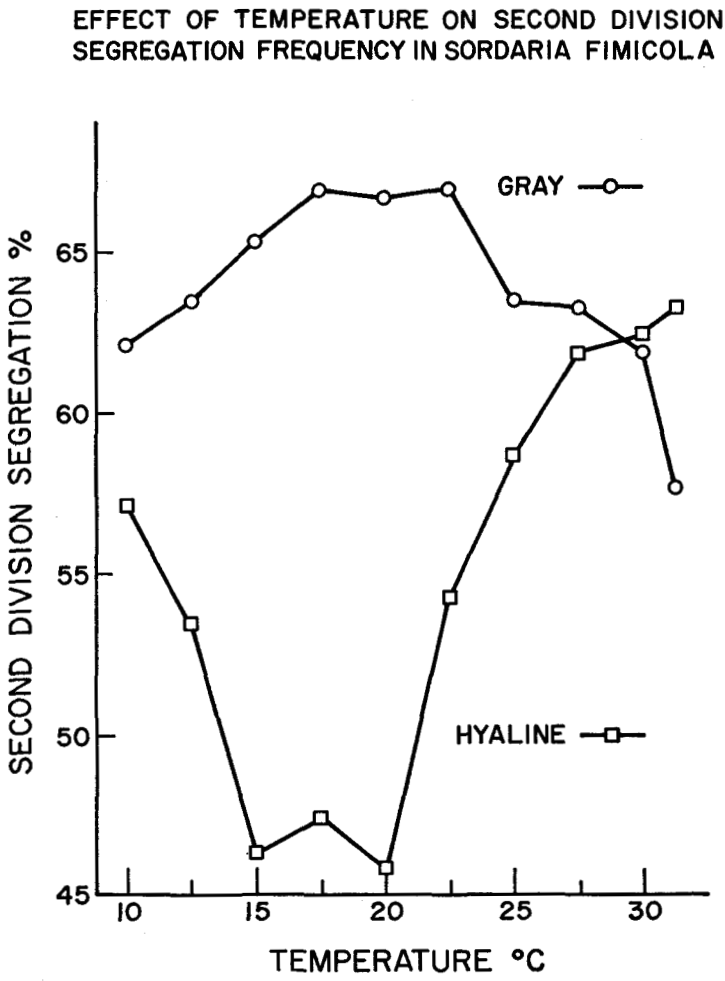



FIGURE 1.—The effect of temperature on second division segregation frequencies.

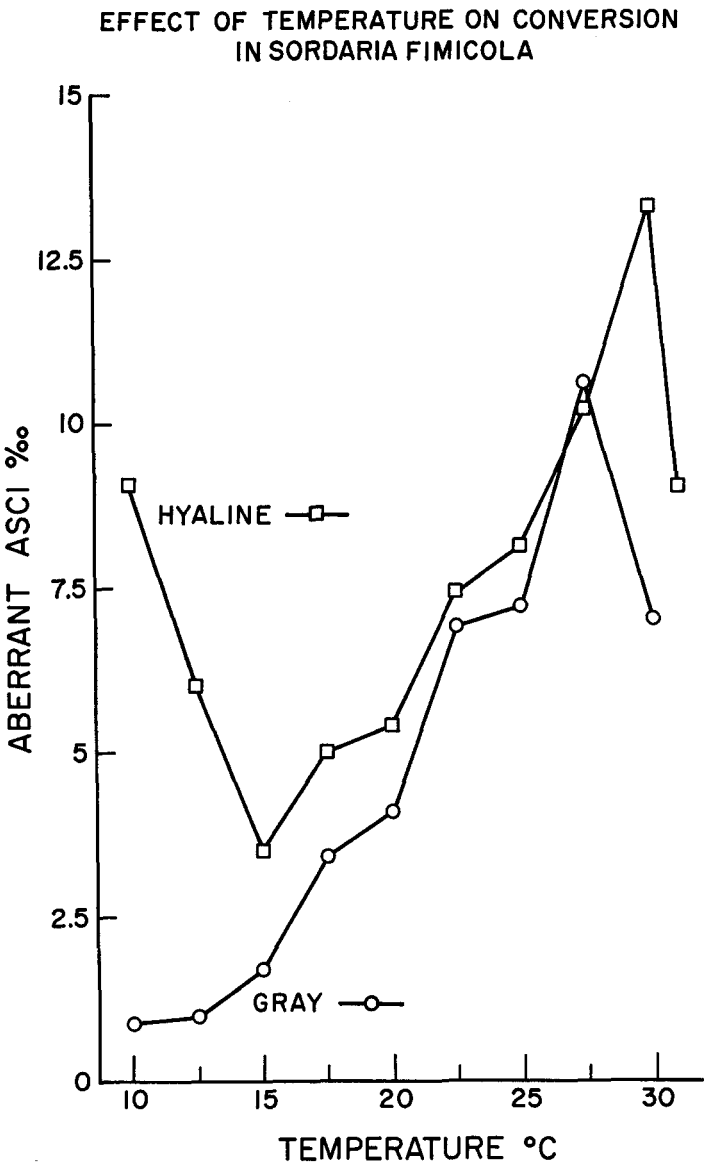



FIGURE 2.—The effect of temperature on conversion frequencies.

different temperatures were often highly significant (Table 1); differences in incubation temperature of only 2.5°C often resulted in MII frequencies for *hyaline* significantly different at the $P = 0.01$ level. In all crosses the expected 1:1 ratios for the two MI ascal classes and the 1:1:1:1 ratios for the four MII ascal classes were obtained (LAMB 1966b and unpublished), showing that the MII frequencies were unaffected by a differential bursting of asci (LAMB 1967) or by spindle overlap at the second division.

TABLE 2

*Temperature coefficients for second division segregation and total conversion frequencies*

| Temperature °C | *hyaline* MII | *hyaline* Conversion | *gray* MII | *gray* Conversion |
|---|---|---|---|---|
| lower range | —1.5 | —6.7 | 1.1 | 3.6 |
| (actual range) | (10–15) | (10–15) | (10–17.5) | (10–15) |
| higher range | 1.3 | 2.3 | —1.2 | 5.0 |
| (actual range) | (20–31) | (15–27.5) | (22.5–31) | (15–27.5) |

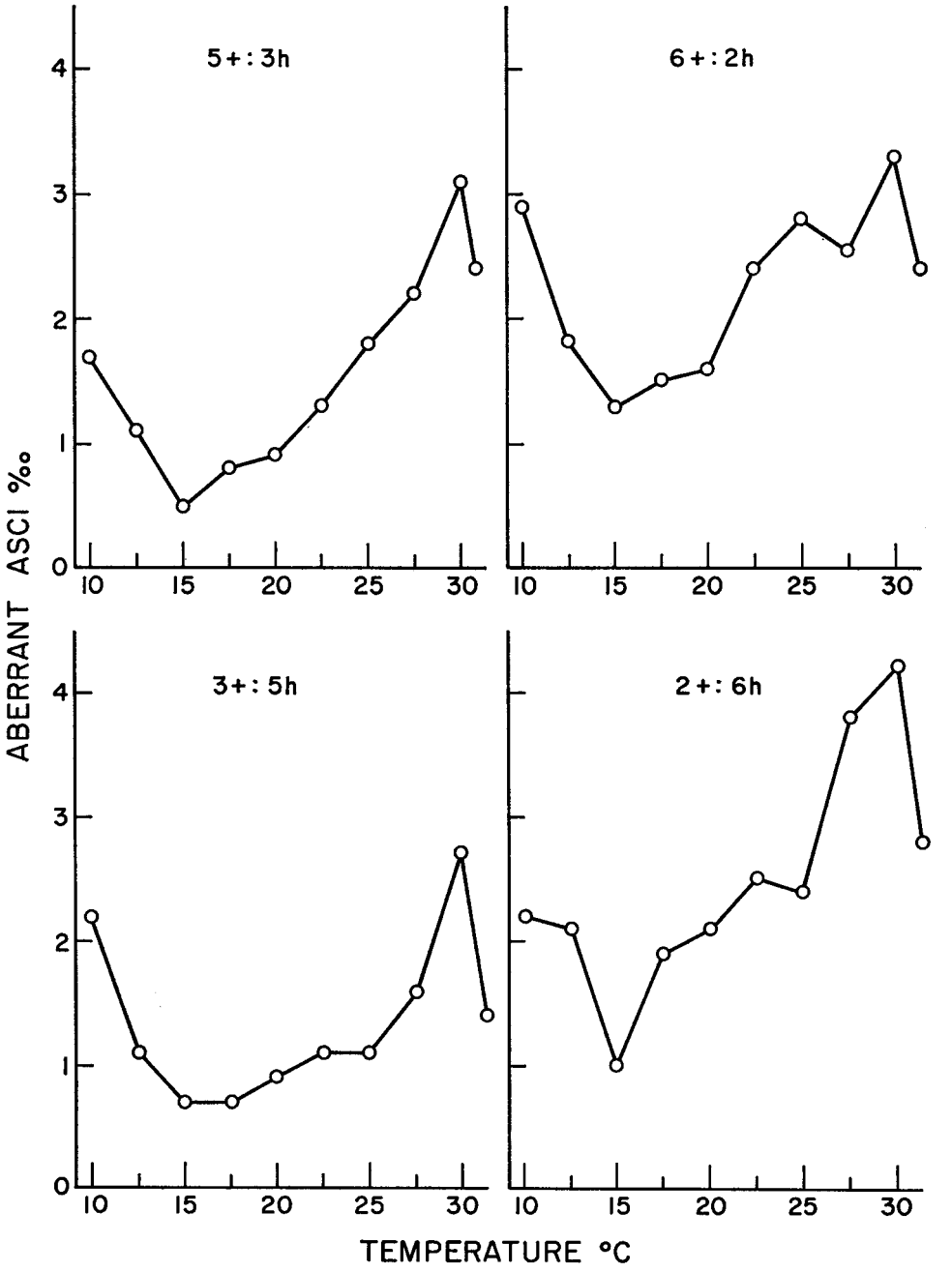
The effects of temperature on total observed conversion frequencies and on individual aberrant-ratio classes are shown in Table 3 and Figures 2 and 3. Trends with temperature for each individual aberrant-ratio class were qualitatively similar for a given locus; that is, the graphs for 5+:3*m*; 3+:5*m*; 6+:2*m* and 2+:6*m* conversion classes are similar in general outline to each other and to that for total conversion frequency for the given locus (quantitative differences between individual aberrant-ratio classes have been detailed previously: LAMB 1968). A striking difference between the two loci was obtained for total conversion frequencies over the lower temperature range: this frequency increased for *gray* with increasing temperature over the range 10–15°C but decreased significantly for *hyaline* over both the intervals 10–12.5°C and 12.5–15°C. The $Q_{10}$s are given in Table 2. Over the range 15–27.5°C, total conversion frequencies showed a similar rise with temperature for both loci although the rate of increase was greater for *gray* than for *hyaline*. Both loci showed a decrease in conversion frequency over the highest interval at which conversion was scoreable: P = 0.01–0.02 for *hyaline*, 30–31°C, and P = 0.05–0.1 for *gray*, 27.5–30°C. For the main portion of the graph, 15–27.5 or 30°C, conversion changes over each 2.5°C interval were mostly significant at the 0.05 level for *gray* but not for *hyaline*.

TABLE 3

*Effect of temperature on conversion frequency*

| Locus: Cross: | | *hyaline* C7+ × C7*h* | | | | | | *gray* $g^+ \times g$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Temperature °C | Total asci | 5+:3*h* °/oo | 3+:5*h* °/oo | 6+:2*h* °/oo | 2+:6*h* °/oo | Aberrant asci °/oo | Total asci | 5+:3*g* °/oo | 3+:5*g* °/oo | 6+:2*g* °/oo | 2+:6*g* °/oo | Aberrant asci °/oo |
| 31 | 5022 | 2.4 | 1.4 | 2.4 | 2.8 | 9.0 | .... | .. | .. | .. | .. | .. |
| 30 | 8381 | 3.1 | 2.7 | 3.3 | 4.2 | 13.3 | 4267 | 2.6 | 1.9 | 1.4 | 1.2 | 7.0 |
| 27.5 | 7375 | 2.2 | 1.6 | 2.6 | 3.8 | 10.2 | 6887 | 3.0 | 2.3 | 3.2 | 2.0 | 10.6 |
| 25 | 7932 | 1.8 | 1.1 | 2.8 | 2.4 | 8.1 | 6079 | 3.1 | 1.8 | 1.3 | 1.0 | 7.2 |
| 22.5 | 7063 | 1.3 | 1.1 | 2.4 | 2.5 | 7.4 | 5932 | 2.0 | 1.7 | 1.9 | 1.3 | 6.9 |
| 20 | 8150 | 0.9 | 0.9 | 1.6 | 2.1 | 5.4 | 8229 | 1.6 | 0.9 | 1.0 | 0.7 | 4.1 |
| 17.5 | 7245 | 0.8 | 0.7 | 1.5 | 1.9 | 5.0 | 8033 | 1.2 | 0.6 | 0.9 | 0.6 | 3.4 |
| 15 | 7659 | 0.5 | 0.7 | 1.3 | 1.0 | 3.5 | 7126 | 0.6 | 0.6 | 0.3 | 0.3 | 1.7 |
| 12.5 | 8286 | 1.1 | 1.1 | 1.8 | 2.1 | 6.0 | 9076 | 0.2 | 0.2 | 0.3 | 0.2 | 1.0 |
| 10 | 8158 | 1.7 | 2.2 | 2.9 | 2.2 | 9.1 | 13014 | 0.2 | 0.2 | 0.3 | 0.2 | 0.9 |

EFFECT OF TEMPERATURE ON CONVERSION CLASSES FOR HYALINE



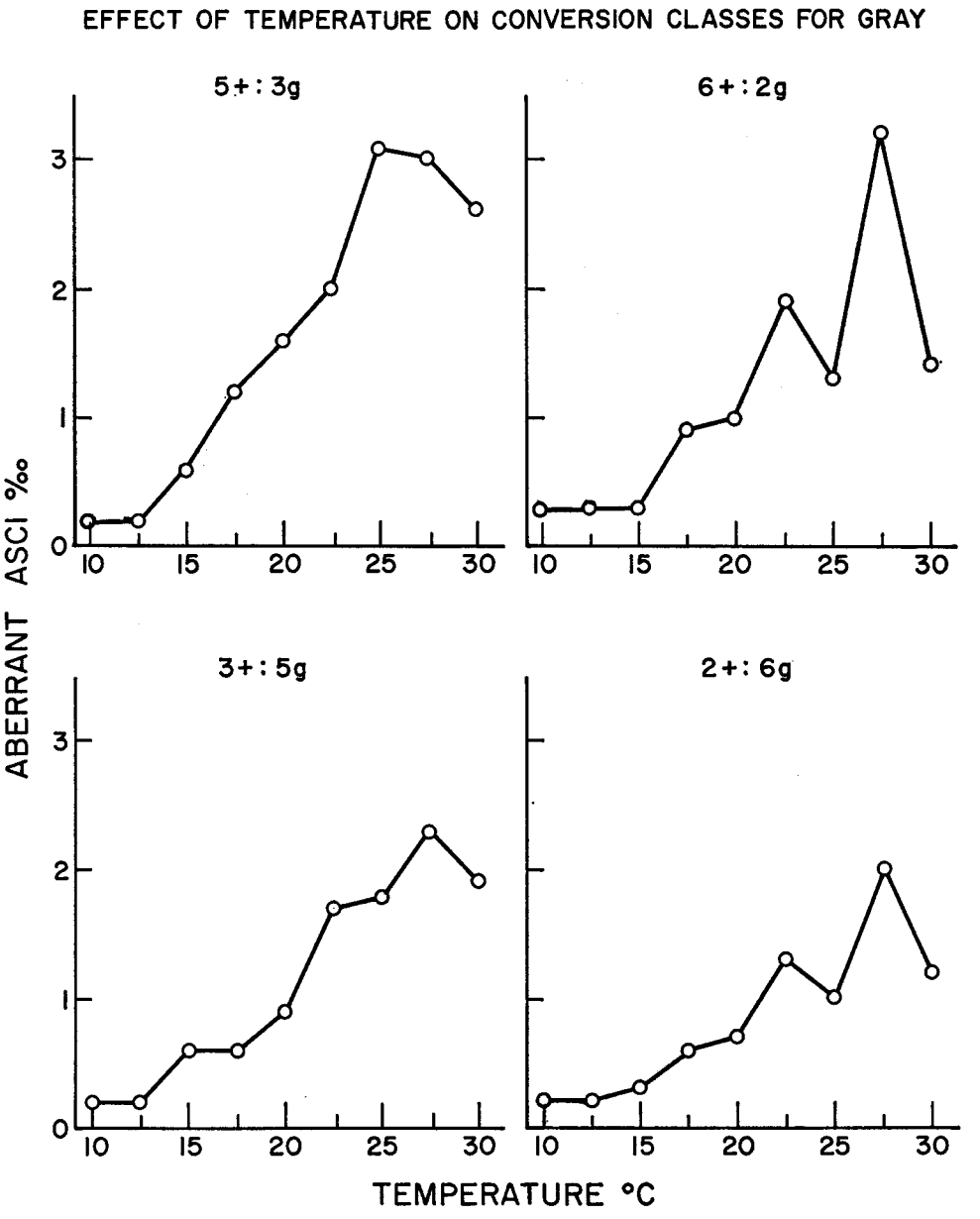



FIGURE 3.—The effect of temperature on the frequencies of individual conversion classes: (a) *hyaline* (b) *gray*

## DISCUSSION

Although there were major differences between loci in their responses, their individual conversion and MII frequencies changed in related ways over the lower temperature range (10–15°C) and in unrelated ways over the higher range

(22.5–27.5°C for *gray*, 27.5–30°C and possibly 15–20°C for *hyaline*). The prediction from hybrid-DNA models of recombination that both related and unrelated changes in conversion and recombination frequencies should occur is therefore supported by these data. Recombination was measured over gene-centromere intervals, so the recombination frequency (RF) changes reflect results of events at a number of different loci. Even if responses at individual loci differ, the use of relatively long intervals, as here, could help average out local differences, assisting the detection of general effects on RFs. Conversion is measured for single sites, so the present comparisons are between general effects of temperature on RFs and site-specific conversion frequency (CF) changes. Possible regional differences in general effects on RFs are discussed later.

Changes in conversion frequency with temperature were generally more marked than those for recombination frequency, in agreement with previous results, but the present data differ in that a negative $Q_{10}$ was obtained for conversion at the *hyaline* locus over the range 10–15°C. Conversion frequencies, like recombination frequencies, may therefore show either or both increases and decreases with increasing temperature.

The possibility of U-curve relations, with both increases and decreases in a frequency over different temperature ranges, affects the interpretations of temperature experiments. Thus studies of only two temperatures (such as that of STADLER 1959) are not sufficient to demonstrate the absence of temperature effects, as the two temperatures might lie at corresponding points on opposite arms of a U-curve (as do 12.5°C and 22.5°C for *hyaline* in Figure 1). No overall $Q_{10}$ value is possible for a U-curve relationship as the value changes over different temperature intervals. In general, a detailed coverage of the maximum temperature range possible should be used when studying effects of temperature. For example, OLIVE (1956) studied the same Sordaria crosses as used here, using only 13°, 23° and 31°C as constant temperatures of incubation; he found a linear relationship between MII frequency for *hyaline* and temperature instead of the U-curve (Figure 1) obtained in a more detailed study here, even though his values were similar to mine at corresponding temperatures.

Over a comparable temperature range, the conversion frequencies found here for *gray* were higher than those of KITANI and OLIVE (1967), which were higher than those of KITANI, OLIVE and EL-ANI (1962). These three sets of observations also differ in the relative frequencies of conversion to wild type and to mutant. There were differences in media and crossing methods, and in the presence of additional markers in several of KITANI *et al.*'s crosses, but none of these factors suggests a satisfactory explanation of the observed disparities. It is possible, however, that the *gray* mutant used here, although a pseudoallele of the *gray* locus, is not identical with the $g_1$ mutant of KITANI and OLIVE (KITANI and OLIVE, personal communication).

In the present study, the difference between the loci in conversion frequency response at 10–15°C was found for all aberrant-ratio classes (Table 3, Figure 3), supporting the evidence from characterization of individual spores that phenocopies were not responsible for this difference. Although different pairs of mis-

paired bases may be involved in conversion at the two loci, the changes amongst various aberrant-ratio classes do not support this as an explanation of the difference in conversion frequency response between loci. Thus if the lower conversion frequency for *hyaline* at 15° than at 10°C were due to a decrease at 15°C in correction efficiency for those mis-paired bases at the *hyaline* site, then the frequency of 5:3 asci for *hyaline* should rise relative to that of 6:2 asci over this interval: from Table 3 it can be seen that the opposite effect was observed (see LAMB 1968, for more detailed discussion). The inability to detect two 4+:4*m* classes in the present study probably made little difference to the total conversion frequency results, for the following reasons: the 4+:4*m* class resulting from correction in both chromatids was expected to vary with temperature in the same way as the 6:2 classes (LAMB 1968), and the 4+:4*m* class with post-meiotic segregation constitutes only a small fraction of all convertant asci (KITANI *et al.* 1962).

Changes in MII frequency with temperature could be caused by changes in cross-over frequency or in interference. There are few reported changes of interference with temperature (MCNELLY 1962; ABEL 1964). No direct interference data were obtained here because crosses with flanking markers for *gray* were not fertile over a sufficient temperature range. Both loci are far enough from their centromeres for double crossovers to occur in these intervals with an appreciable frequency: a given increase in crossover frequency is therefore likely to result in less than a comparable rise in MII frequency. This would partly account for MII $Q_{10}$s for *gray* and *hyaline* being lower than conversion $Q_{10}$s. BARRATT, NEWMEYER, PERKINS and GARNJOBST (1954) gave tetrad mapping functions corresponding to various coincidence coefficients for "chiasma interference", assuming "chromatid interference" is absent. EL-ANI, OLIVE and KITANI (1961) found at 23°C an MII frequency for *gray* of 68% and a centromere distance, from summations over shorter intervals, of about 60 map units (heterogeneity between different crosses makes the exact value uncertain). From the tetrad mapping function graph (BARRATT *et al.* 1961, Figure 5), these values correspond to a coincidence coefficient between 0.5 and 0.6. This value can then be used to relate the present MII frequencies to map distances corrected for multiple crossovers. The $Q_{10}$s for recombination can then be recalculated, giving corrected values for *gray* of 1.3 for the lower temperature range and −1.5 for the higher range, compared with the uncorrected values (in Table 2) of 1.1 and −1.2 respectively. Although these corrected values may not be wholely accurate, as they depend on EL-ANI *et al.*'s map distance and BARRATT *et al.*'s assumptions, these figures show that correction for undetected double crossovers raises numerical values of $Q_{10}$s for recombination in the *gray*-centromere interval. Even the corrected values are still much lower than conversion $Q_{10}$s. If the coincidence value derived above is correct, the flattening off of the MII curve for *gray* at its maximum (17.5–22.5°C, Figure 1) is not due to attainment of the theoretical upper limit of 66.7% but to the absence of temperature effects over that 5°C range.

The main findings to account for in terms of specific recombination models are: that related and unrelated changes in recombination and conversion occurred; that even where related changes occurred, the $Q_{10}$s for recombination and conver-

sion differed, and that results for the two loci differed widely in their changes with temperature. Current hybrid-DNA models suggest three variables: the frequency of breakage at the postulated fixed breakpoints in the DNA strands; the average length of hybrid-DNA formed from such a break, and the relative frequencies of dissociation to form hybrid-DNA in one or in two directions from a break. Changes in the initial breakage frequency will affect the frequency of hybrid-DNA formation and should, on all polaron hybrid-DNA models, produce related effects on recombination (crossover) and conversion frequencies.

Differences in average length of hybrid-DNA formed from a break have similar consequences on various models, but could have different effects on different mutational sites, depending on their distance from a fixed breakpoint. Sites close to a breakpoint should be included in hybrid-DNA nearly every time this is formed in their direction from that point but sites far from one may only occasionally be included. A change with temperature in this variable could thus produce different conversion frequency responses from different mutational sites, those sites furthest from a breakpoint being affected most and those nearest one being affected least. As this variable should not affect recombination, it could—for sites whose conversion is affected by it—be a cause of unrelatedness in recombination and conversion changes.

Changes in the relative frequencies of dissociation in one, and in two, directions have different effects according to different hybrid-DNA models. A relative increase in bi-directional dissociation at the expense of uni-directional dissociation should, on the HOLLIDAY (1964) model, subject to certain assumptions about half-chiasma resolution, increase conversion for all loci by a factor of up to two without affecting recombination frequencies; on the HASTINGS and WHITEHOUSE (1964) model, conversion should increase similarly but recombination should decrease; on the WHITEHOUSE (1966) model, recombination should decrease but the increase in conversion frequencies should be restricted to sites close to the fixed opening points. On all three models a change in this variable would have different effects on recombination and conversion frequencies, which would change in an unrelated fashion and with different $Q_{10}$s.

The three variables postulated in polaron hybrid-DNA models are therefore sufficient to explain related and unrelated changes in recombination and conversion frequencies, differences in their $Q_{10}$s, and certain differences in conversion response between different mutational sites, depending on their positions with respect to fixed break points.

One unexplained point is the difference between *gray* and *hyaline* in recombination response. Different responses of recombination to temperature in different chromosomes and in different regions of a chromosome are known in other organisms (references in MCNELLY-INGLE *et al.* 1966); the linkage relations of *gray* and *hyaline* are unknown as intercrosses are sterile. The difference in U-curve orientation is not likely to result from different distances of the loci (as measured by MII frequencies) from their centromere as these "distances" are identical at the point where the two U-curves intersect in Figure 1. This view is supported by NAKAMURA's (1966) finding that temperature had similar effects

on MII frequencies for *asco* in several Neurospora crosses giving different MII frequencies. Another possibility is that the genetic backgrounds of the *gray* and *hyaline* sets of crosses (described by OLIVE 1956) differ in genes affecting response of recombination to temperature. If the different MII frequency responses of *gray* and *hyaline* reflect differences in response of breakage frequency in the two crosses, then the related changes in MII and conversion frequencies found for both loci at low temperatures have a similar origin. Alternatively, if the breakage frequency responded similarly to temperature in both crosses, then the difference in MII frequency response, and the difference in conversion response between the two loci at low temperatures, require alternative explanations. It is therefore possible that the related changes in recombination and conversion observed for one locus could result from a common cause (changes in breakage frequency) and that the relatedness of changes for the other locus results fortuitously, with separate causes for the changes in recombination and conversion.

The present results are in accord with several different polaron hybrid-DNA models, but, as discussed, these models have testably different predictions. Temperature studies parallel to the present ones might distinguish between such models if crosses using different alleles of the same locus were studied: such results would also eliminate some alternative explanations of the present data.

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## SUMMARY

Hybrid-DNA models of recombination predict that some treatments should cause recombination and conversion frequencies to change in related ways, while others should change them in unrelated ways. This prediction has been tested in crosses of the ascospore-colour markers *hyaline* and *gray* with their respective wild types at different incubation temperatures. Conversion and recombination (second division segregation) frequencies for these loci showed both increases and decreases with increasing temperature, but the response patterns differed for the two loci. For individual loci, conversion and recombination frequencies changed in related ways over the lower temperature range (10–15°C) and in unrelated ways over part of the higher range, confirming the above prediction. The $Q_{10}$s for conversion were higher than those for recombination, but for a particular locus, the frequencies of different aberrant-ratio classes changed in similar ways with temperature. These results are compatible with hybrid-DNA models which postulate fixed points of breakage in DNA and that hybrid-DNA may form in one or both directions from such a break. The predictions of different hybrid-DNA models are discussed.

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