A SELF-PROPAGATING STRUCTURAL CHANGE IN *TRITICUM*

II. The Reproductive Cycle

By O. H. FRANKEL

Wheat Research Institute, Christchurch, New Zealand

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1. INTRODUCTION

DICENTRIC chromatids, broken unevenly in a meiotic anaphase, may yield functional gametes with inverted duplications of part or the whole of a chromosome arm, as was shown in maize by McClintock (1938, 1939, 1941) and inferred in wheat in the first paper of the present series (Frankel, 1949). Chiasmata in such duplications, whether within or between partner chromosomes, may—and the majority do—yield bridges and fragments, a process which results in eliminating the duplication (Frankel, *l.c.*). Yet the new bridges are liable in turn to break unevenly, serving as a source of new duplications not necessarily identical with those to which they owe their existence. Thus we find a *chiasma cycle* from generation to generation, commencing with a duplication chiasma in one generation and leading through an unevenly broken bridge to a duplication chiasma in another.

Dicentric chromatids are of widespread occurrence, both in controlled experiments and in natural populations. It is therefore surprising that inverted duplications arising from bridge rupture have not been observed more frequently ; for at least in plants, and especially in polyploids, they have a chance of survival.

In a dwarf *compactum* type of wheat, Håkansson (1933) illustrated what is probably a homozygote for an inverted duplication. Loops were seen in metaphase I with a frequency of about 10 per cent. ; anaphase I and II were not observed. Derivation and progeny were not recorded.

Richardson (1936) found inverted duplications in *Lilium*. She also illustrated what appears to be a univalent bridge, which may have

originated from chiasma formation in a univalent with a duplicated and inverted segment. Similarly, the likelihood of inverted duplications is suggested where dicentric chromatids are of common occurrence and where there are unusually high frequencies of second anaphase bridges, as in *Tulipa* (Upcott, 1937*a*) and in *Tradescantia* (Bhaduri, 1942). Upcott also found univalent bridges, here, as in *Polygonatum* (Suomalainen, 1947), suggesting an inverted duplication in a univalent.

It must be recognised that whatever the number, the external or the internal relationships of chiasmata, the only structural or genetical change which is brought about by them is the elimination of the duplication. The duplication is perpetuated by non-crossover and normal crossover chromatids, but removed as a fragment when crossing-over leads to bridge formation.

The chiasma cycle preserves the duplication from immediate extinction ; yet each bridge potentially contributes towards the ultimate extinction of the duplication. Not only are there median breaks which fail to yield duplications, but for each duplication chromatid there is a corresponding deficiency chromatid, and some or all of these may be viable. Hence the existence of the duplication is determined by chiasma formation. There is in fact a wider duplication cycle, from the inception of a duplication to its ultimate removal by crossing-over, from the first to the last unevenly broken bridge. The length of this " reproductive cycle " is primarily determined by the chiasma frequency ; where this is high the cycle will be brief.

Is it likely that inverted duplications play a part in the origin of duplications which become part of the stable chromosome complement? Circumstantial evidence comes from " reversed repeats," and, possibly, " doublets " and other associations of small numbers of identical or similar bands in the salivary gland chromosomes of *Drosophila* and *Sciara* (*cf.* recent review by Metz, 1947). The association of a number of chlorophyll genes in the distal sector of the short arm of chromosome 9 (McClintock, 1944, 1946 ; *cf.* also Metz, *loc. cit.*), which is known to yield inverted duplications, is also suggestive ; and so perhaps are the suspected terminal duplications or deletions in *Drosophila ananassæ* (Kikkawa, 1938 ; Dobzhansky and Dreyfus, 1943).

To be incorporated in the stable complement of a species, an inverted duplication, in common with other structural changes, must fulfil three conditions : it must permit survival of the cell and of the organism ; it must have a physiological advantage ; it must become stabilised. It is the last which raises a specific problem in the case of an inverted duplication. Stabilisation is possible only after the elimination of internal crossing-over. This will occur where chiasma formation is inhibited—either through an additional structural change such as translocation or inversion, or by a special genotypic condition such as localisation.

The subject of this paper is the inheritance—and in consequence

the chiasma cycle—of the wheat duplications which have been described previously. Once the cytological types and their frequencies are known, it is possible to predict the duration of the reproductive cycle. This prediction has been tested in a population derived from a known duplication type.

The following abbreviations are used :—

ABC	chromosome (bivalent) in which duplications occur.
BC	arm of above chromosome in which duplications occur
AB	normal arm of above chromosome
LD	gamete with a long duplication
SD	gamete with a short duplication
SD*ef*	gamete with a short deficiency
N	gamete without a duplication
O	gamete lacking the ABC chromosome.

2. THE TRANSMISSION OF CHROMATIDS RESULTING FROM BRIDGE BREAKAGE

In maize the fate of broken bridge chromatids was followed cytologically by observations in pachytene, and genetically by observations of endosperm and plant characters (McClintock, 1939 and 1941). Wheat chromosomes are not suitable for pachytene study, and no genes are known in the duplication arm. The transmission of broken chromosomes was therefore followed by the cytological identification of zygotes in the progenies of crosses and selfings of the duplication types. They are recorded in table 1.

(a) Qualitative

Information on the viability and the nature of the products of bridge breakage is first derived from selfed homozygotes and monosomics for the long duplication, LD/LD and LD/O. In their progenies any D chromosome without the long duplication comes from a broken bridge chromatid. The presence in these families of LD/N, LD/SD, SD/SD, SD/N, N/N and SD/O plants proves (i) that gametes containing chromosomes derived from broken bridge chromatids are functional, and (ii) that bridge breakage produces SD and N gametes.

As noted previously and as might be expected from their origin through chromatid breakage, there is some variation in the size of the short duplications ; but, contrary to the observations by McClintock (1941) in maize, the size varies within narrow limits. The difference between wheat and maize, one may presume, is due to the relative sizes of the chromosomes in relation to those of the cells : maize chromosomes are small, hence their orientation in anaphase is less confined in space than that of the relatively large wheat chromosomes. In wheat it is invariably quite easy to identify

any fragment as originating from either a long or a short duplication ; there are no intergrades between them. This suggests different modes of origin for the two types of duplication. The question must be asked whether the long duplication ever arises from bridge breakage.

TABLE 1

Crosses and selfings in the duplication strain

Parents	Number of progenies	LD/LD	LD/N	LD/SD	SD/SD	SD/N	N/N	LD/O	SD/O	N/O	Tot
(*a*) 42-chromosome types											
/N × LD/LD	2	...	18	...	...	3	2	...	...	...	2
/N × LD/N	8	...	35	...	...	4	50	...	...	1	9
/N × LD/SD	1	...	3	...	...	5	...	...	...	...	
D/LD × SD/SD	1	...	1	3	1	...	1	...	...	...	
D/LD . .	11	58	18	17	1	6	2	1	1	...	10
D/N . .	19	21	68	1	...	11	55	...	...	1	15
D/SD . .	4	4	6	14	7	7	1	...	...	...	3
D/SD . .	4	...	...	...	20	10	1	...	1	1	3
D/N . .	10	...	1	2	4	42	35	...	...	...	8
/N . .	5	...	...	...	...	...	35	...	...	...	3
(*b*) Monosomics											
D/O × N/N	2	...	9	...	...	1	9	...	...	18	3
/N × LD/O	3	...	13	...	...	2	2	...	...	...	1
/N × SD/O	2	...	...	...	...	9	3	...	...	...	1
/O × N/N .	2	...	...	...	...	...	15	...	...	21	3
/N × N/O .	2	...	...	...	...	...	13	...	...	...	1
D/O . .	10	4	11	...	...	...	1	63	7	18	10
D/O . .	4	...	...	...	4	5	2	...	25	2	3
/O . .	8	...	...	...	...	...	30	...	...	101	13

Note.—N/N is either White Fife or Tuscan.

Information on this point can be obtained from the progeny of crosses and selfings of plants with the short duplication ; an LD chromosome must be the result of bridge breakage. Among 167 plants raised from selfed SD plants and from SD crossed with N/N, three plants were found which carried an LD chromosome. This proves that a long duplication may arise from bridge breakage.

Whenever an SD chromosome occurs as the result of an unevenly broken bridge, a chromosome with a corresponding short deficiency (SD*ef*) should arise with equal frequency. The deficient chromosome would, however, be indistinguishable from a normal one.

(*b*) *Quantitative*

(1) *The proportion of functional crossover gametes.*—We have seen that, with rare exceptions, the chromosomes resulting from a chiasma in an inverted duplication are either normal (which possibly includes short-

deficiency chromosomes) or have a short duplication. The frequency of crossing-over is known from observations in meiosis (*cf.* Frankel, *loc. cit.*) ; it is now possible to relate this to the frequencies of functional non-crossover and crossover gametes. While meiotic observations were confined to male cells, zygotic ratios provide information on both sexes.

Evidence on the proportions of functional pollen grains carrying non-crossover and crossover chromosomes is available from LD/LD ♂ crossed with N/N ♀ and from LD/O selfed and crossed with N/N ♀ (*cf.* table 1).

(*a*) N/N ♀×LD/LD ♂. The proportions of functional non-crossover and crossover gametes were as follows :—

18 LD : 3 SD : 2 N

or 0·78 non-crossover : 0·22 crossover, against 0·64 : 0·36 observed in meiosis.

(*b*) LD/O selfed. Pollen grains lacking the ABC chromosome are inviable ; hence 41-chromosome plants in the progeny of selfed LD/O are derived from ovules without the ABC chromosome, fertilised by pollen grains with LD (non-crossover), SD or N (crossover) chromosomes. The observed proportions were :—

63 LD : 7 SD : 18 N

and hence the ratio of functional non-crossover : crossover pollen grains was 0·72 : 0·28, against 0·6 : 0·4 observed in meiosis.

(*c*) N/N ♀×LD/O ♂. This cross produces only 42-chromosome plants. The proportions of functional gametes were as follows :—

13 LD : 2 SD : 2 N

a ratio of 0·76 : 0·24, against 0·6 : 0·4 in meiosis.

If (*b*) and (*c*) are combined, the ratio of non-crossover : crossover gametes is 76 : 29 or 0·72 : 0·28, against 0·6 : 0·4 in meiosis. The difference is statistically significant ($P < 0{\cdot}01$).

By combining all data for LD ♂ gametes in (*a*) to (*c*), the frequency of male functional crossover gametes obtained is 0·27. It is now possible to use the progeny of selfed LD/LD for obtaining information on the corresponding frequency in the female gametes.

The observed zygotic frequencies (table 1) are compared with those calculated on the basis of a ratio of 0·27 functional crossover gametes in the male, and of an output of female gametes according to the following assumptions (table 2) :—

(i) The frequency in the female is the same as in the male, *viz.* 0·27.

(ii) There is no elimination of crossover gametes in the female, hence the ratio of functional gametes is identical with the gametic output in meiosis, *viz.* 0·36 (observed in pollen mother cells).

(iii) The frequency of functional female crossover gametes is 0·5 as in LD/O ♀.

The first assumption provides the best fit ; yet the possibility that female gametes with broken chromosomes function at a higher rate than male gametes (assumption 2) is not excluded. This indeed is more than likely to be the case since selfed LD/LD plants are fully fertile, which could not occur if female gametes were eliminated at the rate of 25 per cent. required by assumption (1).

TABLE 2

Zygotic types in the 102 offspring of selfed LD/LD, *with frequencies according to assumptions 1-3, derived from male and female gametes formed with and without crossing-over in meiosis.*

Female gametes \ Male gametes	Crossovers (N, SD)	Non-crossovers (LD)
Crossovers (N, SD)	N/N, SD/N, SD/SD (1) 7·2 (2) **9·8** (3) *12·8*	LD/N, LD/SD (1) 19·9 (2) **26·5** (3) *38·3*
Non-crossovers (LD) . . .	LD/N, LD/SD (1) 19·9 (2) **17·6** (3) *12·7*	LD/LD (1) 54·9 (2) **48·0** (3) *38·3*

	N/N, SD/N, SD/SD	LD/N, LD/SD	LD/LD	P
Observed . .	9	35	58	...
Assumption 1 . .	7·2	39·8	54·9	>0·5
Assumption 2 . .	**9·8**	**44·1**	**48·0**	<0·2
Assumption 3 . .	*12·8*	*51·0*	*38·3*	<0·001

Evidence which in general confirms these results comes from selfed LD/N and SD/SD ; but here the presence of N and SD as both non-crossover and crossover chromosomes renders adjustments necessary which reduce the significance of observations.

It is concluded that the frequency of male functional gametes with a chromosome broken in meiosis is 0·27, or about 70-75 per cent. of the output of crossover chromatids in meiosis, and that it is the same or slightly higher in female gametes. Approximately one-quarter of gametes with broken chromosomes are non-functional.

(2) *The point of bridge breakage.*—It has been shown above that the main distinguishable derivatives of broken chromatid bridges are SD and N type chromosomes. The distinction is based on the presence or absence of internal duplication pairing and hence is of a preliminary nature ; for N type chromosomes may be expected to include any of the following : (*a*) true N chromosomes derived from a bridge with median breakage point ; (*b*) chromosomes with deficiencies

(SD*ef*), corresponding to the duplication SD and resulting from the same breakage ; and, possibly, (*c*) duplications too small to form an internal chiasma, and (*d*) the corresponding deficiencies. These chromosome types cannot be distinguished ; but it is possible to obtain a general idea of the proportions of median or near-median breaks yielding types (*a*), (*b*) or (*c*), and sub-median breaks yielding SD and SD*ef*.

For this purpose the observed zygotic ratios are interpreted in the light of two alternative assumptions : the first that SD*ef* gametes are functional, the second that they are non-functional. In the first case there should be a frequency of SD*ef* corresponding to that of SD, the balance of N type chromosomes being the result of median breakage ; in the second case all N type chromosomes derive from median breakage. In either case an unevenly broken bridge yields one SD and one SD*ef* (= N type) chromosome ; but an evenly broken bridge yields two N chromosomes.

(i) N/N ♀×LD/LD ♂—3 SD/N : 2 N/N, or 3 SD : 2 N.
SD*ef* functional—2 N are SD*ef* ; O even : 2 uneven breaks.
SD*ef* non-functional—1 even : 3 uneven breaks.

(ii) LD/LD selfed—2 N/N : 6 SD/N : 1 SD/SD.
Ratio of SD : N, in both sexes—8 SD : 10 N.
SD*ef* functional—8 N are SD*ef* ; 1 even : 8 uneven breaks.
SD*ef* non-functional—5 even : 8 uneven breaks.

(iii) LD/LD selfed—17 LD/SD : 18 LD/N, or 17 SD : 18 N.
SD*ef* functional—17 N are SD*ef* ; 1 even : 17 uneven breaks.
SD*ef* non-functional—9 even : 17 uneven breaks.

(iv) N/N ♀× LD/N ♂—35 LD/N : 4 SD/N : 50 N/N.
When allowance is made for non-breakage N chromosomes, the following proportions are obtained :—

SD*ef* functional—1 even : 4 uneven breaks.
SD*ef* non-functional—2 even : 4 uneven breaks.

Summarised, the ratios of uneven and even breaks are as follows :—

SD*ef* functional—0 : 2, 1 : 8, 1 : 17, 1 : 4.
SD*ef* non-functional—1 : 3, 1 : 1·6, 1 : 1·9, 1 : 2.

The conclusion is reached that the majority of broken chromosomes are the result of uneven bridge breakage, whether short deficiencies are viable or not.

3. MONOSOMICS

In the progenies of plants carrying an inverted duplication monosomics are not uncommon, no doubt owing to the failure of pairing of the BC arm and to the resulting high frequency of non-conjunction. Six 41-chromosome plants were found among 534 plants derived from selfings and crosses of 42-chromosome plants with LD or SD duplications. The meiotic behaviour of LD/O and SD/O has

been described in the previous paper. The special interest regarding their zygotic output lies in the differential rates of functional gametes, both between crosses and selfings, and between male and female gametes.

(a) *Chromosome numbers*

The progenies from crosses and from selfings of the monosomics N/O, LD/O and SD/O are summarised in tables 1 and 4. Table 3 gives details for those plants for which both crosses and selfings are available.

TABLE 3

*Monosomics : crosses * and selfings of the same plants*

Parents	42-chromosomes	41-chromosomes
N/N × N/O (1/12)	7	0
reciprocal	7	11
N/O (1/12) selfed	3	9
N/N × N/O (1/17)	6	0
reciprocal	8	10
N/O (1/17) selfed	5	16
N/N × LD/O (25/8)	10	0
reciprocal	12	7
LD/O (25/8) selfed	6	15
N/N × LD/O (25/10)	7	0
reciprocal	7	11
LD/O (25/10) selfed	4	8
N/N × LD/O (126/4)	12	0
LD/O (126/4) selfed	0	20
N/N × SD/O (125/4)	8	0
SD/O (125/4) selfed	7	8
N/N × SD/O (126/1)	4	0
SD/O (126/1) selfed	1	9

* In the crosses of N/O and LD/O, N/N is White Fife ; in those of SD/O, N/N is Tuscan.

TABLE 4

Monosomics : summary of crosses and selfings

Crosses			Selfings		
	42-chromosomes	41-chromosomes		42-chromosomes	41-chromosomes
N/N × N/O	13	0	...	...	...
reciprocal	15	21	N/O	17	69
N/N × LD/O	17	0	...	...	...
reciprocal	19	18	LD/O	16	88
N/N × SD/O	12	0	SD/O	11	27
42 × 41	42	0	...	...	...
reciprocal	34	39	X/O	44	184
	0·47	*0·53*		*0·19*	*0·81*

The transmission of the monosome differs in male and female gametes, as is evident from reciprocal crosses ; and in crosses and selfings, as shown by the cross 41 ♀×42 ♂ *versus* selfed monosomics (table 4).*

Nullisomics for the ABC chromosome have failed to occur in the progenies of the selfed monosomics totalling 273 plants. This does not rule out altogether the possibility that nullisomics may be viable, since some occur in progenies of monosomics in wheat with a frequency as low as 0·9 per cent. (Sears, 1944). Yet, if they occur, their frequency is extremely low ; and this, together with the lack of monosomics in crosses of 42-chromosome ♀×monosomic ♂, indicates that pollen deficient for the D chromosome does not function. There is no direct evidence for this interpretation, since the mature pollen of monosomic plants was found to be normally developed ; yet the alternative assumption that nullisomics are eliminated through zygotic lethality requires that 20-chromosome pollen should fail to function with normal 21-chromosome ovules after crossing, but be fertile with its own 21-chromosome ovules after selfing. That this is improbable is shown below.

The evidence so far discussed is derived from progenies of selfed monosomics and of crosses of 42-chromosome ♀×monosomic ♂ (table 4). Here the analogy with other monosomes with inviable nullisomics is complete ; pollen grains without the ABC chromosome fail to function ; ovules are produced at the rate of four with 20-chromosomes to one with 21-chromosomes. It was found, however, that this ratio does not apply when a monosomic ♀ was crossed with a normal ♂. Here the ratio closely approximated one 20-chromosome ♀ :

* The inheritance of a monosome depends on the rate of its inclusion in microspores and megaspores, on the viability of deficient gametes, on competition between normal and deficient pollen grains, and on the viability of the deficient zygotes. In hexaploid oats, three monosomes are transmitted equally through both sexes at rates between 6 and 14 per cent. Frequencies of inclusion in tetrad cells agree with zygotic frequencies. Nullisomics are viable, though some are semi-lethal (Nishiyama, 1931 ; Philp, 1935, 1938). In hexaploid wheat, Sears (1944) has obtained all 21 monosomics and 17 nullisomics. Female transmission, uniform for all monosomes, is about 25 per cent., the discrepancy from the possible 50 per cent. being due to loss of the univalent in meiosis ; on the male side transmission varies from 1 to 15 per cent., the low value being attributed to competition with normal pollen. Watkins (1925) found a primary ratio in microspores of one-quarter to one-third lacking the univalent. He concludes that since the chance of a univalent being included in the innermost megaspore is less than random, the frequency of inclusion is likely to be lower on the female than on the male side. These primary ratios are modified either by partial pollen sterility or by slower pollen-tube growth of the defective grains. The case of the B series speltoids and fatuoids in wheat and oats, both monosomics, is more extreme. Here defective pollen as a rule fails to function ; there are no or few nullisomics and an excess of monosomics on selfing (Nishiyama, 1931). In *Nicotiana Tabacum* all the 24 monosomics have been obtained, but no nullisomics. The primary ratio for microspores is about 80 per cent. defective to 20 per cent. normal for all monosomics, and the same is believed to occur on the female side ; but differences in pollen and ovule development between the monosomic types result in a wide range of transmission rates in both sexes (Clausen and Cameron, 1944). Greenleaf (1941) found in a cytological study of embryo-sac development in *Nicotiana* monosomics that $n-1$ embryo-sacs had a slower rate of development than n, and also a higher frequency of abortion before reaching the eight-nucleate stage.

In diploid monosomics, defective pollen grains as a rule fail to function whereas eggs often are fertile. This is the case in *Nicandra physaloides* where pollen grains lacking the isochromosome die but deficient ovules are functional (Darlington and Janaki-Ammal, 1945).

one 21-chromosome ♀ (table 4). Two explanations are possible: (i) the true ratio of functional ovules is as in the cross, *viz.* 1 : 1. Then the ratio of 4 monosomic : 1 normal in the progeny of selfed monosomics requires that 20-chromosome pollen, non-functional in crossing, should be functional in selfing, with a frequency of three 20-chromosome : one 21-chromosome pollen grains (table 5).

TABLE 5

Zygotic ratio from selfed monosomics, explained on assumption that defective pollen grains are functional on selfing but non-functional on crossing

Female gametes \ Male gametes	3 20-chromosomes	1 21-chromosomes
1 20-chromosomes	[3] 40-chromosomes	1 41-chromosomes
1 21-chromosomes	3 41-chromosomes	1 42-chromosomes

This assumption requires that three-eighths of the zygotes resulting from a selfed monosomic should be lethal. However, grain development of selfed monosomics is normal without any signs of partial sterility; and plant establishment in the progeny was 91 per cent. of the seed sown.

(ii) The true ratio of functional ovules in the monosomic is four 20-chromosome : one 21-chromosome. Then three-quarters of the 20-chromosome ovules, though functional with their own pollen, fail to function when crossed with 21-chromosome normal pollen. Here, therefore, there should be 60 per cent. lethal zygotes. Such lethality is hard to prove with grains resulting from crossing where seed setting is always uncertain; and plant establishment was normal, at the rate of 90 per cent. of the seed sown.

Both explanations assume differential compatibilities: the first, that 20-chromosome pollen is compatible with 21-chromosome ovules carried by the monosomic, but incompatible with those carried by a normal plant; the second, that the 20-chromosome ovules of the monosomics are more compatible with their own 21-chromosome pollen than with that of normal 42-chromosome plants. The evidence of ovule fertility disproves the first assumption; but the second is by no means established. It should be tested by using a N/N plant extracted from the duplication stock in place of White Fife. This is now in progress.

(*b*) *Crossover frequencies*

It has been previously shown that the monosomic with the long duplication (LD/O) has an output of 0·24-0·28 of functional pollen grains with a crossover ABC chromosome, which is similar to the

output of the homozygote LD/LD (0·22). On the female side, there is evidence from crosses with White Fife ♂ (table 1). Monosomics derive their one ABC chromosome from the N/N male parent and are normal; 42-chromosome plants are LD/N, SD/N and N/N, in the proportion shown in the first line :—

	Non-crossover	Crossover		Ratio non-crossover : crossover
	LD	SD	N	
LD/O ♀ .	9	1	9	0·9 : 1
LD/O ♂ .	13	2	2	3·3 : 1

The result of the reciprocal cross—which consists only of 42-chromosome plants—is shown in the second line. The figures are small, but the difference is significant ($P > 0{\cdot}01$). On the male side, the proportion of functional non-crossover and crossover gametes is about 3 : 1, on the female side about 1 : 1. It has been shown before that in the homozygote LD/LD the proportion of crossover ovules is between 0·27 and 0·36, but not 0·5 as in the monosomic LD/O. If the primary ratio in megaspore cells is the same in the monosomic as in the homozygote, then the deficiency of functional non-crossover ovules is due to differential elimination; but LD/O heads, which on this assumption should show partial sterility, are fully fertile.

This leaves the assumption that the primary ratio in LD/O megaspore cells is atypical. Here again there are two possibilities. (i) Internal duplication pairing is more frequent in the megaspores than in the microspores of the monosomic and in the megaspores of the homozygote. In view of the constancy of crossover values observed throughout this study, this seems improbable. (ii) A crossover chromatid has a greater chance than an LD chromatid of reaching the innermost megaspore cell.

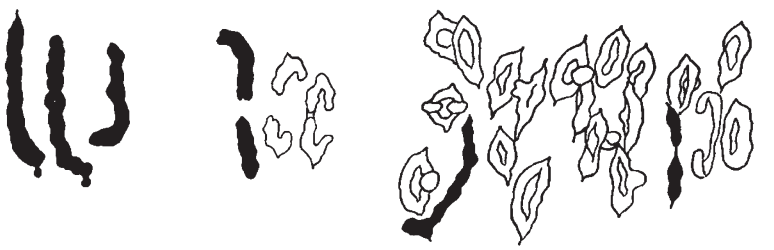
Owing to the difficulty of obtaining the large numbers required for establishing quantitative differences, no observations on megaspore development have been made; but whatever the cause, the data indicate preferential segregation favouring the inclusion of crossover chromatids in the egg.

From the absence of inversion crossovers in *Drosophila*, Sturtevant and Beadle (1936) concluded that a first division bridge remains intact so that crossover chromatids are excluded from the terminal nucleus which forms the egg. Darlington and La Cour (1941) obtained cytological confirmation in *Lilium* and *Tulipa*, and, recently, Carson (1946) in *Sciara*. The former authors point out, however, that the non-inclusion of inversion crossovers does not apply where a chiasma proximal to the inversion causes the formation of a second division bridge. That in the present study there is no differential

distribution of crossover chromatids resulting from second division bridges is confirmed by the similarity of crossover ratios in the pollen grains and ovules of the homozygote LD/LD. The monosomic, however, shows preferential inclusion of crossover chromosomes in the ovule, the opposite in fact of the Sturtevant and Beadle effect. Here, as in the case of preferential segregation of knobbed chromosomes in the megasporogenesis of maize (Rhoades, 1942 ; Longley, 1945), no explanation can be given.

4. TELOCENTRICS

Telocentrics involving the duplication chromosome have been found independently on two occasions. In both instances the duplication arm was missing. Both were found as heterozygotes in the progeny of normal plants ; in the first the normal partner chromosome carried the long duplication, in the second it carried the short duplication (fig. 1). In the latter case the ABC chromosome



(*a*) (*b*) (*c*)

FIG. 1.—Telocentric, with BC arm missing, paired with SD : (*a*) metaphase I. (*b*) anaphase I. (*c*) complete metaphase cell with telocentric bivalent as above and another homozygous telocentric bivalent. × 1280.

was not the only telocentric. A telocentric bivalent was found side by side with the AB telocentric (fig. 1*c*). This pair usually forms a chiasma. The majority of the progeny carried this second telocentric as a bivalent, the remainder as a univalent. At the time of its discovery, preparations of some of the antecedents had been discarded ; yet the origin of the AB telocentric could be traced to the two preceding generations, since the third, and all sibs of the original plant, 29/7, and of its parent, were normal.

The parents and descendants of the two AB telocentrics were as follows :—

(*a*)

126/2 (1941-42) : LD/O

Plot 31 (1943-44) : 1 N/N, 2 LD/O, 1 LD/TC *

Plot 22 (1944-45) : 1 N/N, 1 LD/SD, 1 LD/N, 1 LD/TC

(*b*)

6/12 (1944-45) : SD/N

| Plot 29 (1945-46) : 1 SD/SD, 3 SD/N, 1 SD/TC * |

| Plot 2 (1946-47) : 4 SD/N, 3 SD/TC, 1 N/N, 1 N/TC,* 1 SD/O |

The expectation in the progeny of a heterozygote for a telocentric is 0·25 normal : 0·5 heterozygous telocentric : 0·25 homozygous telocentric. In the two progenies of heterozygous telocentrics the proportions were as follows :—

3 : 1 : 0
5 : 4 : 0

The absence of homozygous telocentrics and the deficiency of heterozygotes, together with the inviability of pollen lacking the ABC chromosome, suggest that it is the BC arm itself which is required for the pollen to be functional.

An AB telocentric may arise through misdivision of the centromere (Upcott, 1937*b* ; Darlington, 1940) in a univalent or non-conjoined bivalent ; and possibly through breakage of a dicentric chromatid at one of its centromeres. The former is frequent in LD/O and SD/O plants. Bridge breakage at or near a centromere has been observed (fig. 3) ; it can be inferred from the occurrence of the long duplication in the progeny of short-duplication plants.

Misdivision, telocentrics and isochromosomes are of frequent occurrence in wheat monosomics as well as in types with incomplete pairing (Love, 1940, 1943 ; Chin and Chwang, 1942 ; Sears, 1944, 1946 ; Smith, 1947). Sears found telocentrics for one or both arms in fifteen of the seventeen identified monosomics in common wheat. Thus in general polyploidy provides a wide safety margin, and the high degree of intolerance in relation to the BC arm deficiency is the exception rather than the rule ; and even in this instance where a deficiency is a pollen lethal, an excess has no apparent effect. However, as expected, in the diploid *Triticum monococcum* deficiencies and duplications arising from chromosome fragmentation, have serious physiological effects on size and other body characters, on fertility, and on gametic output (Smith, *loc. cit.*).

5. THE CHIASMA CYCLE AND THE ORIGIN OF THE INVERTED DUPLICATIONS

(*a*) *The chiasma cycle*

It has already been shown that short-duplication and normal plants occur in the progeny of long-duplication plants, and, as a rare event, long-duplication plants in that of short-duplication ones.

* LD/TC = bivalent consisting of an ABC chromosome with the long inverted duplication and one lacking the duplication arm ; similarly, SD/TC and N/TC.

It is now possible to describe the system which leads from a duplication in one generation to a duplication—but not necessarily the same—in the next, a repetitive process of structural change which simulates the orderly process of hereditary transmission.

Fig. 2 illustrates the chiasma cycle which is found in the BC arm of *Triticum*. A chromatid bridge breaks either at the centre, (*a*), near the centre, (*b*), or at or near one of the centromeres, (*c*). Break (*a*) yields two normal chromatids, break (*b*) a short duplication and a corresponding deficiency, break (*c*) a long duplication and a telocentric (or acentric).

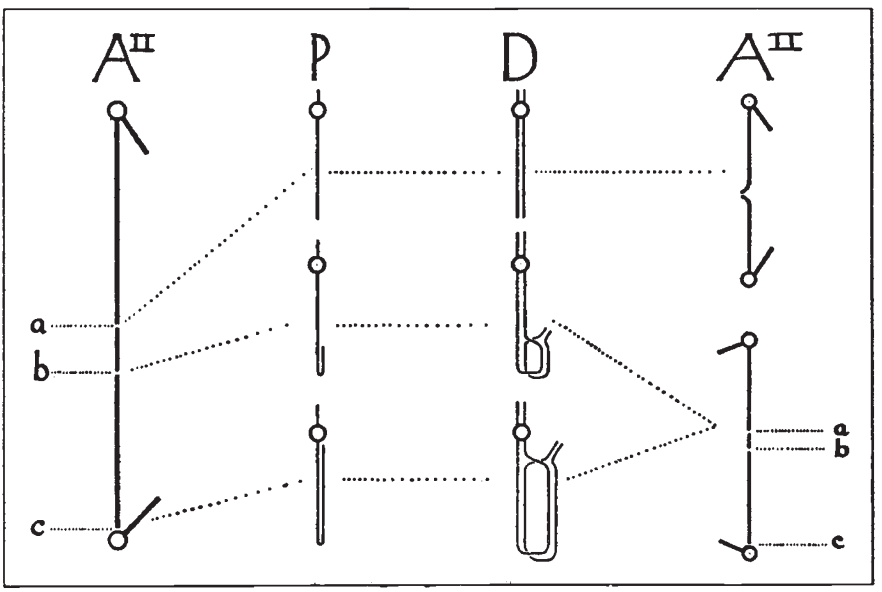


FIG. 2.—The chiasma cycle.

The new duplications—short or long—in turn are liable to be involved in inversion chiasmata, the majority of which, as has been shown in the previous paper, result in the elimination of the duplication as a fragment. When this occurs a bridge is formed thus closing the cycle, for this bridge breaks in (*a*), (*b*) or (*c*).

The frequencies of these events cannot be directly ascertained since the point of bridge rupture cannot be determined with precision by observation in anaphase. The functional gametes which carry chromosomes derived from bridge rupture can, however, be found in the next generation. It has already been shown that 27 per cent. of pollen grains carry a chromosome broken in the previous meiosis and that the proportion is the same or slightly higher in the ovules. The majority of breaks were found to occur near the centre—within less than one-tenth of the distance between the centre and a centromere—and the remainder at the centre itself.

That bridges are broken at—or very near—a centromere has been

seen in first-division bridges and in univalent bridges (fig. 3) ; centromere breakage of second-division bridges would scarcely be observable. Weakness at the centromere is not uncommon. Breakage at the centromere in anaphase, giving a telocentric and an apparent acentric, was found in *Tradescantia*, and centromere breakage of bridge chromatids in *Tulipa* (Darlington and Upcott, 1941*b*). Centromere weakness in metaphase of meiosis was also revealed by both X-ray and mustard gas treatment (Darlington and Koller, 1947).

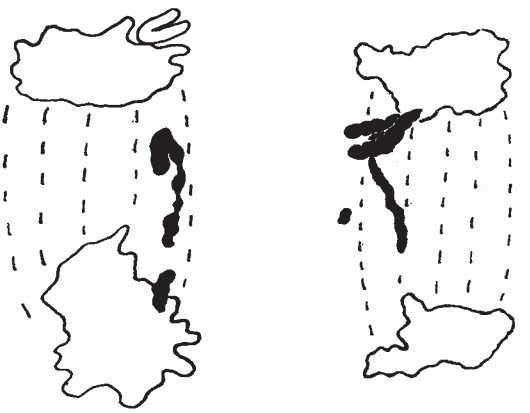


FIG. 3.—Bridge chromatids in anaphase I broken at or near a centromere : (*a*) univalent bridge, × 1700 ; (*b*) first-division bridge, × 1470.

More precise evidence comes from plants carrying the long duplication which are found sporadically in progenies of short-duplication plants. This occurred three times among the 167 plants identified in progenies of SD plants and in crosses SD × normal. An SD/N plant, 32/10 (1943-44), had the following progeny :—

4 N/N, 5 SD/N, 1 SD/SD, 1 **LD**/SD, 1 **LD**/N

The third exceptional plant occurred in the progeny of 24/13 (1945-46), another SD/N plant :—

1 N/N, 3 SD/N, 1 **LD**/SD

The exact frequencies with which broken bridges give SD and LD gametes cannot be stated, since crossover and non-crossover SD are indistinguishable ; but if the frequencies of SD gametes in the progenies of LD/LD, LD/N and LD/O are used to estimate the frequencies of SD crossovers in the corresponding SD/SD, SD/N and SD/O progenies, their number is calculated as 17·1, against the observed frequency of 3 LD gametes. Hence of the bridges which are broken unevenly, about six-sevenths break near the centre of the bridge and one-seventh at one of its centromeres.

(b) *The origin of the duplications*

Three sets of direct evidence are available. First, the distribution of the duplication when discovered ; second, observations in F_1 and F_2 from the cross of the parent varieties, Tuscan and White Fife ; and third, the occurrence of short duplications in the progeny of long-duplication plants, and of long duplications in that of short-duplication plants.

In 1941-42, when the first cytological examination was made, seed from plants grown in 1935-36 was used, all of which belonged to the progeny of a single plant raised in 1934-35. The identification of the 1941-42 progenies identified in turn their parent plants of 1935-36 and, through these, the 1934-35 plant from which they derived—probably a heterozygote (LD/N) or a monosomic (LD/O). Nothing is known of its sister plants ; hence our information does not extend beyond the presence of one LD gamete in the 1933-34 generation, which was the F_5 of the original cross. The reconstructed family tree, from 1933-34 onwards, is shown in fig. 4.

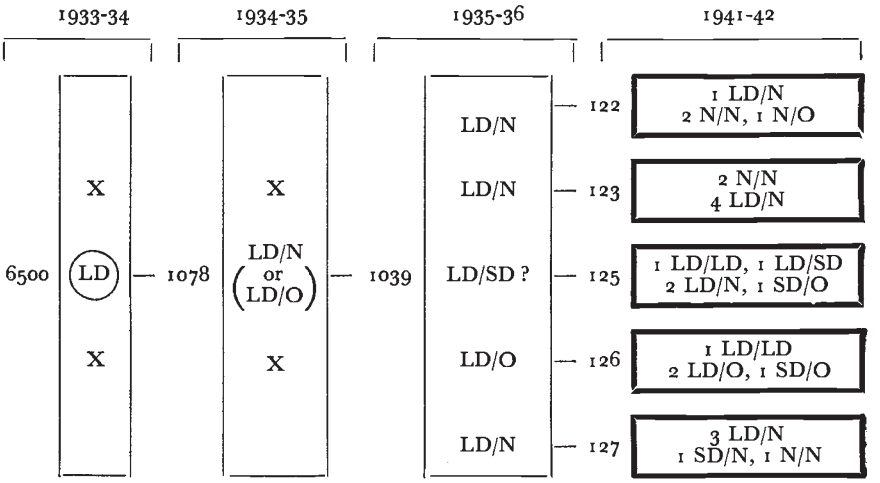


FIG. 4.—The derivation of the long duplication. Heavy frames observed, light frames inferred.

Seed of earlier generations was no longer available. Hence the original cross, Tuscan × White Fife, was repeated in 1943-44, and the F_1 and F_2 were examined. Chromatid bridges were found in both meiotic divisions of both generations. With the exception of one b' with which a very small fragment was found, visible fragments were absent. The frequencies are given in table 6.

The nature of these bridges cannot be defined with certainty. It is unlikely that they are due to crossing-over in small distal inverted segments, as inferred by Sax (1937) in *Tradescantia* and by Darlington (1937) in *Rhoeo*, since second-division bridges are too frequent to be accountable by inversion crossing-over. Moreover, the occurrence of

sporadic second-division bridges in N/N and other types suggests a common cause.

TABLE 6

Frequencies of first and second division bridges in parents, F_1 and F_2

Plant	First division			Second division		
	Number of		Bridge frequency	Number of		Bridge frequency
	cells	bridges		cells	bridges	
Tuscan	...	...	...	990	0	0·00 per cent.
White Fife	...	...	...	980	1	0·10 ,,
F_1	114	1 *	0·88 per cent.	1323	9 †	0·81 ,,
F_2	133	1	0·75 ,,	1031	5	0·49 ,,

* Bridge with very small fragment ; all other bridges without fragments.
† One of the nine had two bridges, the remainder one.

In addition to the chromatid bridges resulting from chiasma formation in the defined types of duplications, bridges with which no visible fragments are associated are found infrequently though regularly in all cytological types examined in this study. Bridges of this type occur mainly in anaphase II. They can be identified with certainty in types without inverted duplications and, in duplication types, in those cells in which they coincide with bridges resulting from crossing-over in the inverted duplication. Of 129 normal plants derived from the duplication strain, 71 had no bridges in counts varying from 50 to 100 anaphase II cells ; 58 had bridges, with an average frequency of 3 per cent. and a maximum of 10 per cent. In all normal plants, bridge frequency in 5152 cells was 2 per cent. ; 98 cells had single bridges and two had two bridges.

Is it likely that some at least of these bridges are due to crossing-over in inverted duplications too small to produce a visible fragment? This is unlikely to apply to all bridges without fragments. The bridge frequency for the long duplication is 40 per cent., for the short duplication 32 per cent. ; since the latter often approaches the limit of visibility, it is improbable that frequencies for a slightly shorter duplication would fall off to less than one-tenth.

It is in fact not possible to ascertain whether any of the bridges without visible fragments are formed by the duplication bivalent. That they are not confined to this bivalent is established, since in long-duplication heterozygotes, anaphase II cells with two bridges and one fragment, and in a homozygote a cell with three bridges and two fragments have been observed. In a monosomic a cell with three bridges and one fragment was found.

The alternative assumption of spontaneous sister reunion is consistent with the observed facts ; it is also consistent with observations

in meiosis of a variety of organisms (*cf.* Darlington and La Cour, 1945, pp. 243*ff*). In itself neither assumption is of direct relevance; for if, as is suggested, the inverted duplications originate from unequal bridge rupture, the fact that bridges occur is relevant rather than the cause of their occurrence.

Between the rare bridges in F_1-F_2 and the LD gamete in F_5 there is a gap in our direct evidence. Yet the facts presented in the preceding section help to bridge it. First, short duplications arise regularly from broken bridges; nearly one-half of all functional gametes resulting from bridge rupture have a short duplication. Secondly, long duplications arise also from broken bridges, though only one-seventh as often as the short duplications. This suggests that the duplications arose from bridges—presumably of the type observed in F_1 and F_2—by means of a two-phase process: first, a sub-median break, originating a short duplication, resulted in raising the level of bridge frequency; and secondly, as a sequel, a centric break produced the long duplication.

(c) *The healing of broken chromatid bridges*

In maize, McClintock (1938, 1939, 1941) found that chromatid bridges broken in meiosis fail to heal in endosperm and in gametophytic tissue, forming a breakage-fusion-bridge cycle which is ended only by fertilisation when as a rule broken chromosome ends heal. *Narcissus bulbocodium* is apparently a more extreme case: here healing does not take place at all, even after years of breakage and fusion in somatic tissue (Fernandes and Neves, 1941).

In *Triticum*, as in maize, chromosomes broken in a meiotic anaphase are found in functional gametes. Contrary to the observations in maize, however, broken chromosome ends fail to fuse. No bridges were found in the first pollen grain mitosis. If every pollen grain carrying a broken chromosome were to form a bridge in the following mitosis, the frequencies of bridges would be 0·2 in LD/N and 0·36 in LD/LD (*cf.* Frankel, 1949). The number of cells examined and the number of bridges expected on the assumption of a breakage-fusion-bridge cycle are as follows:—

	Number of cells observed	Number of bridges expected
LD/N . .	85	17·0
LD/LD . .	49	17·6
Total . .	134	34·6

The probability that the absence of bridges is due to chance is infinitely small.

Thus in wheat, unlike maize, there is no sister reunion of chromatids broken in meiosis; healing apparently is rapid and permanent. This

is not surprising, for, as Darlington and Upcott (1941*b*) have shown, " healing of sister ends is variable and is both internally and externally conditioned." The nature of these conditions which, as is now seen, are sufficiently specific to cause healing of broken ends in one, sister reunion in another homologous tissue of related forms, is yet to be determined.

6. THE REPRODUCTIVE CYCLE

The preceding sections have dealt with the origin, the gametic output and the inheritance of the inverted duplications. It is now possible to approach the questions of their distribution in successive generations of a population and of their possible role as an evolutionary mechanism.

The zygotic output of the duplication types (*cf.* table 1) allows to predict the fate of the duplications, provided assumptions are made regarding the survival and reproductive rates of the types involved. It is assumed (1) that the proportions found in this study are a true expression of the proportions occurring in the progenies

TABLE 7

Percentages of cytological types in successive generations in the progeny of LD/N (*see fig. 5*)

Generation	LD/N	LD/LD	LD/SD	LD/O	SD/N	SD/SD	SD/O	N/N	N/O
1	100·0	...	...	...	...	...	...	...	...
2	43·31	13·38	0·67	0·0	7·0	0·0	0·0	35·03	0·67
3	21·26	13·33	2·88	0·13	7·42	0·58	0·13	53·55	0·81
4	12·03	10·69	3·52	0·21	6·66	1·36	0·24	64·47	0·81
5	7·78	8·03	2·13	0·23	5·92	1·92	0·32	72·79	0·81
6	5·18	5·75	2·27	0·22	4·97	1·94	0·36	78·45	0·79
7	3·68	4·15	1·91	0·19	4·23	1·91	0·37	82·77	0·76
8	2·69	3·02	1·49	0·15	3·59	1·78	0·35	86·22	0·72
9	1·98	2·20	1·13	0·12	3·02	1·43	0·32	89·17	0·67
10	1·47	1·62	0·46	0·09	2·46	1·28	0·28	91·70	0·66

TABLE 8

Cytological types in the fifth generation from an LD/N *plant*

	LD/N	LD/LD	LD/SD	LD/O	SD/N	SD/SD	SD/O	N/N	N/O	Total
Observed	1	1	...	...	4	1	...	29	...	36
Expected	*2·80*	*2·89*	*0·77*	*0·08*	*2·13*	*0·69*	*0·12*	*26·20*	*0·29*	*35·97*

$\chi^2 = 1{\cdot}08$; $P < 0{\cdot}30$

of the various types ; (2) that these remain constant from generation to generation ; (3) that all plants survive to seed production ; (4) that all types have equal rates of reproduction. Then, starting with the type LD/N, the proportions of the various types up to the tenth generation are shown in table 7, and the proportions of LD

and SD arms in fig. 5. It will be seen that the frequency of the long duplication declines first rapidly and later more gradually, and that the short duplication, after an initial rise, follows the trend of the former. In extending the graphs beyond the tenth generation it is found that the long duplication will soon be extinct, survived by the short duplication by only a generation or two.

In a population derived from an LD/N plant whose progeny was grown without selection for 4 generations, 36 plants, taken at random,

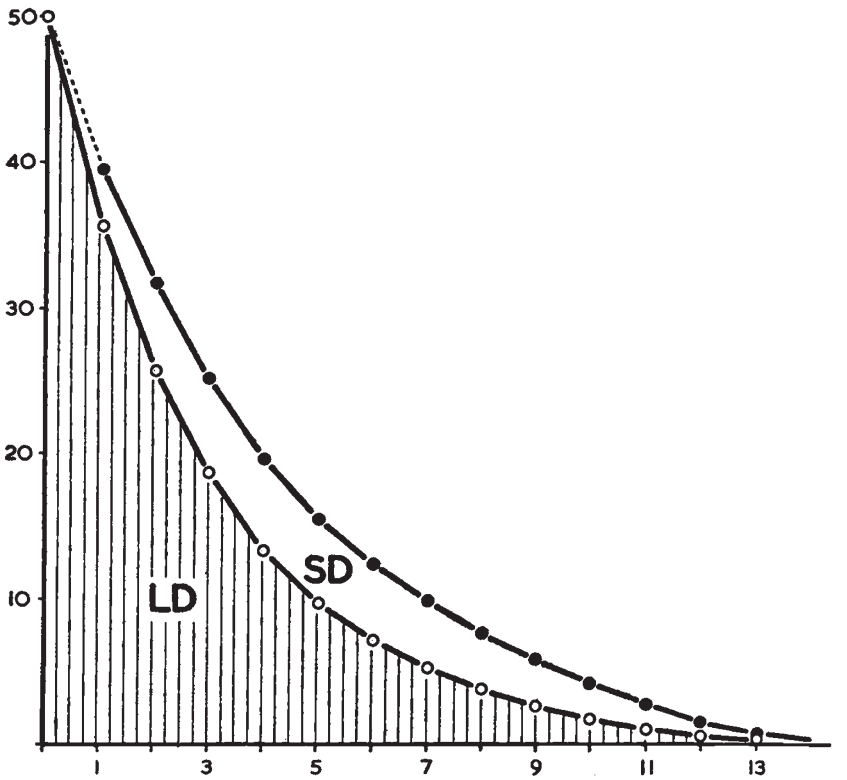


FIG. 5.—Frequencies of LD and SD gametes expected in successive generations in the progeny of LD/N.

were examined in the fourth. The proportions of cytological types are compared with the expected ratios in table 8. The small representation in all duplication classes, necessitating their being combined, reduces the significance of χ^2; yet the fit of observed and expected ratios is striking. This confirms the validity of our assumptions. In particular it shows that the observed duplications have little if any physiological significance. It also proves that, left to themselves, they are removed rapidly and completely.

The persistence of an inverted duplication—the duration of the reproductive cycle—will depend on the rate of duplication crossing-over, internal as well as fraternal, and on the selective value of the

duplication. The case reported here is extreme in exhibiting very nearly the maximum rate of crossing-over combined with an absence of selective advantage. Crossover values in maize (McClintock, 1941) are similarly high. It remains to be seen whether they are substantially lower in other organisms. This in fact, should it be the case, would explain why inverted duplications have not been discovered more frequently. It is possible that duplications occur which are below the minimum size for chiasma formation in inverted segments, yet there is no evidence for this, and it should be noted that in *Triticum* even the short duplication has a high chiasma frequency.

If crossing-over in an inverted duplication occurs at all, ultimately, however low its frequency, it is bound to eliminate the duplication unless the latter has a strong positive selective value or unless it is transformed or transferred by a secondary change such as inversion or translocation. Hence the shorter its duration, the smaller the chance of its ultimate survival.

If inverted duplications possess an evolutionary significance, their closest analogues are perhaps the supernumerary chromosomes (*cf.* discussions by Darlington and Upcott, 1941*a*, and White, 1945, pp. 118*ff*). Both are self-destroying : supernumeraries by failure of pairing and by structural changes, inverted duplications by crossing-over. Both are capable of enriching the chromosome complement, the former with centromeres, the latter with " repeat " sectors— " apart from polyploidy . . . the only known process which may lead to an increase of the number of genes in the germ plasm of organisms " (Dobzhansky, 1941, p. 129). Both owe their existence to accidents though of a widely different nature ; both have their life cycles, though of a different order. Compared with the subtle and orderly adaptability of polygenic systems or even with the storage and release of gene mutations in inversions, both constitute crude evolutionary mechanisms ; but if and when they come into play, they would constitute major and irreversible steps affecting the foundations of the genetic structure.

There is yet another possibility of an evolutionary role for inverted duplications. Major changes in the chromosomes rarely fail to have a profound influence on other parts of the chromosome complement. It is not too much to expect that large duplications, though themselves of a transitory nature, may be the cause of secondary and more permanent changes. They may in fact be yet another destabilising evolutionary mechanism. Evidence of a major genetic change which coincided with the *Triticum* duplications will be presented in a third paper.

7. SUMMARY

1. This paper presents evidence on the transmission and evolutionary history of the self-propagating inverted duplications which were described previously.

2. The origin of the duplications is traced back to rare bridges without or with minute fragments in the F_1 and F_2 of the cross in which the duplications were found. An uneven bridge rupture, resulting in a short duplication, would raise the bridge frequency in the offspring sufficiently for the rarer event of a centromere break to occur and produce a long duplication.

3. Homozygotes for the long duplication (LD/LD) produce functional gametes with long (LD), short (SD) and without (N) duplications, The SD and N gametes arise from uneven and even bridge rupture ; but the N gametes may include short deficiency as well as normal gametes.

4. The frequency of functional gametes from LD/LD with a chromosome broken in the previous meiosis is about 27 per cent. in the male and the same or slightly more in the female. The majority of breaks are uneven but close to the centre of the bridge.

5. SD/SD, SD/N and SD/O plants normally yield SD and N gametes, but LD gametes are produced as rare exceptions. These are believed to arise from bridge rupture at or near a bridge centromere.

6. Crossing-over removes the duplications ; but, by causing bridge formation, it is instrumental in initiating new duplications, not necessarily of the original length. Thus LD can give SD and *vice versa*. There is a " chiasma cycle " from generation to generation.

7. Monosomics LD/O, SD/O and N/O produce 20-chromosome ovules, but 20-chromosome pollen grains are either non-functional or very rare ; hence no nullisomics have been found.

8. Monosomics have different proportions of functional gametes in selfings and crosses : 20-chromosome ovules are more compatible with their own 21-chromosome pollen than with that from a normal 21-chromosome plant.

9. In the LD/O monosomic, functional gametes carrying a chromosome from crossing-over in LD constitute about one-quarter on the male side, but one-half on the female side. A crossover chromatid thus has a greater chance of reaching the functional megaspore cell than has one carrying the duplication : this is the opposite of the Sturtevant and Beadle effect.

10. A telocentric produced by the loss of the duplication arm has been found on two occasions ; it is lethal as a homozygote.

11. Whether inverted duplications have evolutionary significance, *i.e.* whether they have a chance of incorporation in the chromosome complement, will depend in the first instance on the cessation of inversion crossing-over, through a coincident structural or genetical change. The chance of such an occurrence will be proportional to the length of the reproductive cycle.

12. If a heterozygote for the long duplication (LD/N) is propagated without selection, the duplications are calculated to have a reproductive cycle of 13 generations for LD and a further one for SD (fig. 5). Random sampling in the fifth generation was in accordance with expectation.

13. The evolutionary analogies between inverted duplications and supernumerary chromosomes are discussed. The latter may be a source of centromeres, the former of repeats.

14. Inverted duplications may be yet another destabilising evolutionary mechanism. Evidence of a genetic change associated with duplications is brought in a third paper.

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