

ON THE GENETICS OF SILVERING IN THE GUINEA PIG
WITH ESPECIAL REFERENCE TO INTERACTION AND LINKAGE^{1,2}

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THE genotypes of the major color varieties of a guinea pig colony, that had been almost self-contained since 1916, have been discussed in a number of papers (most recently, WRIGHT 1949a). The present paper will be concerned with a rather troublesome pair of alleles, *Sisi*, in which the heterozygote overlaps both homozygotes, its effects in interaction with other genes, and possible linkage relations. The most striking interaction effect, one with a hitherto unrecognized gene, will be reserved for a later paper.

The major color factors

The color factors that have been recognized in this stock may be characterized briefly as follows in terms of the effect on self-colored intense black ($E aa B C P S Gr Si$), self-colored intense brown ($E aa bb C P S Gr Si$), or on self-colored intense yellow or "red," ($ee C F S Gr Si$).

E, e^p, e $e^p e^p$: tortoise-shell (black and yellow), recessive to E (self black) and occasionally overlapping; ee self yellow, recessive to E ; $e^p e$ intermediate tortoise-shell.

A, a A —: agouti; black hairs with subterminal yellow bands on back; belly yellow, usually with some basal black; A dominant, no effect at birth in self-yellows (ee) or in yellow of tortoise-shell.

B, b bb : brown in place of black in fur, skin and eyes, b recessive. Accumulation of intensity factors ($C P F$ and modifiers) beyond a certain point, results in a peculiar form of dilution known as dinginess.

C, c^k, c^d, c^r, c^a $c^k c^k$: very slight dilution of black (or brown), marked dilution of yellow.

$c^d c^d$: moderate dilution of black (or brown), yellow much as with $c^k c^k$.

$c^r c^r$: between $c^k c^k$ and $c^d c^d$ in dilution of black (or brown) in fur and skin, but eye color reduced more than by $c^d c^d$. White in place of yellow.

$c^a c^a$: albinism. White coat but developing dark pigmentation of feet, ears and nose; pink eyes.

C is completely dominant, while heterozygotes between lower c alleles are intermediate.

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- P,p* *pp*: pink-eyed. Strong dilution of black (or brown) but no effect on yellow, *p* recessive in most combinations.
- F,f* *ff*: fading yellow. Dilution of yellow much as in $c^k c^k$ at birth but fading later; no effect on black (or brown with a minor qualification) in the presence of *P*. In *E pp ff* there is replacement of sepia or brown by pale brownish cream, if *C* is present, otherwise by white. Gene *f* is not completely recessive.
- S,s* *ss*: spotted. Colored areas on white ground, *s* incompletely recessive.
- Gr, gr* *grgr*: grizzled. No effect at birth; progressive whitening of dorsal hairs later, *gr* incompletely recessive. Gene *gr* was not present in colony during period of these studies.
- Si, si* *sisi*: silvered. Stationary sprinkling and blotching with white; slight dilution in unsilvered areas, *si* incompletely recessive. This pair is the main subject of the present paper.

Other loci, involved in linkage tests: It will be convenient to describe briefly here the effects of four loci, not concerned with color (except that *St* tends to produce a white spot on the forehead, which *R*, in conjunction with *m*, tends to inhibit (Bock 1950). These loci have been used in linkage tests with *Si, si*.

- R,r* *R*:- Rough fur. Reversal of hair direction at least on toes, *R* fully dominant.
- M,m* *M*: (more fully *M(R)*, modifier of effect of *R*). *R-MM* shows low grade roughness (Rough E); *R-Mm* an intermediate grade (Rough C or D); and *R-mm* high grade roughness (Rough A or B). All are usually distinguishable in progenies.
- St,st* *St*:- "Star." Strong forehead rosette. There is reciprocal partial inhibition by *R* and *St*. *St* is dominant (except in *R-mm St st*).
- Px,px* *Px*: "Pollex." In *Pxpx* there is a tendency toward atavistic pentadactyly, of which presence of the thumb is most characteristic. This is independent of the common multifactorial atavistic little toe. *PxPx* is a lethal monster with short abnormal legs, hind legs rotated 180°, and up to 44 digits. There is also microphthalmia, and usually harelip and protruding brain.

Grades of intensity: Intensity of coat color has been recorded in the routine records made at birth by comparison with standard squares of dorsal skin (about 3' × 3'). These were chosen so that each grade is barely distinguishable from the preceding. Yellows have been graded from 1 for a pale "cream," barely distinguishable from white, to 13 for intense "red." The intensity modifiers necessary for grades 12 and 13 were absent from the colony during the period of the present studies. Sepias were graded by a second series of fur samples from 1, very pale sepia, barely distinguishable from white, to 21 for intense black. Browns differed so little in quality of coat color that they could be and were graded by the same series as the sepias.

Earlier conclusions on the genetics of silvering: Most of the inbred strains with which the author has worked (WRIGHT 1922) have shown no trace of silvering.

One, however, (No. 34) consisted wholly of strongly silvered and brindled blacks ($e^h e^h aa BB CC PP FF SS GrGr sisi$). Crosses of this strain with nonsilvered ones produced young that were usually slightly silvered on the belly. The proportions of wholly unsilvered and of strongly silvered young increased in F_2 , but the upper 25 percent was much lower in average amount of silvering than strain 34. The results were interpreted as indicating multifactorial heredity (WRIGHT 1917).

IBSEN (1932), in a list of color factors of the guinea pig, attributed what seems to have been the same sort of silvering to an incompletely dominant gene, *Ro* (roan), but presented no data.

PICTET and FERRERO (1940) presented data on what also seems from their description and photographs to have been the same condition. They concluded that silvering is a heterogeneous category involving two independent pairs of alleles: dominant ventral whitening (*V*) and recessive dorsal silvering (*d*). They advanced the supplementary hypothesis that the type combination $vvDd$ is lethal if both parents are $VvDd$, but not otherwise, to account for the absence of nonsilvered offspring from matings of such parents. Analysis of their data (WRIGHT 1947) indicated that these hypotheses were not acceptable and that the data were compatible with the hypothesis that there is a single basic gene for silvering, complicated by one or more modifiers that increase the degree of silvering and in so doing extend it from belly to back. Grades of silvering were not, however, given in PICTET and FERRERO's paper in sufficient detail for demonstration of the mode of inheritance.

Evidence for the hypothesis stated above was given by WRIGHT (1947) from the results of backcrosses, generation after generation, of nonsilvered or very slightly silvered segregants (*Sisi*) to a pure silvered strain (*sisi*). The gene *Si* maintained itself in spite of the continued attempt at dilution while strongly silvered segregants, mated *inter se* produced only silvers of highly varying grades.

IBSEN and GOERTZEN (1951) presented data that supported essentially the same hypothesis except that in their experiments some silvering (or "roan") was usually present in heterozygotes so that they preferred to treat the gene as dominant (*Ro*), while in my experiments reported in 1947, silvering was either absent or so doubtful in most heterozygotes that silvering was most conveniently treated as recessive (*sisi*). It was recessive in these experiments to about the same degree as spotting (*ss*) or grizzling (*grgr*) in both of which the heterozygotes may show traces and occasionally considerable of the "recessive" character and thus may overlap both homozygotes.

Grades of silvering: The following grades of silvering have been applied separately to back and belly, with the following definitions (1947). The total grade that will be used in this paper is the sum. A grouping was used in 1947.

- grade 0 No silvering.
- grade 1 Trace of silvering (irregular dilution or few white hairs).
- grade 2 Slight but unmistakable silvering in a small area only.
- grade 3 Silvering extensive but over less than half the area.

- grade 4 Strong silvering or blotching with white over more than half of the area, but not approaching self white.
- grade 5 Pure white predominates over the whole area.
- grade 6 Pure white (ventral). Pure white except on head (dorsal).
(new)

Evidence for single essential gene for silvering: The upper six rows of Table 1 largely repeat some of the data in the 1947 paper on the results of mating a silver strain I-13 with homozygous nonsilvers, with F₁ and successive low grade backcross segregants, and matings of the F₂ type. The table is, however, here restricted to young in which the ground color was black or black-red tortoise-shell, because of the greater uncertainty of grading on other backgrounds. This has led to removal of only a few individuals from the earlier table. Several records from later litters are added.

It may be noted that 63 percent of F₁ did not show even a trace of silvering. Only one is recorded as showing more than grade 2.

There are no significant differences among the successive backcrosses ($\chi^2 = 13.4$, ten degrees of freedom) but there is a bimodality in the last group (third to fifth backcross), absent in the first and second, that is suggestive. These results were interpreted as indicating that there is a single major gene, *Si*, that maintains its integrity through continued attempts at dilution. About 56 percent of the lower half of the total backcross population (roughly those that are *Sisi*) are still nonsilvers, and 95 percent of the upper half (largely *sisi*) are more silvered than all but one of the F₁ individuals, i.e., are of grade 4 or more.

TABLE 1

Grades of silvering in F₁ from matings between a silvered strain, I-13, and miscellaneous homozygous nonsilvered; in successive backcrosses (BC) of F₁ or low grade BC segregants to I-13; in F₂ or (BC)² from matings between low grade BC segregants; from extracted silvers mated inter se or with I-13 (Ro early), and inbred derivatives (Ro late) from one mating of preceding; from descendants of outcrosses of Ro to other silvers (RoLF, RoXR). The average grades of the lower and higher parents, weighted by numbers of offspring, are given

	Number matings	Lower parent			Higher parent			Grade of silvering							Total
		Geno.	Source	Av.	Geno.	Source	Av.	0	1-	3-	5-	7-	9-	11-	
F ₁	7	<i>SiSi</i>	(misc)	0	<i>sisi</i>	(I-13)	7.3	43	24	1	68
1BC	10	<i>Sisi</i>	(F ₁)	0.2	<i>sisi</i>	(I-13)	6.4	36	25	17	18	7	6	..	109
2BC	10	<i>Sisi</i>	(1BC)	1.0	<i>sisi</i>	(I-13)	6.8	14	14	13	12	7	1	..	61
3-5 BC	5	<i>Sisi</i>	(2-4BC)	0.9	<i>sisi</i>	(I-13)	6.4	12	15	4	7	8	6	..	52
F ₂	4	<i>Sisi</i>	(F ₁)	0.0	<i>Sisi</i>	(F ₁)	0.4	13	6	2	..	1	22
(BC) ²	8	<i>Sisi</i>	(BC)	0.7	<i>Sisi</i>	(BC)	1.0	25	47	9	10	4	95
Ro(early)	10	<i>sisi</i>	(BC,Ro)	6.1	<i>sisi</i>	(BC,Ro)	7.5	..	5	9	32	31	11	..	88
Ro(late)	9	<i>sisi</i>	(Ro)	7.8	<i>sisi</i>	(Ro)	8.9	3	74	38	..	115
RoLF	16	<i>sisi</i>	(LF,Ro)	7.0	<i>sisi</i>	Ro	8.7	..	2	8	31	71	44	(10)*	156
RoXR	8	<i>sisi</i>	(Ro)	8.2	<i>sisi</i>	(XR,Ro)	10.1	1	32	40	17	90

* RoLF produced ten white or near-white offspring that differed discontinuously and are not included in the total.

Those of the upper half are not, however, as strongly silvered on the average as the silvered strain Ro, derived from them and the parental silver strain I-13. It appears that there is multifactorial heredity at least in the sense that there are independent genes that modify somewhat the effects of segregation of the postulated major pair of alleles.

This impression is strengthened by comparison of these backcross arrays with the data of the F_2 type (matings between F_1 's or between low grade segregants from the backcrosses (BC)²). The upper 25 percent from the latter (roughly the *sisi* segregants) are much lower in average grade than the supposed *sisi* segregants from the backcrosses and of course still lower than the silver strains.

The distributions of the F_2 type are indeed so compact as to raise the question whether there may not, after all, be two loci with approximately equal effects. The persistence of a nearly or quite unsilvered class through the backcrosses could be due to selection of such low grade segregants that *both* type alleles were nearly always retained. On this view the original matings were of the type $Si_1Si_1, Si_2Si_2 \times si_1si_1, si_2si_2$ producing Si_1si_1, Si_2si_2 in F_1 and the successive backcrosses were largely or wholly $Si_1si_1, Si_2si_2 \times si_1si_1, si_2si_2$ by selection of the former. Such a hypothesis would obviously account well for the compact distribution of the F_2 type.

This compactness can also be accounted for, however, by segregation of a mere modifier of silvering (in a 1:2:1 ratio in F_2 as opposed to 0:2:2 in the backcross) in addition to that of a single essential gene for silvering. The relatively wide spread of the backcross arrays, the suggestion of bimodality in the later backcrosses point toward the latter hypothesis.

The modifiability of silvering is clearly shown by the significant difference between the distribution of the earlier ten matings of strain Ro, derived from high grade segregants and that of the later nine matings, tracing to a single mating of the earlier group.

Outcrosses (RoLF) were made to silvered reds of a strain (LF) in which silver of different origin was occurring. The character of the silvering seemed so different, consisting sometimes apparently of mere irregular dilution of red, that there was considerable doubt as to whether it was the same condition. The black-red crossbreds were, however, typical silvers. The distribution of silvering in these matings and inbred descendants (excluding a few reds for which the grades are less reliable) did not differ much from that in pure Ro, except for the production (by four matings) of five dark-eyed self-whites and five dark-eyed whites with strongly silvered sepia or yellow spots on one or both cheeks. The latter differs discontinuously from the strongest silvers in RoLF or Ro. The dark-eyed whites could not be accounted for as extreme spotted (*ss*) or as dark-eyed whites of genotype *eec^rc^r* (of which eight were produced by another of the matings). The ratio of ten white or near-white to 26 silvered black-reds and reds from these four matings suggests segregation of a recessive modifier that completely or almost completely eliminates all color from the coat of an animal of genotype *sisi*. Three of

this type had appeared in LF and many in other experiments which will be discussed in a later paper.

A mating, XR127, between rather high grade silvers (the sire from an outcross of Ro, the dam from F₂ of an outcross of RoLF) produced 19 silvers over the usual range (2 to 9) and one much more extreme (called grade 11) with pure white belly and dorsal silvering largely but not wholly restricted to the head. It was not, however, as extreme as the near whites from RoLF. This animal, a male, was mated with a female from Ro to start a group of eight matings (RoXR) with young of decidedly higher average grade than in any other silvered strain. In two of the matings both parents were of grade 11 and the average of their 12 offspring was 10.8, including three so nearly white that they were called grade 12. While these seem to bridge the gap between ordinary silvers and the whites and near whites of RoLF, they cannot be considered the same as the latter. As will be brought out elsewhere, males of the latter near-white or white category are sterile, and the near white males of RoXR are fertile.

On treating Ro, RoLF (near whites and whites excluded), and RoXR as a single strain, the regression of 436 offspring on midparent is .40 (.35 on sire, .43 on dam), indicating that about 40 percent of the variability is genetic and 60 percent nongenetic (including errors of grading) on the simplest hypothesis (additive modifiers with intermediate heterozygotes).

Further evidence has been given by matings of silvers from Ro and RoLF with animals with no silvering or merely a trace from a strain (A), made for the purpose of testing linkage of *Si,si* with certain loci. Strain A consisted of agoutis that were self-colored except for occasional silvering. The young in F₁ (Table 2) were agoutis and in the backcrosses, agoutis, agouti-reds, blacks, and black-reds. Four of the F₁ matings are interpreted as *SiSi* × *sisi*, eight as *Sisi* × *sisi*, and one (in which the A parent was of grade 2, higher than in any of the other cases) as *sisi* × *sisi*.

The results in F₁ and in the first backcross are rather similar to those of the previous set, except that the proportion, with no silvering at all, is less. Assignment of grade 1 instead of 0 is often, however, doubtful and especially in agoutis which have a yellow belly. The second backcross is more strongly bimodal than

TABLE 2

Grades of silvering in F₁ of cross between silvers of strain Ro or RoLF and nonsilvers or low grade silvers from strain A; two successive backcrosses of F₁ or low grade 1BC to Ro or RoLF

	Number matings	Lower parent			Higher parent			Grade of silvering							Total	
		Geno.	Source	Av.	Geno.	Source	Ave.	0	1-	3-	5-	7-	9-	11-		
F ₁	4	<i>SiSi</i>	(A)	0.0	<i>sisi</i>	(Ro,RoLF)	7.4	18	17	5	40
F ₁	8	<i>Sisi</i>	(A)	0.2	<i>sisi</i>	(Ro,RoLF)	8.5	8	28	21	15	4	3	79
F ₁	1	<i>sisi</i>	(A)	2.0	<i>sisi</i>	(Ro,RoLF)	6.0	..	4	..	4	8
1BC	13	<i>Sisi</i>	(F ₁)	0.7	<i>sisi</i>	(Ro,RoLF)	7.8	14	49	33	37	35	9	(1)*	..	177
2BC	3	<i>Sisi</i>	(1BC)	2.0	<i>sisi</i>	(Ro,RoLF)	8.7	2	26	4	6	20	4	62

* A black-eyed white in 1BC, both parents of which traced to RoLF, is not included in the total.

even the third to fifth backcrosses in the previous set. This may be due to the fact that the low grade parent in each of the three matings had more than a trace of silvering (grade 2) though all proved to be *Sisi*. Apparently both parents in these matings had the same major modifiers favoring strong silvering, with the consequence that segregation was more nearly unifactorial than in the first backcross or in the earlier experiment. The fact that the mean of the lower half of this distribution was as low as 1.7, little more than a trace of silvering, confirms the view that there is a single basic factor for silvering. It may be added that matings have been made between silvers of as diverse origins as could be found in the colony. The results in all cases have indicated a single basic gene for silvering in this colony.

Interaction effects: As already noted, the effects of *sisi* are most conspicuous, and the grades accordingly most reliable, on a black ground. The trace of silvering of grade 1 is usually confined to the posterior belly and up to grade 4 silvering is in general confined to the belly except for a slight extension up the sides. There is sometimes great irregularity, and thus there may be black with only a trace of silver, if any, in an area on one side of the midline of the belly, white with a mere sprinkling of black hairs on the other. In the higher grades, the back may be black rather uniformly sprinkled with white, but the head and feet wholly black. More often there is irregularity: perhaps a white streak in the midline immediately surrounded by silvered black, or perhaps a compact spot of very strong silver on one shoulder or side, the rest, areas of self black and black with light silvering. Conversely the entire back may be strongly silvered except for a compact spot of black or lightly silvered black. Only in the highest grades, in which the belly and back are almost pure white does silvering invade the feet and head spots. Grades of intensity of color have been based on areas free of silvering.

Table 3 shows in condensed form the grades of silvering, their mean and the mean grades of intensity in unsilvered areas from genotypes that segregated out in all matings of type *sisi* × *sisi*, following outcrosses of strain Ro and RoLF, except that the yellows of genotype *C ff* are from matings of type *sisi* × *sisi* in strains of LF or RoLF and the agoutis and blacks in the last two rows are from the single mating XR127, on which RoXR was based.

The blacks show a rather high average grade of silvering (6.3) though not as high as in Ro (7.1), RoLF (7.3) or RoXR (8.9), undoubtedly because the favorable modifiers in these selected strains have been partly dissipated in the outcrosses. There is a slightly subnormal intensity (20.8, where 21.0 is standard intense black).

The browns show much silvering, but of lower average grade (4.9) than the blacks. The browns were difficult to grade satisfactorily because all of them were "dingy," a condition which somewhat simulates silvering (WRIGHT 1947). In dingy browns there is a sprinkling throughout the coat of hairs that are very pale brown but not white, except that there is intense brown for about a millimeter at the tip. The condition is due to factors *C*, *F*, and *P* (and modifiers) that intensify brown in most combinations but produce this peculiar form of dilution in higher

TABLE 3

Distribution of grades and mean grade of silvering and mean intensities in various colors and genotypes from matings of sisi × sisi, except that eight eeCff sisi from Sisi × sisi are added to those from sisi × sisi for mean intensity. The agoutis and blacks in the last two rows are from a single mating (XR127). The 1949 norms (unsilvered) are given in the last column. In all genotypes with E, this may be replaced by e^p

Color	Genotype	Grade of silvering							silvering		intensity		
		0	1-	3-	5-	7-	9-	11-	no.	m.	no.	m.	1949 norm
Black	<i>E B C P</i>	..	3	9	16	36	6	..	70	6.3	60	20.8	21.0
Brown	<i>E bb CC PP</i>	2	8	13	30	15	1	..	69	4.9	40	12.7	15.3
Pale Sepia	<i>E B C pp</i>	2	3	3	14	14	6	..	42	5.9	39	9.7	9.7
Dark Sepia	<i>E Bc^dc^dP</i>	1	11	11	2	..	25	6.6	24	17.5	18.1
Light Sepia	<i>E Bc^dc^uP</i>	..	4	2	2	8	2.9	8	13.7	14.5
V.P. Sepia	<i>E B c^dc^d pp FF</i>	..	1	..	5	6	4.8	6	6.2	4.7
V.P. Sepia	<i>E B c^dc^u pp FF</i>	4	4	0.0	4	2.5	2.7
Red	<i>ee-C-FF</i>	1	6	10	9	10	4	..	40	5.1	39	9.5	10.6
Yellow	<i>ee-C-ff</i>	1	1	2	1	..	5	6.6	13	6.1	6.8
Cream	<i>ee-c^dc^u-FF</i>	1	1	2	4	4.0	4	4.2	4.2
Agouti	<i>A E B C P</i>	4	1	3	2	..	10	6.3
Black	<i>aa E B C P</i>	..	1	1	3	3	1	1	10	6.1

combinations and most in *CC FF PP* which all of the browns in Table 3 were. The low intensity of these silvered and dingy browns (12.7) in comparison with 1949 norm (15.3) is undoubtedly due largely to the dinginess. All animals with more than a trace of dinginess were excluded in the data for the 1949 average.

There was no significant correlation between the grades of silvering and of dinginess ($-.05 \pm .13$). It is, however, probable that the grade of silvering tended to be reduced slightly by confusion with dinginess. There is no satisfactory evidence for any real interaction.

The pink-eyed pale sepias are not substantially less silvered than the blacks (5.9 *vs.* 6.3) and have the same average intensity (9.7) as the 1949 norm for their genotype. The apparent absence of any dilution may, however, be due to an unduly low 1949 norm since modifiers that reduce the intensity of pale sepias were important in the early history of the stock, but not later. The average for nonsilvered pale sepias during the period of these studies was about 10.4. With respect to the grade of silvering, that for the belly was often doubtful because of the paleness of the ground color. The conclusion that seems warranted is that the effects of *pp* and *sisi* are approximately additive.

The silvered dark-eyed sepias with *c^dc^d* also show substantially the same grade of silvering as the blacks (6.6 *vs.* 6.3). They are distinctly below the 1949 norm for their genotype in intensity (17.5 *vs.* 18.1). The apparently greater dilution of color with *c^dc^d* than with *C*, may merely reflect a saturation effect in intense black. The simplest interpretation is again that there is no interaction, but greater dilution of *c^dc^d* than *C* by *sisi* is at least suggested.

The few light sepias ($c^d c^a$) from these matings show a decidedly low grade of silvering but only slightly more dilution than the 1949 norm. This low grade of silvering is borne out by observations of some 200 dark-eyed and red-eyed light sepias ($c^d c^a$ and $c^r c^a$) that have been produced from matings from which silvered segregants were expected. Not one of them was recorded as having more than a trace of silvering on the belly. The four cases in Table 3 with silvering of grades 3 to 6 seem in fact to have been the only definitely silvered light sepias of genotypes $c^d c^a$ or $c^r c^a$ to have been recorded in any mating. Among three other cases of $c^d c^a$ from $sisi \times sisi$, not in the series tabulated, not one showed a trace of even ventral silvering.

The way in which silvering seems to go out of sight in most matings when combined with $c^d c^a$ in a sepia may be illustrated by a pair of matings in which one of the most strongly silvered $c^d c^d$ sepias (grade 9) in Table 3, a female, was mated with an intense yellow ($ee C c^a SiSi$). A son, sepia 13-yellow 4, $c^d c^a Sisi$ was mated back to her. None of the 13 offspring showed more silvering than grade 2. Four were dark sepias (one grade 16, three grade 17) identified as $c^d c^d$ by yellow areas of grade 7, and nine were light sepias (three grade 12, six grade 13) identified as $c^d c^a$ by light yellow spotting of grade 4 or less. The absence of overt silvering in $c^d c^d$ of higher grade than 2 (and only one of this grade) is surprising but may have been a chance result. The absence in the $c^d c^a$'s (again only one as high as grade 2) is highly unlikely as a chance event. The lighter ones (grade 12) may have been $sisi$ and the others (grade 13) $Sisi$, but exact assignment gives more weight to the grades in individual cases than is warranted.

The absence of overt silvering in most $c^d c^a$ and $c^r c^a$ sepias cannot be merely an illusion due to their light color since dorsal silvering is conspicuous in most pink-eyed sepias of genotype $EC pp FF sisi$ which are considerably lighter. Moreover, the color of $c^d c^a$ and $c^r c^a$ sepias differs little from that of browns in which dorsal silvering is usually conspicuous in spite of the complication from dinginess. It seems to be certain, therefore, that there is an interaction between $sisi$ and $c^d c^a$ (and probably also $c^r c^a$) by which silvering is much reduced. Its presence in four young from the Ro outcrosses of Table 4 but absence elsewhere in the colony may be due to more favorable modifiers in the former derived from the selected silvers of Ro.

There is also evidence from analysis of reflectionmeter readings of intensity, not presented in this paper, that the intensity of $c^d c^a$ and $c^r c^a$ sepias is usually reduced more than indicated in Table 3 for the former. This effect is especially apparent in combination with another modifier, dm .

There were six pale-sepia yellows ($c^d c^d pp$) from these matings of $sisi \times sisi$. Five showed moderately strong silvering while one showed only a trace. Four pale sepia-yellows of genotype $c^d c^a pp$ from these matings showed no recognizable silvering. There was no difference in intensity from the norm that could be relied upon but again the norm was undoubtedly based in part on animals with modifiers favoring dilution. As far as these data go, they confirm the absence of inter-

action effects of pp and $c^d c^a$ on $sisi$ and the tendency toward suppression of silvering when $c^d c^a$ is combined with $sisi$.

These matings produced 40 silvered intense yellows ($ee CFF$). These include some with silvering as strong as observed in blacks but the average is considerably lower. The silvered intense yellows are also considerably lighter in color than the norm. Low grade silvering is difficult to grade in these since silvering is manifested more by a rather uniform lightening of the color of the belly than by intermingling of white and colored hairs. There is sometimes, however, marked irregularity in intensity. As with all of the other light colors, a microscopic study of the distribution of pigment within and among hairs would be required to determine how much real difference there is from the effect of silvering in blacks. To a first approximation the effects are additive.

Matings of $ee CC ff sisi$ interse produced four silvered fading yellows all of high grade in an early series of experiments (LF) and one of these segregated out from a mating of $ee CC Ff sisi$ interse in RoLF. The average (6.6) is about the same as for silvered blacks in the Ro outcrosses. Five $ee CC ff sisi$ segregants from matings of $Sisi \times sisi$ (and $ff \times ff$ or $Ff \times ff$) were also well silvered. The average grade of silvering for all ten was 6.0. The average grade of intensity of these and three others from the first group, born dead and not graded in silvering, was 6.1 which is somewhat lighter than the norm (6.8). There is no evidence for anything other than additive effect of ff and $sisi$.

No yellows of genotype $ee c^d c^d FF sisi$ were produced by the Ro outcrosses. A great many have been produced in other series in which dilution factor dm was often present. High grade silvering has often been present but as with the intense yellow offspring from silvered parents, they rather often show no evidence of silvering except a decided lightening of the color on the belly and some lightening of that on the back.

Four light yellows of genotype $ee c^d c^a FF sisi$ were produced. While two showed no more than a trace of silvering, two were conspicuously silvered on the back as well as almost white on the belly. A mating (L257) between two light yellows of grade 4 (both $ee c^d c^a sisi$) and four matings derived from this in two generations of brother-sister mating produced 39 light yellow young of grades 3 and 4 (average 3.56) as well as albinos. Nine young of grades 5 and 6 (average 5.36) came from two of the matings that were $c^d c^a \times c^d c^a$, and are interpreted as $c^d c^d$. These averages are decidedly lighter than the norm. Several were described as having very light but not white bellies, and a few as being somewhat irregular in intensity on the back, but silvering with white was not recognized in any of them. There is also evidence that light yellows of genotypes $c^k c^r$, $c^k c^a$, and $c^d c^r$ are closely similar. These results agree with those from the $c^d c^a$ sepias that there is a nonadditive interaction between $sisi$ and lower combinations in the c-series under which silvering with white is largely suppressed, but dilution, especially of the belly, is enhanced.

The combination of medium silvering ($sisi$) with low to medium spotting (ss) shows an approximately additive effect in blacks: spots of pure black and of

lightly silvered black on a white ground of the same extent, as if silvering were absent. Low grade silvering is often undetectible in spotted animals since pigment tends to be eliminated more on the belly in the latter than in other regions, except feet and nose. In high grade spotted animals, spots are likely to be restricted to the region about the eyes and ears. As these same regions are those least likely to be silvered, even rather high grade silvering may be undetected in high grade spotting.

On the other hand the fact that high grade silvering may be responsible for large, pure white areas means that animals that would be only low to medium grade spotted otherwise, may appear to be high grade spotted because of this effect of *sisi*. In silvered medium spotted animals, there are apt to be one or more spots of smaller size than are found on unsilvered spotted. In this sense, silvering may act as a member of the group of modifiers of spotting.

There are indications, moreover, that there is some genuine nonadditive interaction such that silvering tends to invade areas (such as the eye-ear region) in high grade spotting to a greater extent than in the absence of such spotting. There is also evidence of interaction in tricolors. An unspotted tortoise-shell ($c^p c^p SS$) is usually a black with scattered small clumps of yellow, or isolated yellow hairs. The interaction, if any, with silvering is merely what one would expect from the appearance of silvering in self-blacks and in self-reds. Thus sprinkling with white is more conspicuous in the black areas while dilution is more conspicuous in the yellow areas of tortoise-shells. In tricolors, ($e^p e^p ss$), the tortoise-shell pattern is profoundly modified (WRIGHT 1917; ILJIN 1928; CHASE 1939). The amount of yellow is greatly increased and there is a tendency toward separate black and yellow spots on the white ground or else of black spots on a ground that is in part yellow and in part white. A streak between two black areas is often white at one end, separated sharply from yellow at the other.

The boundaries of spots of strong and weak silvering in tricolors tend to be the same as those between black and yellow. Examination of the records of the patterns of tricolors in Ro and its outcrosses revealed only four cases in which silvering was stronger on the black side of such a boundary but 14 cases in which silvering was stronger on the yellow side (contrary to the usual situation in tortoise-shells). The latter cases suggest that the effect of *ss* that favors yellow also favors silvering.

Presumably the same sort of interaction occurs in black piebald ($E-ss$) and tends to increase both the strength of silvering and the amount of white. It is probably no accident that the most extreme spotted inbred strain in the colony (#13) with 97.8 percent as the median percentage of white, frequent silvering of the head spots, and 24 percent self-white (WRIGHT and CHASE 1936) turned out to be *ss sisi* on outcross to self-colored animals. It was in fact the source of the silvering in strains I-13 and Ro.

It should be emphasized that these interaction effects are second order ones. To a first order, silvering and spotting are additive.

The last two rows of Table 3 compare the amount of silvering in agoutis and

blacks (some of them tortoise-shells), from a single mating XR127. There is evidently no recognizable difference.

Tests for linkage of Sisi with other loci: Tests for possible linkage have been made previously in every possible pair among the following loci: *S, E, A, B, C, P, F, R, M, St, Px*, and *Sex* (WRIGHT 1941 and 1949b). A significant deviation from 50 percent recombination has been found in only one case *viz.* *R* and *Px* with 43.8 percent recombination among 1015 young. None of these genes showed any indication of partial sex linkage of any sort. We consider here tests for linkage of *Si*.

The prevailing genes in strain Ro and RoLF were e^p , a , *B, C, P, F, S, si, r, and *px*, but *ee, c^rc^r* and *ss* segregated out from some matings. *R* was present in some matings and *M* and *m*, which are unrecognizable except in the presence of *R*, were both present. Strain A was characterized by *E, A, B, C, P, F, S, R*, and *St*. Both *M* and *m* were present. Many animals were *Ppx*. Silvering as already stated was not uncommon. Backcross progenies from *Ro* × *A* gave coupling data for *Si* in relation to *E, A, R, St*, and *Px* but not always from the same mating.*

A considerable number of matings were made between silvers from Ro and nonsilvers that were *bb, c^dc^d, ff, pp*, or *ss*, sometimes in combination. The F₂ repulsion data from these matings was much less satisfactory than the backcross data because of the greater amount of overlap characteristic of F₂, as already discussed. Double recessive strains *bb sisi* and *pp sisi* (used in the discussion of interaction) were, however, established in time to permit the obtaining of some backcross coupling data.

Search through the records for matings of backcross types yielded some repulsion data as well as a few supplementary coupling data.

The linkage tests for *M* and *Si* had to be based on a rather small number of matings from which certain classes of rough-furred young could be shown by pedigree analyses to give valid evidence.

In the progenies of the backcross type, the cleavage between those treated as *Sisi* and those treated as *sisi* was in general made between silver grades 3 and 4 in order to give reasonably good 1:1 ratio. There were four large progenies, however, (not involving the selected silvered strains) in which this cleavage was made between 2 and 3 or between 1 and 2 for the same reason. In the case of the F₂ repulsion data, cleavage had to be made between grades 1 and 2 in all cases to give reasonably good 3:1 ratios. The same cleavage was used throughout for any given mating.

The distribution of grades is given in condensed form in Tables 4 to 6. The estimates of the number of recombinants (parentheses) and nonrecombinants depend on the points of cleavage chosen for the separate matings as indicated above and thus cannot be obtained from the distributions as given.

The matings of *Sisi* male by *sisi* female have been examined for possible partial sex linkage of the expected type. Neither the coupling nor the repulsion data indicate linkage. Altogether, there are estimated to be 277 recombinants in 528 young or 52.5 percent (Dev = 1.1 SE). The reciprocal matings have also been

TABLE 4

Backcross tests for linkage of Si with sex (heterogametic male or heterogametic female) Px, R, St, E, A, B, P, and C. The number of recombinants, as given by the chosen points of cleavage, are put in parenthesis under Sisi and sisi

Mating type ♂ × ♀	No. matings	Grade of silvering								Total	Sisi sisi		Percentage recomb.	Dev. SE	
		0	1-	3-	5-	7-	9-	11-							
♂ C <i>Sisi</i> × <i>sisi</i>	24	{ ♂	21	49	27	25	29	11	2	164	74	(90)	51.4	52.5	1.1
♀ C <i>sisi</i> × <i>Sisi</i>	20	{ ♀	17	52	27	35	29	5	2	167	(80)	87			
♂ R <i>siSi</i> × <i>sisi</i>	20	{ ♂	29	26	14	19	13	6	1	108	(57)	51	54.3		
♀ R <i>sisi</i> × <i>Sisi</i>	8	{ ♀	15	24	15	21	8	5	1	89	39	(50)			
♀ R <i>sisi</i> × <i>Sisi</i>	8	{ ♂	11	7	6	6	5	1	..	36	18	(18)	52.2	54.2	1.5
♀ C <i>sisi</i> × <i>siSi</i>	29	{ ♀	11	5	2	6	9	33	(18)	15			
♀ C <i>sisi</i> × <i>siSi</i>	29	{ ♂	32	42	24	24	4	5	2	133	(79)	54	54.8		
♀ C <i>sisi</i> × <i>siSi</i>	29	{ ♀	24	36	20	22	15	2	..	119	60	(59)			
♀ C <i>Px Si</i> × <i>px si</i>	6	{ <i>Pxpx</i>	2	13	4	12	4	1	..	36	16	(20)	55.3	51.2	0.3
♂ R <i>Px si</i> × <i>px si</i>		{ <i>pxpx</i>	7	11	5	9	8	40	(22)	18			
♀ R <i>px si</i> × <i>Px si</i>	2	{ <i>Pxpx</i>	3	2	1	2	3	1	..	12	(6)	6	39.3		
♀ R <i>px si</i> × <i>Px si</i>	2	{ <i>pxpx</i>	5	6	..	2	2	1	..	16	11	(5)			
♀ R <i>px si</i> × <i>Px si</i>	2	{ <i>Pxpx</i>	1	1	4	6	(1)	5	52.9		
♀ R <i>px si</i> × <i>Px si</i>	2	{ <i>pxpx</i>	2	2	4	3	11	3	(8)			
♂ C <i>RSi</i> × <i>r si</i>	22	{ <i>Rr</i>	26	50	28	32	39	8	..	183	91	(92)	49.3	48.9	0.5
♀ C <i>r si</i> × <i>RSi</i>		{ <i>Rr</i>	24	50	30	43	26	13	..	186	(90)	96			
♀ C <i>r si</i> × <i>RSi</i>	10	{ <i>Rr</i>	13	10	8	5	3	1	..	40	27	(13)	47.3		
♀ C <i>r si</i> × <i>RSi</i>	10	{ <i>rr</i>	12	13	9	9	6	2	..	51	(30)	21			
♂ C <i>St Si</i> × <i>st si</i>	10	{ <i>Stst</i>	7	18	21	12	11	2	..	71	36	(35)	44.7	46.4	1.2
♀ C <i>st si</i> × <i>St Si</i>		{ <i>stst</i>	8	15	15	11	14	7	..	70	(28)	42			
♀ C <i>st si</i> × <i>St Si</i>	13	{ <i>Stst</i>	13	17	12	14	3	3	..	62	36	(26)	48.3		
♀ C <i>st si</i> × <i>St Si</i>	13	{ <i>stst</i>	12	18	9	11	7	1	..	58	(32)	26			
♂ C <i>E Si</i> × <i>e^p si</i>	14	{ <i>Ee^p</i>	8	31	20	25	21	4	..	109	55	(54)	48.7	51.4	0.6
♂ R <i>e^p si</i> × <i>E Si</i>		{ <i>e^pe^p</i>	7	44	17	18	27	10	..	123	(59)	64			
♂ R <i>e^p si</i> × <i>E Si</i>	1	{ <i>Ee^p</i>	..	2	..	3	1	6	(2)	4	57.1		
♀ C <i>e^p si</i> × <i>E Si</i>	1	{ <i>e^pe^p</i>	..	2	1	2	1	2	..	8	2	(6)			
♀ C <i>e^p si</i> × <i>E Si</i>	19	{ <i>Ee^p</i>	12	20	14	22	7	6	..	81	35	(46)	53.5		
♀ R <i>e^p si</i> × <i>E Si</i>		{ <i>e^pe^p</i>	18	23	15	20	9	4	..	89	(45)	44			
♀ R <i>e^p si</i> × <i>E Si</i>	1	{ <i>Ee^p</i>	9	11	1	..	4	25	(15)	10	56.4		
♀ R <i>e^p si</i> × <i>E Si</i>		{ <i>e^pe^p</i>	2	8	2	1	1	14	7	(7)			
♂ C <i>A Si</i> × <i>a si</i>	20	{ <i>Aa</i>	17	49	18	24	25	9	..	142	77	(65)	43.1	43.7	2.4
♂ R <i>a si</i> × <i>A Si</i>		{ <i>aa</i>	9	39	31	36	33	7	..	155	(63)	92			
♂ R <i>a si</i> × <i>A Si</i>	1	{ <i>Aa</i>	6	8	2	1	1	18	(10)	8	48.7		
♀ C <i>a si</i> × <i>A Si</i>	1	{ <i>aa</i>	5	11	1	..	3	1	..	21	12	(9)			
♀ C <i>a si</i> × <i>A Si</i>	6	{ <i>Aa</i>	2	3	..	2	1	2	..	10	5	(5)	42.9		
♀ C <i>a si</i> × <i>A Si</i>		{ <i>aa</i>	3	3	3	4	3	2	..	18	(7)	11			
♂ C <i>B Si</i> × <i>b si</i>	2	{ <i>Bb</i>	..	1	2	..	1	1	..	5	1	(4)	55.6	50.0	0.0
♂ R <i>b si</i> × <i>B Si</i>		{ <i>bb</i>	..	1	..	2	1	4	(1)	3			
♂ R <i>b si</i> × <i>B Si</i>	1	{ <i>Bb</i>	1	1	(0)	1	50.0		
♀ C <i>b si</i> × <i>B Si</i>	1	{ <i>bb</i>	1	1	0	(1)			
♀ C <i>b si</i> × <i>B Si</i>	4	{ <i>Bb</i>	1	6	2	3	1	13	7	(6)	55.6		
♀ R <i>b si</i> × <i>B Si</i>		{ <i>bb</i>	3	1	..	1	5	(4)	1			
♀ R <i>b si</i> × <i>B Si</i>	3	{ <i>Bb</i>	5	2	3	2	1	13	(7)	6	42.9		
♀ R <i>b si</i> × <i>B Si</i>		{ <i>bb</i>	4	2	..	2	8	6	(2)			
♂ C <i>P Si</i> × <i>p si</i>	5	{ <i>Pp</i>	3	5	5	10	8	3	..	34	11	(23)	60.8	53.9	1.0
♂ R <i>p si</i> × <i>P Si</i>		{ <i>pp</i>	6	12	8	12	1	1	..	40	(22)	18			
♂ R <i>p si</i> × <i>P Si</i>	1	{ <i>Pp</i>	7	6	4	3	20	(8)	12	40.0			
♀ C <i>p si</i> × <i>P Si</i>	1	{ <i>pp</i>	8	8	3	1	20	12	(8)				
♀ C <i>p si</i> × <i>P Si</i>	5	{ <i>Pp</i>	3	6	4	6	2	2	..	23	9	(14)	54.9		
♀ C <i>p si</i> × <i>P Si</i>		{ <i>pp</i>	1	11	5	7	2	2	..	28	(14)	14			
♂ C <i>C Si</i> × <i>c^d si</i>	2	{ <i>Cc^d</i>	..	2	..	3	5	2	(3)	55.6		
♂ C <i>c^d si</i> × <i>C Si</i>		{ <i>c^dc^d</i>	..	1	1	1	1	4	(2)	2			

examined on the improbable hypothesis that the female may be heterogametic. There is no indication of linkage (174 estimated recombinants in 321 or 54.2 percent (Dev = 1.5 SE).

In the case of *Si* and *Px*, there is no indication of linkage from either coupling or scanty repulsion data. Altogether 62 recombinants in 121 young are indicated or 51.2 percent (Dev = 0.3 SE).

Only coupling data were obtained for *Si* and *R*. There is no indication of linkage either in tests of F_1 males or F_1 females, or in both combined (225 recombinants in 460 young or 48.9 percent, Dev = 0.5 SE).

Similarly there is no indication of linkage of *Si* with *St* in backcross coupling tests of either F_1 males or F_1 females. The estimated proportion of recombinants altogether is 121 in 261 or 46.4 percent (Dev = 1.2 SE).

In the case of *Si* and *M*, four matings were found within the backcrosses to I-13, five matings were found in the backcrosses of A to *Ro* and one additional mating (XR161) was found in the records, which, by pedigree analysis, could give information (Table 5). No information is given by the smooth young. All of the matings were of the type *Sisi* × *sisi* but only two were *Mm* × *mm* and two *MM* × *Mm* permitting use of all of the rough-furred young. Among the others, two were *Mm* × *Mm*, three were *Mm* × *M-* and one was *Mm* × *m-*, where the dash represents uncertainty. In these last six cases, only high grade (*Rmm*) and low grade (*RMM*) roughness gives information on linkage. The cleavage between those interpreted as *Sisi* and as *sisi* was taken at the same points as in the other tests (between grades 3 and 4 in three cases, between grades 2 and 3 in five cases, including one not otherwise used, and between grades 1 and 2 in two cases).

On this basis there are 20 recombinants in 92 usable offspring or 21.7 percent (Dev = 5.4 SE). This clearly demonstrates linkage if the assignment of genotypes is acceptable. No plausible shifts in the points of cleavage chosen for *Sisi* and *sisi* were found to have any important effect on the result. Another complication is the occasional overlap of *Rm* and *RM*. Thus the last mating in Table 5; *mm* × *Mm*, produced one offspring called Rough E which is usually *R-MM* but occasionally *R-Mm* with which it must here be counted. Examination of the pedigrees for possible errors of this sort, revealed none which would affect the result appreciably. The female of XR161 was a pale cream of grade 1 in which silvering cannot be recognized except by the extreme dilution. She could have been *Sisi* (*dmdm*) instead of *sisi* (*Dmdm*) from her parentage (*dm* being a modifier of intensity). In this case only the silvered young should be counted, removing two recombinants and eight nonrecombinants from those used. The ratio of silver to nonsilver (9:10) makes the interpretation in the table more probable.

In the case of *Si* and *E*, considerable coupling data and a few repulsion data were obtained for both sexes with no indication of linkage in any. The total estimated number of recombinants was 234 in 455 or 51.4 percent (Dev = 0.6 SE).

There is some indication of linkage of *Si* and *A*. Altogether there are estimated to be 159 recombinants in 364 or 43.7 percent (Dev = 2.4 SE). The probability of as great a derivation in this direction from accidents of sampling is about .008.

TABLE 5

Ten matings which give information on possible linkage of Si and M. All young are included, but those which give no information on linkage are in parentheses. In formulae of parents, genes from sire in numerator, from dam in denominator. Uncertain allele represented by dash, C coupling, R repulsion. The totals indicate 21.7 percent recombination

	♂	♀		R-mm	RMm	RMM	Sm (rr)	Total	Non Rec.	Rec.
Ro38	$\frac{si\ m}{Si\ M} \times \frac{si\ M}{si\ —}$	$\frac{Si\ si}{si\ si}$	Sisi	3	(4)	7	3	..
(♂ C)	$\frac{Si\ M}{si\ —}$	$\frac{si\ —}{Si\ M}$	sisi	..	(2)	0	(5)	7
Ro51	$\frac{si\ m}{Si\ M} \times \frac{si\ M}{si\ —}$	$\frac{Si\ si}{si\ si}$	Sisi	1	(3)	4	1	..
(♂ C)	$\frac{Si\ M}{si\ —}$	$\frac{si\ —}{Si\ M}$	sisi	1	(1)	2	..	1
SiAll	$\frac{si\ M}{Si\ M} \times \frac{Si\ M}{si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	..	0	2	(2)	4	2	..
(♀ C)	$\frac{si\ M}{Si\ M}$	$\frac{si\ m}{Si\ M}$	si si	..	2	0	(0)	2	2	..
SiA51	$\frac{Si\ m}{si\ M} \times \frac{si\ M}{si\ M}$	$\frac{Si\ si}{si\ si}$	Si si	..	1	..	(1)	2	1	..
(♂ R)	$\frac{si\ M}{si\ M}$	$\frac{si\ M}{si\ M}$	si si	..	2	..	(6)	8	..	2
Ro16	$\frac{si\ M}{si\ —} \times \frac{si\ M}{Si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	..	(1)	..	(4)	5
(♀ R)	$\frac{si\ —}{Si\ m}$	$\frac{Si\ m}{Si\ m}$	si si	..	(2)	2	(3)	7	2	..
SiA47	$\frac{si\ M}{Si\ m} \times \frac{si\ M}{si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	7	(7)	?	(4)	20	7	2
(♂ R)	$\frac{Si\ m}{si\ m}$	$\frac{si\ m}{si\ m}$	si si	1	(9)	7	(2)	19	7	1
SiA39	$\frac{si\ M}{si\ m} \times \frac{si\ M}{Si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	10	(6)	4	..	20	10	4
(♀ R)	$\frac{si\ m}{Si\ m}$	$\frac{Si\ m}{Si\ m}$	si si	3	(8)	5	..	16	5	3
SiA43	$\frac{Si\ m}{si\ M} \times \frac{si\ m}{si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	7	1	..	(18)	26	7	1
(♂ R)	$\frac{si\ M}{si\ M}$	$\frac{si\ m}{si\ m}$	si si	..	11	..	(10)	21	11	..
Ro2	$\frac{Si\ m}{si\ M} \times \frac{si\ —}{si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	1	(2)	..	(4)	7	1	..
(♂ R)	$\frac{si\ M}{si\ m}$	$\frac{si\ m}{si\ m}$	si si	0
XR161	$\frac{si\ M}{Si\ m} \times \frac{si\ m}{si\ m}$	$\frac{Si\ si}{si\ si}$	Si si	8	2	10	8	2
(♂ R)	$\frac{Si\ m}{si\ m}$	$\frac{si\ m}{si\ m}$	si si	4	5	9	5	4
									72	20

The probability for a random pair of loci to show linkage with recombination as great as 43.7 percent is, however, also small, noting that the guinea pig has 33 pairs of chromosomes and assuming that recombination percentages are distributed uniformly between zero percent and 50 percent. This probability is .0019 ($= .030 \times .063$). The probability for such a pair of loci to be in a different chromosome and yet to show as little recombination as 43.7 percent is .0078 ($= .970 \times .008$) or four times as great. The Si and A loci cannot perhaps be considered as a random pair since they show next to the strongest indication of linkage among nine somewhat adequately tested cases discussed here. Nevertheless it is clear that it is at least as likely that this is a deviation due to accidents of sampling as that it is due to linkage. There are, however, other possibilities.

One such possibility is that there is linkage between *A* and a modifier of silvering that makes for a low grade in comparison with its allele from the high grade selected strain Ro. The difference between the mean grades of silver of *Aa*(4.0) and *aa*(4.2) in the first backcross generation in which one might expect linkage to be shown most clearly, is however, less than in the remainder of the coupling data (second backcross and miscellaneous matings) (*Aa* 3.5, *aa* 4.4).

The most probable explanation seems to be a slight systematic bias in grading silvered agoutis as compared with silvered blacks. Traces of silvering are more easily observed on the black belly of *aa* than on the yellow belly of *Aa*. Such a bias would be most serious in the low grades which are thus likely to be underestimated in agoutis. These grades were not represented to an important extent in the previously discussed comparison of *Aa* and *aa* from *sisi* × *sisi*.

The evidence for random assortment of *A* and *M* (50.4 percent recombination among 607 young, WRIGHT 1941) and that for strong linkage of *Si* to *M* (ca. 22 percent), presented here, also make it unlikely that *Si* and *A* are in the same chromosome.

Table 6 shows the results in F_2 from matings of *BB sisi* × *bb SiSi*. It is evident that recombination occurs. If cleavage between *Si*- and *sisi* is made between grades 1 and 2, the estimated proportion of double recessives, seven in 125, excluding seven near whites is approximately that expected under random assortment (expected 7.8). There is, however, so much overlap between *Sisi* and *sisi* in F_2 due to segregation of modifiers that little stress can be put on an F_2 ratio. A double recessive strain was established, and a few backcross data obtained which are of more value (Table 4). The coupling and repulsion data from F_1 males and females

TABLE 6

F₂ data on possible linkage of Si with B, P, F, S, and C. Near-white (unclassifiable but with excess likelihood of being sisi in parentheses). Trace of silvering difficult to recognize in most cases. Any silvering probably unrecognizable in ffpp. Cleavage in all cases between grades 1 and 2

Type of F_2 mating	Number matings		Grade of silvering					Near W	Total	0-1	2-9	
			0	1-	3-	5-	7-					9-
Repulsion	9	<i>B-</i>	46	25	6	7	4	..	(5)	88	63	25
		<i>bb</i>	24	10	1	1	1	..	(2)	37	30	7
Coupling	3	<i>P-</i>	8	9	3	1	1	1	...	23	16	7
		<i>pp</i>	4	3	..	1	8	7	1
Repulsion	3	<i>P-</i>	23	14	1	1	2	..	(1)	41	34	7
		<i>pp</i>	16	4	1	1	22	18	4
Repulsion	5	<i>F-P-</i>	23	17	2	2	2	..	(2)	46	37	9
		<i>ffP-</i>	12	3	(4)	15	13	2
		<i>F-pp</i>	8	3	..	1	12	9	3
		<i>ffpp</i>	6	6	6	0
Repulsion	8	<i>S-</i>	58	36	11	4	2	111	81	30
		<i>ss</i>	19	6	..	2	(9)	27	19	8
Repulsion	3	<i>C-</i>	4	10	5	1	2	1	...	23	14	9
		<i>c^dc^d</i>	2	6	..	1	9	8	1

all indicate that recombination occurred freely. The over-all number of recombinants is estimated at 25 in 50 or exactly 50.0 percent.

In the case of *Si* and *P*, F_2 data were obtained for both coupling and repulsion (Table 6). On making the cleavage between 1 and 2, the repulsion data yielded four in 63. There is clearly no indication of linkage. Both coupling and repulsion data were also obtained (Table 4) from backcrosses to the double recessive strain derived from F_2 . Again there is no indication of linkage (89 estimated recombinants in 165 young or 53.9 percent) ($Dev = 1.0 SE$).

As noted earlier, spotting (*ss*) on the one hand interferes with the expression of *sisi* by eliminating color from the regions in which silvering tends to be strongest, and on the other, there are indications of an interaction effect by which *ss sisi* tends toward self-white or near-white somewhat more frequently than *ss Si-*. For both reasons simple linkage tests are certain to be unsatisfactory. However, matings were made between *SS sisi* from strain Ro and unsilvered spotted animals *ss SiSi* and carried to F_2 . As far as they go, the results indicate that recombination occurred at random. The arbitrariness of the cleavage between *Ss* and *ss* (between 4 and 5 parts of white in 20), and between *Sisi* and *sisi* (between silver grades 1 and 2) and the production of nine black-eyed whites or near whites (*ss*), that could not be graded in silvering, make this ratio highly uncertain. The double recessive strain (inbred strain 13) was not on hand at the time linkage was being tested and no backcrosses were made. The fact that *SS sisi* was easily extracted from outcrosses of strain 13 (to produce strain I-13) indicates that linkage is not close.

An F_2 test for possible linkage of *Si* and *F* was attempted from matings of *FF sisi* \times *ff SiSi*. Unfortunately both *ss* and *pp* segregated from F_2 to complicate classification. There were six near whites (of which four were *ss ff*) in which silvering is unrecognizable. Silvering would probably also be difficult or impossible to recognize in *E ff pp* which is very pale cream. These are tabulated separately. Among those with *P-* and not near white, only two double recessives, *ff sisi*, were recognized among 61 young, and these were borderline silvers (grade 2). The data are thus compatible with any degree of recombination. No double recessive strain was established at this time and no backcross data are on hand. The fact that there was no difficulty in producing double recessives at an earlier period (strain LF referred to in connection with possible interaction effects) shows that recombination can occur.

Tests for linkage of *Si* with *C* were delayed by failure to recognize that *sisi* is usually not recognizable with confidence in $c^d c^a$. Only a few F_2 young were obtained from the mating *CC sisi* \times $c^d c^a SiSi$. There was one clear case of a double recessive (silver grade 5) among 32 young and no border line cases. In a mating of backcross type (coupling) there were five recombinants among nine young (cleavage between grades 2 and 3). There is an abundance of data indicating easy transfer of *si* from one *c* allele to another but uncertainties of classification make these useless for calculation of recombination percentage.

The best evidence at present that *Si* is not linked with *S*, *F*, or *C* comes from

the evidence for rather strong linkage with M and the earlier evidence that M shows random assortment with these (52.9 percent with S in 363 backcross young, 56.7 percent with F in 157 backcross young, and 48.7 percent with C in 275 backcross young).

SUMMARY

The character "silver" in the guinea pig ranges from a few white hairs on the belly almost to self-white. Whatever the grade, it is present at birth and not progressive. Data have been given in a previous paper indicating that self or low grade silvering maintains itself through repeated backcrosses to a high grade silver strain as if dependent on a single incompletely dominant gene. This result is confirmed here by data from another cross, carried to the second backcross. In the latter the distribution was definitely bimodal. F_2 from self by high grade silver gave no clear indication of unifactorial segregation because of segregating modifiers.

The existence of genetic modifiers is shown by the rapid advance under selection. The regression of offspring on midparent was .40 in a group of related strains that extended over the entire range.

The silvering character is often highly irregular especially in intermediate grades in which corresponding areas on the right and left sides may differ greatly. It is convenient to distinguish this "blotching" effect from the silvering in the narrow sense. There is also some dilution of the intensity of color in nonsilvered (as well as silvered) areas. The silvering is most conspicuous on a black ground, while the dilution is barely perceptible in blacks. The effect of the gene seems to be essentially the same in browns (bb), pale sepias (pp), and dark sepias ($c^d c^d$) although silvering becomes more difficult to recognize on the paler backgrounds, and dilution becomes more conspicuous (perhaps merely because of saturation in blacks). In light sepias ($c^d c^a$, $c^r c^a$), however, silvering tends to disappear and uniform dilution becomes the most characteristic effect. Silvering may be extreme but is usually less expressed in intense yellow (ee) or dilute yellows ($ee c^d c^d$ and $ee ff$) than in black while dilution is more conspicuous.

In still paler yellows ($c^k c^r$, $c^k c^a$, $c^d c^r$, $c^d c^a$), silvering is rarely expressed at all as scattered white hairs but merely as dilution, especially on the belly which tends to be a very pale cream color but not actually white. There is believed to be a real interaction effect with the lower combinations of the c -series. There are also minor interactions with spotting (ss) as well as mere interference in the expression of the two white patterns.

There is no sex linkage of Si of any sort. Rather strong linkage (22 percent recombination) is indicated with locus M (modifier of rough fur). Tests for linkage of Si with Px , St , R , E , B , and P indicated random assortment. Apparently significant linkage of Si and A (Deviation $2.4 \times$ standard error) was probably due merely to underestimation of low grade silvering on the yellow bellies of agoutis. Tests for linkage of Si with S , F , and C were inadequate but gave no indication of linkage as far as they went. Previously reported tests (not including Si)

have indicated random assortment among all of the other genes above except for a weak linkage between *R* and *Px* (43 percent recombination). These appear to be indicators of 11 different chromosomes, with only two cases of linkage *R-Px* and *Si-M*. The only other suggestion of linkage in the guinea pig (and this is doubtful) is between *A* and one of the components of multifactorial polydactyly.

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