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A REVIEW OF GENETIC LINKAGE IN THE GUINEA-PIG

Roy ROBINSON

St. Stephen's Road Nursery
Ealing, London, W.13

SUMMARY

The published data on tests for linkage are reviewed and statistically analysed for independent inheritance of 15 different loci. Estimates are derived from the combined data for (1) the closest linkage compatible with the apparent random assortment or (2) the crossover fraction where random assortment is contradicted. Linkage is evident for the gene pairs *Px* and *R* and *m* and *si*.

INTRODUCTION

Although still extensively utilised in many fields, domestic Guinea-pigs, *Cavia cobaya*, have declined somewhat from favour as genetic material. This is unfortunate since it is a useful animal in several respects. The purpose of this communication is to analyse and collate the published data on genetic linkage. If the Guinea-pig is to play a more vital role in rodent genetics, a critical review of the present position would seem opportune. In this regard, the Guinea-pig will be brought into line with the Mouse (CARTER and FALCONER, 1952), Rabbit (ROBINSON, 1956), Rat (ROBINSON, 1960) and *Peromyscus* (ROBINSON, 1964).

MATERIAL AND TECHNIQUE

The material consists of genetic segregation data for 15 mutant genes. There have been tested in 83 combinations out of the possible 105; this is a rate of investigation of 69 per cent, far higher than that for the other species mentioned above. The statistical technique employed is the system of scoring first explicitly introduced by FISHER (1946). For further details of the method, see ROBINSON (1956).

RESULTS

1. *Independent segregation*

The mutant genes, or the loci which they represent, are listed in table 1. The main independence data are arranged in table 2. This tabulation gives the estimated recombination fraction for the pooled data, together with the score

TABLE 1 (TABLEAU 1)

Mutants of the guinea-pig which have been employed in linkage studies
Mutants du Cobaye qui ont été employés dans des études de linkage

Symbol *Symbole*	Designation *Appellation*	Prime characteristic *Principale caractéristique*
a	Non-agouti	Coat colour
b	Brown	Coat colour
c	Albino	Coat colour
e	Yellow	Coat colour
f	Faded	Coat colour
l	Long hair	Hair texture
m	Rough modifier	Hair texture
p	Pink-eye	Coat colour
Px	Polydactyly	Skeleton
R	Rough	Hair texture
s	Piebald	White spotting
si	Silver	Coat colour
sm	Salmon-eye	Coat colour
St	Star	Hair texture

and amount of statistical information for each pair of genes. The column headed phase balance discloses the percentage of information derived from coupling segregation. Perfect balance is indicated by an index of 50, a value which postulates that inviability or other interactions between genes should not bias the estimation.

Fig. 1 serves the double function of (*a*) indicating the extent of the linkage testing and particularly high-lighting those gene pairs which remain to be investigated, and (*b*) showing the strength of linkage which would be compatible with the observed segregation of the gene pair at the 5 per cent level of significance. This is approximated by multiplying the standard error by 1,96 and subtracting the quotient from the recombination fraction. The compatible linkage value is then expressed as a percentage.

With one exception, none of the tested pairs of genes listed in table 2 have shown any indication of linkage. The exceptions are the genes *e* and *f*. The combined data on the segregation have produced the significant recombination

TABLE 2 (TABLEAU 2)

Quasi-independent segregation
Segrégations quasi-indépendantes

Loci *Loci*	Recombination fraction *Fréquence de recombinaison*	Score *Note*	Information *Quantité d'information*	Phase balance *Équilibre des phases*	References *Références*
a-b	0.49 ± 0.02	— 41.33	4510.22	98	SOLLAS (1909), CASTLE (1916), IBSEN (1923), GREGORY (1928), WRIGHT (1941)
a-c	0.47 ± 0.02	— 63.56	1874.37	100	CASTLE (1916), IBSEN (1923), WRIGHT (1941)
a-e	0.49 ± 0.01	— 57.11	5497.93	98	SOLLAS (1909), CASTLE (1913, 1916), IBSEN (1923), WRIGHT (1941)
a-f	0.45 ± 0.03	— 62	1308	100	WRIGHT (1941)
a-m	0.48 ± 0.02	— 68	2940	99	WRIGHT (1916, 1941)
a-p	0.49 ± 0.02	— 20	3008	96	IBSEN (1923), GREGORY (1928), WRIGHT (1941)
a-Px	0.46 ± 0.02	— 46	1292	100	WRIGHT (1941)
a-R	0.51 ± 0.01	40	5544	98	WRIGHT (1916, 1941), IBSEN (1923)
a-s	0.51 ± 0.02	18	2824	100	WRIGHT (1941)
a-si	0.44 ± 0.03	— 92	1456	89	WRIGHT (1959)
a-sm	0.51 ± 0.05	4	420	60	GREGORY (1928)
a-St	0.52 ± 0.02	34	2108	84	WRIGHT (1949)
a-♂	0.50 ± 0.02	— 5	2277	32	WRIGHT (1941)
b-c	0.50 ± 0.03	— 5.78	1346.22	100	CASTLE (1916), IBSEN (1923), WRIGHT (1941)
b-e	0.50 ± 0.02	4.33	4420.44	95	SOLLAS (1909), CASTLE (1961), IBSEN (1923), WRIGHT (1941)
b-f	0.54 ± 0.03	58	1316	100	WRIGHT (1941)
b-m	0.49 ± 0.03	— 14	1756	100	WRIGHT (1941)
b-p	0.50 ± 0.02	— 6.67	2826.67	100	IBSEN (1923), GREGORY (1928), WRIGHT (1941)
b-Px	0.56 ± 0.03	52	920	100	WRIGHT (1941)
b-R	0.49 ± 0.02	— 28	3504	100	IBSEN (1923), WRIGHT (1941)
b-s	0.50 ± 0.02	4.22	3526.67	100	WRIGHT (1941)
b-si	0.54 ± 0.05	18	434.67	79	WRIGHT (1959)
b-sm	0.50 ± 0.05	2	468	45	GREGORY (1928)
b-St	0.46 ± 0.03	— 44	1216	68	WRIGHT (1949)
b-♂	0.52 ± 0.03	44.67	2470.67	49	WRIGHT (1941)
c-e	0.50 ± 0.02	51.56	2822.22	100	CASTLE (1916), IBSEN (1923), WRIGHT (1941)
c-f	0.50 ± 0.04	3.44	887.11	19	WRIGHT (1941)
c-l	1.25 ± 0.5	3.56	4.47	100	CASTLE (1913)
c-m	0.49 ± 0.03	— 14	1100	100	WRIGHT (1941)
c-p	0.50 ± 0.03	13.42	5148.28	98	IBSEN (1922, 1923), WRIGHT (1941)
c-Px	0.48 ± 0.04	— 16	776	100	WRIGHT (1941)
c-R	0.48 ± 0.02	— 59.78	2566.22	100	CASTLE (1913), IBSEN (1923)
c-s	0.47 ± 0.02	— 59.22	2014.67	100	WRIGHT (1941)
c-si	0.36 ± 0.11	— 10.44	75.11	55	WRIGHT (1959)
c-St	0.51 ± 0.02	24	2232	54	WRIGHT (1949)
c-♂	0.49 ± 0.02	— 28.67	2230.67	60	WRIGHT (1941)
e-f	0.47 ± 0.04	— 19	728	100	WRIGHT (1941)
e-m	0.48 ± 0.02	— 60	2856	100	WRIGHT (1941)
e-p	0.50 ± 0.02	— 4	3376	100	IBSEN (1923), WRIGHT (1941)
e-Px	0.48 ± 0.03	— 36	1560	100	WRIGHT (1941)

TABLE 2 (contd)

Loci *Loci*	Recombination fraction *Fréquence de recombinaison*	Score *Note*	Information *Quantité d'information*	Phase balance *Équilibre des phases*	References *Références*
e-R	0.49 ± 0.01	— 82	6004	100	IBSEN (1923), WRIGHT (1941)
e-s	0.50 ± 0.02	8	2832	100	WRIGHT (1959)
e-si	0.41 ± 0.02	— 22	2304	88	WRIGHT (1959)
e-St	0.51 ± 0.02	22	2516	95	WRIGHT (1949)
e-♂	0.50 ± 0.02	— 6	3332	37	WRIGHT (1941)
f-m	0.57 ± 0.04	42	628	100	WRIGHT (1941)
f-p	0.50 ± 0.04	— 4.44	800.44	85	WRIGHT (1941)
f-Px	0.46 ± 0.04	— 41	728	100	WRIGHT (1941)
f-R	0.52 ± 0.03	30	1308	100	WRIGHT (1941)
f-s	0.49 ± 0.03	— 10	900	100	WRIGHT (1941)
f-si	0.50 ± 0.09	— 0.44	147.56	0	WRIGHT (1959)
f-St	0.52 ± 0.04	12	552	100	WRIGHT (1949)
f-♂	0.46 ± 0.03	— 42	1062	67	WRIGHT (1941)
l-R	0.38 ± 0.27	— 1.78	14.22	100	CASTLE (1913)
m-p	0.49 ± 0.03	— 10	1332	100	WRIGHT (1941)
m-Px	0.50 ± 0.04	— 2	796	100	WRIGHT (1941)
m-R	0.48 ± 0.02	— 74	3188	97	WRIGHT (1916, 1941)
m-s	0.53 ± 0.03	42	1452	100	WRIGHT (1941)
m-St	0.48 ± 0.03	— 24	1072	7	WRIGHT (1949)
m-♂	0.49 ± 0.03	— 24	1696	38	WRIGHT (1941)
p-Px	0.55 ± 0.04	38	780	100	WRIGHT (1941)
p -R	0.49 ± 0.02	— 22	2996	100	IBSEN (1923), WRIGHT (1941)
p-s	0.49 ± 0.02	— 20.67	2406.67	100	WRIGHT (1941)
p-si	0.54 ± 0.04	— 30.44	828.89	67	WRIGHT (1959)
p-sm	0.50 ± 0.05	— 2	396	57	GREGORY (1928)
p-St	0.52 ± 0.02	26	1724	84	WRIGHT (1949)
p-♂	0.49 ± 0.02	— 15.33	2542.67	64	WRIGHT (1941)
Px-s	0.52 ± 0.05	6	380	100	WRIGHT (1941)
Px-si	0.51 ± 0.05	60	484	63	WRIGHT (1959)
Px-st	0.47 ± 0.02	— 54	1948	51	WRIGHT (1949)
Px-♂	0.53 ± 0.03	28	1096	100	WRIGHT (1941)
R-s	0.53 ± 0.02	78	2982	100	WRIGHT (1941)
R-si	0.49 ± 0.02	— 20	1840	100	WRIGHT (1959)
R-St	0.47 ± 0.02	— 104	3952	59	WRIGHT (1949)
R-♂	0.51 ± 0.02	30	3340	100	WRIGHT (1941)
s-si	0.50 ± 0.10	— 0,43	98.61	0	WRIGHT (1959)
s-St	0.50 ± 0.03	— 4	848	89	WRIGHT (1959)
s-♂	0.47 ± 0.02	— 63.67	1862.67	86	WRIGHT (1941)
si-St	0.46 ± 0.03	— 38	1033	100	WRIGHT (1959)
si-♂	0.53 ± 0.02	52	2112	63	WRIGHT (1959)
St-♂	0.48 ± 0.02	— 58	2572	65	WRIGHT (1949)

fraction of 0.439 ± 0.029. However, WRIGHT (1941) is cautious in accepting the result as evidence for linkage because, of the two crosses involved, that which contributed most significantly is one in which *f* is most difficult to classify. In the cross where misclassification is not a problem, the recombination fraction is 0.474 ± 0.037, an insignificant value. The two genes could probably bear further investigation.

IBSEN (1922) reported significant excess recombination between *c* and *p*. However, the excessive recombination was only apparent for one of the two reported crosses and, when the two are combined, the results become insignificant.

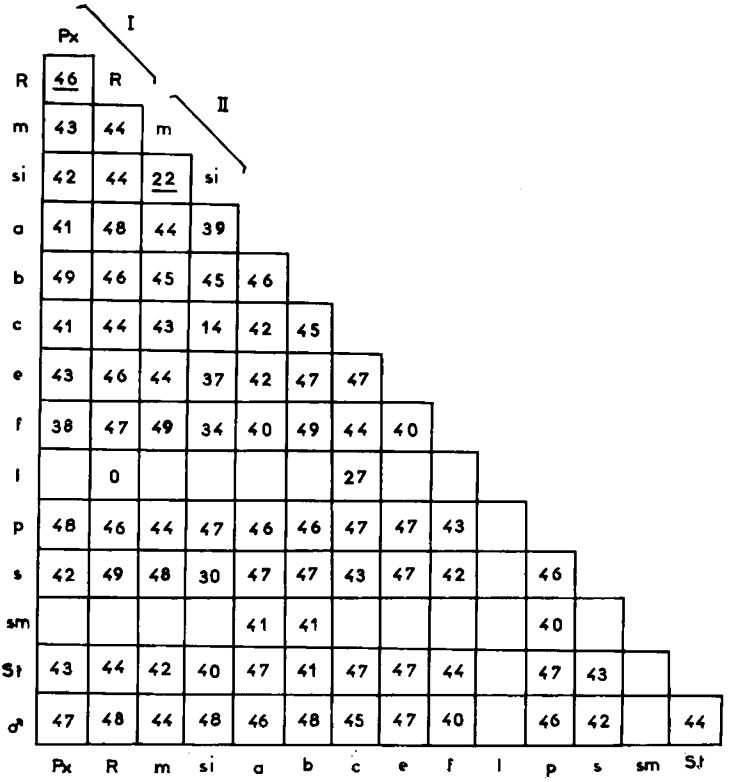

FIG. 1. — Summary of extent of linkage tests. Two groups have been found and the recombination percentage shown is the average of those of table 3. The percentage shown for the other genes are the closest linkage compatible with the available data.

FIG. 1. — *Résumé des tests de linkage. Deux groupes de linkage on été trouvés (Px, R* et *m, si), le pourcentage de recombinaisons indiqué est la moyenne de ceux du tableau 3. Les pourcentages relatifs aux autres gènes sont ceux qui présentent les liaisons les plus étroites parmi les données disponibles.*

The crosses are not straightfoward and it may be wondered if phenotypic overlapping may have occurred. Later data by IBSEN (1923) and WRIGHT (1941) on the joint segregation of the two genes revealed nothing unusual.

2. *Linkage*

Two pairs of linked genes have been discovered to-date. Table 3 gives the genes concerned and the amount of recombination observed, according to linkage phase and sex of the diheterozygous parent. The discovery of only two linked pairs is remarkable considering the number of genes examined and the systematic manner with which most of the genes have been compared with each other.

TABLE 3 (TABLEAU 3)

Established linkage
Relations de linkage démontrées

Linkage Group *Groupe de linkage*	Gene Pair *Paires de gènes*	Phase *Phase*	Sex *Sexe*	Recombination fraction *Fraction recombinée*	References *Références*
I	*Px-R*	C	♂	0.424 ± 0.025	WRIGHT (1941, 1949)
		R	♂	0.453 ± 0.028	WRIGHT (1941, 1949)
		C	♀	0.484 ± 0.036	WRIGHT (1941, 1949)
		R	♀	0.563 ± 0.056	WRIGHT (1941, 1949)
II	*m-si*	R	♀	0.203 ± 0.052	WRIGHT (1959)
		R	♀	0.250 ± 0.078	WRIGHT (1959)

C = coupling, R = repulsion.

The first linkage to be discovered was that between *Px* and *R* (WRIGHT, 1941, 1949). The *Px* gene has variable expression and penetrance of a nature which cannot be easily compensated by statistical manipulation. WRIGHT (1941) discusses the problem and divides the data into three groups, the last group being regarded as very unreliable for linkage estimation. This group has been rejected from the analysis since the contribution in any case is small. A curiosity of the data is the large but sub-significant heterogeneity between the four segregations of the table. This is due largely to the high rate of recombination for females of repulsion phase. No obvious reason can be deduced for the high rate but it could, of course, be due to the variable penetrance. If the repulsion female data are included, the mean recombination is 0.457 ± 0.016; if these are excluded, the mean is 0.447 ± 0.017. A sex difference in recombination is evident between the sexes but, in the main, this is due to the exceptional female data referred to above. If these are ignored, the sex difference falls appreciably.

The second case of linkage involves the genes *m* and *si*. The expression of *si* is variable and can be difficult to score upon certain genetic backgrounds (WRIGHT, 1959). However, this merely interferes with the estimation of the linkage strength and not with its existence. The sex difference in recombination is insignificant.

Two forms of polydactyly are known in the guinea-pig. That due to the dominant gene *Px* (*PxPx* is lethal, *Px* + is polydactylous of variable expression) and another which is due to the combined effects of three or four mainly recessive genes (WRIGHT, 1934). The results of WRIGHT (1941) suggest that one of these may be linked to *s*. WRIGHT states that if recessive polydactyly is assumed to be caused by a single gene, a recombination fraction of 0.443 ± 0.029 would be consistent with the data.

3. *Karyology*

Karyotypes of the guinea-pig have been produced by several investigations within recent years (AWA *et al.*, 1959; OHNO *et al.*, 1961; WATSON *et al.*, 1966 and DOBRIJANOV and GOLJDMAN, 1967*a*, *b*). The haploid number of chromosomes is 32, a relatively large number for a rodent. The karyotype consists of a large subtelocentric chromosome, which is easily identifiable, and numerous medium to small elements with few (or no) distinguishing features. The majority seem to be either telocentric or subtelocentric. The overall picture is that of fragmentation in the evolution of the present complex. The *X* is a large telocentric body while the *Y* is a small acrocentric, scarcely different in size from the small autosomes.

The large numbers of chromosomes and their small size would imply that linkage between known genes will be infrequent. Though the number of mutant genes so far investigated are few, the results support the implication.

DISCUSSION

It only remains to stress a few points. The present analysis has not produced any novel results. Most of the general comments made earlier with respect to the analysis of the Rabbit and Rat data (ROBINSON, 1956, 1960) are applicable to the guinea-pig. Most of the pairs of genes tested to date for the guinea-pig have precluded the likelihood of linkage up to 40 per cent. Beyond this linkage value, diminishing returns becomes a serious problem in that progressively larger numbers of progeny have to be examined. One solution would be to make the collection of data incidental to some other aspect of research.

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RÉSUMÉ

ÉTUDE DU LINKAGE CHEZ LE COBAYE

Les données publiées concernant les tests de linkage relatif à 15 loci sont revues et analysées statistiquement. On distingue les paires de loci où l'appariement semble se faire au hasard de ceux où l'hypothèse du hasard doit être exclue. Le linkage apparaît évident pour les paires de loci *Px* et *R* et *m* et *si*.

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