Genet. Res., Camb. (1983), **42**, *pp.* 169–182
With 1 *plate and* 8 *text-figures*
Printed in Great Britain

Quantitative genetic variation in the skeleton of the mouse

I. Variation between inbred strains

BY D. P. LOVELL[1] AND F. M. JOHNSON[2]

[1] *MRC Laboratory Animals Centre, Woodmansterne Road, Carshalton, Surrey, SM5 4EF, England*

[2] *Laboratory of Biochemical Genetics, National Institute of Environmental Health, Sciences Research Triangle Park, North Carolina 27709, USA*

(*Received 15 March 1983 and in revised form 25 July 1983*)

SUMMARY

A series of six bones from samples of mice from eleven inbred strains and one F_1 hybrid were measured using a simple apparatus. The bones examined were the mandible, os coxae, femur, tibia–fibula, scapula and humerus. Considerable variation in the shape of each bone was found and successful discrimination between the strains was obtained. Correct strain classification ranged from 87 % for the scapula to 98 % for the os coxae. Gross abnormalities and quantitative variants were identified.

As the pattern of discrimination is different for each bone, the use of other bones in addition to the mandible may improve resolution in the identification and quality control of mouse stocks. The objective and precise identification of abnormal and variant bones suggests that the method may be useful for population studies and for the detection of induced skeletal abnormalities in toxicological investigations.

1. INTRODUCTION

The skeleton of the mouse is a source of considerable genetic variation (Grüneberg, 1963). Much of this variation is discontinuous or the result of the pathological effects of mutant genes.

The skeleton, in particular the mandible, has been used for some time in the identification of mouse strains (Festing & Lovell, 1980) and recently for rat strains (Lovell & Festing, 1982). The skeleton has also been proposed as a possible character that could be used in a search for mutant genes showing quantitative effects (Festing & Wolff, 1979). Selby & Selby (1977) have reported that offspring of males subjected to irradiation by γ-rays have skeletal abnormalities resulting from induced dominant mutations and that these mutations are transmissible from generation to generation.

This report is a survey of various inbred strains of mice to examine a series of bones using a technique similar to that developed by Festing (1972) for the mandible. The aim is to detect variation in the skeleton resulting from genetic and environmental causes that can subsequently be used in comparisons between strains, populations and experimental groups.

2. MATERIALS AND METHODS

Skeletons were prepared from groups of inbred strains of mice (Table 1). As in previous studies (Festing, 1972) the mice were killed, eviscerated, boiled for a few minutes and the flesh digested with papain; the selected bones were cleaned with hydrogen peroxide and any remaining fat removed by soaking in acetone. Six

Table 1. *Details of the mice used in this study*

Group	Genotype	Age range (days)	No. of males	No. of females
1	C57BL/6J	71–4	18	18
2	C57BL/6J	111–14	14	18
3	C57BL/6J	Adult*	5	—
4	C57BL/6J	Adult**	12	—
5	DBA/2J	70–4	22	11
6	DBA/2J	110–12	19	9
7	B6D2F$_1$	194	23	15
8	BALB/cJ	70–140	44	—
9	CBA/J	60–158	65	3
10	C3H/HeJ	94–103	4	4
11	P/J	71–126	10	10
12	PL/J	70–84	7	4
13	RF/J	70–129	20	20
14	SM/J	60–85	12	12
15	ST/J	66–99	7	12
16	SWR/J	70–136	14	21
Total			296	157

* Control males treated with buffer only and ** ethylnitrosourea-treated males from experiment reported by Johnson & Lewis (1981).

bones – the mandible, os coxae, femur, tibia–fibula, scapula and humerus – were examined. The bones were placed in a standard way touching two glass slides fixed at right angles over a sheet of 0·25 mm graph paper. The heights and lengths of particular features of the bones were measured using the horizontal and vertical glass slides as baselines. Fig. 1 shows the measurements made on each bone. Only eleven measurements were made of the mandible compared with thirteen made by Festing (1972). The measurements made on the first molar were ignored, and those measurements taken on the scapula do not correspond exactly to those used by Berry, Jakobson & Peters (1978).

All the groups of mice, except one, were derived from the production colonies at the Jackson Laboratories and were purchased during 1979–80 for various studies performed at the NIEHS. One group, the B6D2F$_1$ hybrids, were produced at the NIEHS as part of a programme to investigate the mutagenicity of procarbazine (Johnson *et al.* 1981). The animals were offspring of the control males from this experiment. One of the C57BL/6J groups (No. 4) were from males treated with ethylnitrosourea (Johnson & Lewis, 1981); a second group (No. 3) were from the saline-treated controls.

All animals were offered NIH-32 diet (Ziegler Bros., Inc., P.O. Box 95, Garner, PA 17324) and water *ad lib*. They were maintained under conditions conforming to the AALAS guidelines for the care and maintenance of laboratory animals.

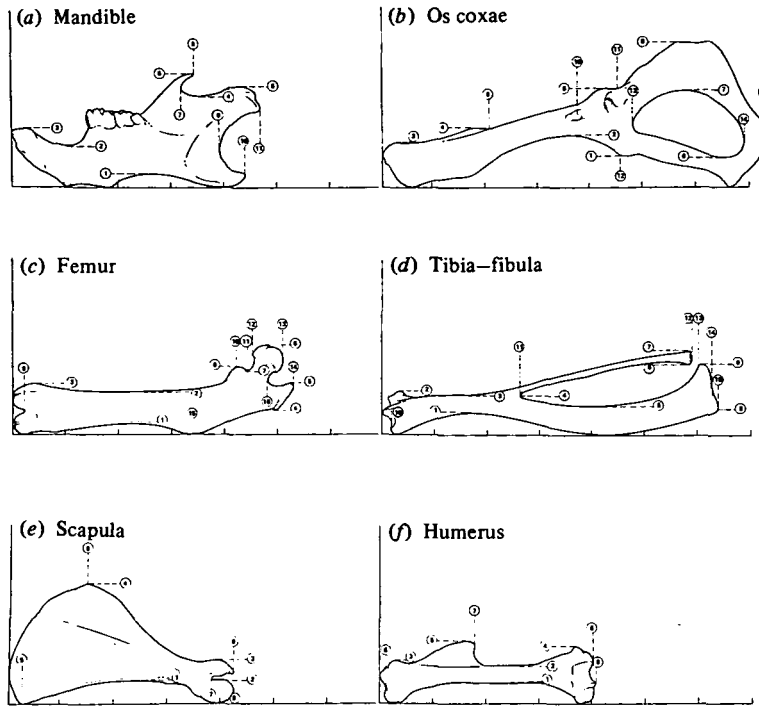


Fig. 1. Measurements made on each (*a*) mandible, (*b*) os coxae, (*c*) femur, (*d*) tibia–fibula, (*e*) scapula, (*f*) humerus. Measurements were made at right angles from the horizontal or vertical base lines to the broken line joining the number to the feature on the bone.

The data collected were analysed using a stepwise discriminant analysis programme BMDP7M. Dixon & Brown (1979) give details of the statistical methods employed. A simple correction for overall size was made by expressing each measure as a proportion of the sum of all the measurements made on that bone (Fig. 2). The analyses were carried out on 29 samples. The C57BL/6J and DBA/2J mice of different ages (groups 1–4) were analysed as separate samples, as were males and females from each strain. Classification in the BMDP7M programme is performed by comparing the generalized Mahalanobis distance (D^2) calculated for each bone with the group means and classifying the bone into that group to which it is nearest. The Mahalanobis D^2 is a measure of the distance between two points representing multivariate data. A more conservative test was also carried out by excluding the bone 'under test' from its group mean and then comparing it with all the group means. This is referred to as the 'Jack-knife' technique. In large samples the distribution of the individual values of Mahalanobis D^2 should approximate a chi-squared distribution, with degrees of freedom equal to the number of measurements used in the discrimination between the groups. All bones that produced Mahalanobis D^2 approaching the appropriate chi-squared value for $P = 0{\cdot}05$ were re-examined to determine why their shape differed from the group mean. A bone was considered abnormal if its Mahalanobis distance from its group mean was greater than the appropriate chi-square value for $P = 0{\cdot}001$.

The BMDP7M programme produced a series of discriminant functions which

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

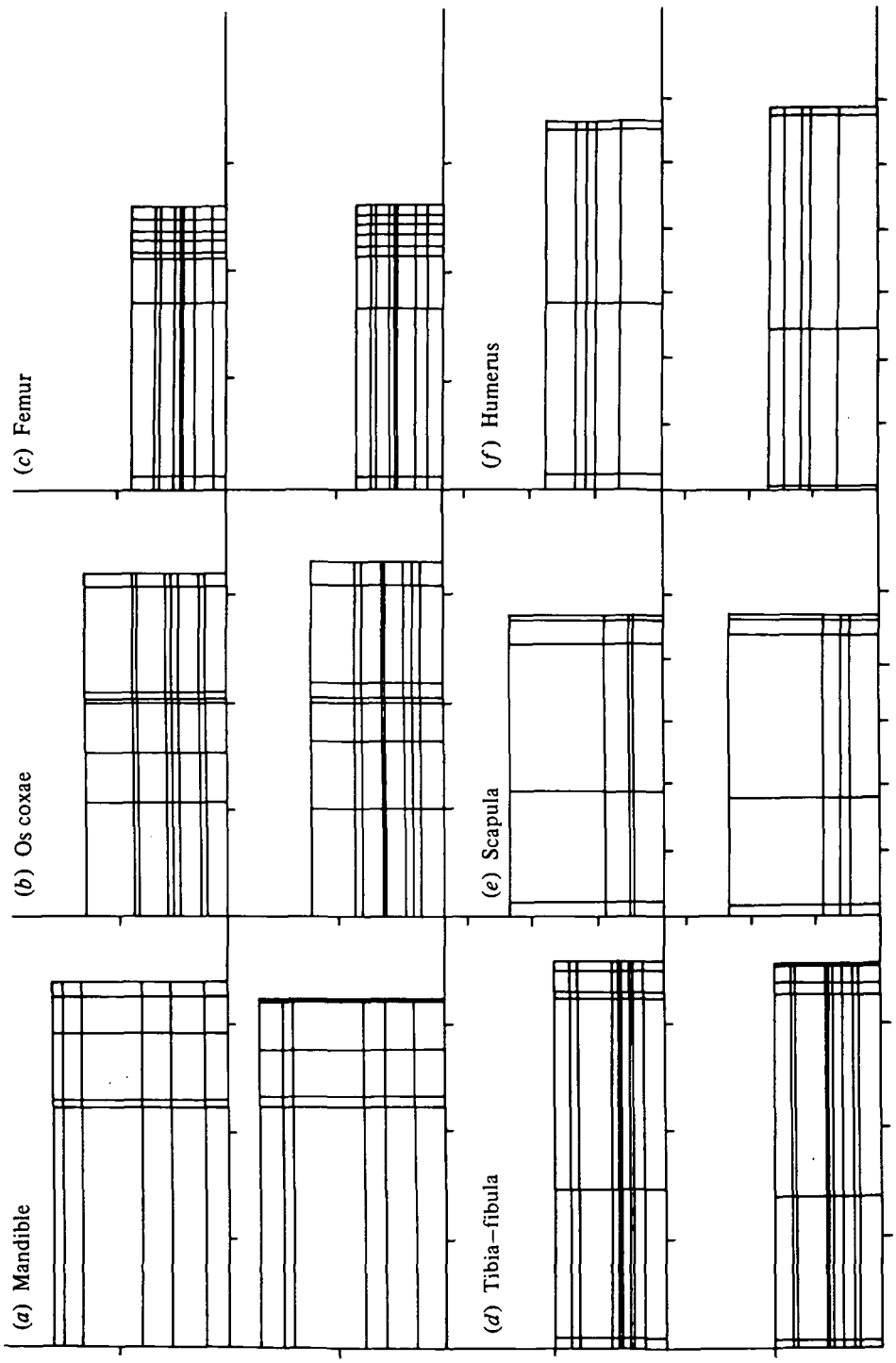


Fig. 2. Diagram of relative mean heights and lengths made on male BALB/cJ (upper) and CBA/J (lower) for each of the six bones. The values for each measurement are expressed as a proportion of the sum of the values and are represented on either horizontal or vertical lines. The division on the axis represents 5% of overall size.

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

give a maximum discrimination between the strains used for each of the six bones. A set of canonical variates (CVI, CVII . . .) which describe bone shape are derived from these functions. A full description of the statistical methods used is given by Kendall (1975).

3. RESULTS

Data from less than 30 out of 453 animals were left out of the analysis of each bone because the bone was either missing, broken or grossly abnormal. All the bones from two animals were excluded; these, a BALB/cJ and CBA/J, were consistently misclassified as from the other strain. It was concluded that the labels had been muddled, as the skeletons were prepared on the same day. Another BALB/cJ mouse had small bones, some of which were abnormally shaped and were left out of the analyses. Three other grossly abnormal bones were excluded; other abnormal bones (D^2 value $P < 0{\cdot}001$) were left in the subsequent analyses.

A total of over 30000 measurements were made and analysed. Fig. 2 shows an example of the differences in shape that exist for each of the six bones between two inbred strains of mice. In this paper the main features of the variation in bone shapes are reported. A further description of the genetic variation found and the discriminant functions produced by the analyses will be the subject of another paper.

There was some discrimination between the different age groups of C57BL/6J and DBA/2J. The proportion of bones misclassified into the wrong age groups but correct genotypes ranged from 23 % with the os coxae to 10 % for the scapula and tibia–fibula. In the results presented below these bones were considered to be assigned to the correct genotypes.

Table 2 and Figs. 3–8 show that successful discrimination was obtained between strains. Discrimination, measured by the successful assignment of an animal to its correct strain (regardless of sex or age group), was most successful with the tibia–fibula (98·4 %). The proportion of bones classified correctly was only slightly reduced when the more conservative 'Jack-knife' technique was used.

Sexual dimorphism was most obvious in the bones of the pelvic girdle and hind limb but less obvious in the mandible, scapula and humerus (Figs. 3–8). The degree of sexual dimorphism appears to depend upon the strain. For instance, a larger difference exists in the shape of the tibia–fibula between male and female $B6D2F_1$ hybrids compared with male and female P/J mice. A fuller analysis of this dimorphism was limited by the small sample sizes of several of the groups. An analysis of the effect of age and sex on the shape of the six bones has been carried out in larger samples from two of the inbred strains, C57BL/6J and DBA/2J, and will be published elsewhere.

The pattern of discrimination between strains is different for each bone. Only the first two canonical variates for each bone (accounting for 57·7–71·6 % of the variation) are shown in the figures, but up to six canonical variates, depending on the bone, are needed to explain 90 % of the variation (Table 2).

Table 2. *Summary of discriminant analyses carried out on each bone*

	Mandible	Os coxae	Femur	Tibia/fibula	Scapula	Humerus
Percentage of animals correctly classified for sex and strain	88·0	98·2	95·4	91·9	75·3	73·5
Percentage of animals correctly classified for strain	96·1	98·2	97·3	98·4	87·4	89·3
Percentage of animals correctly classified for sex and strain using 'Jack-knife'	78·0	96·6	89·1	86·0	67·1	67·1
Numbers of measures used in discrimination	10	13	14	13	8	7
Percentage of total variation explained by first two canonical variates	71·6	58·7	65·1	52·7	69·5	65·7
Total number of bones in study	440	441	439	432	429	441
Number of canonical variates required to explain more than 90% of variation	5	6	6	6	5	4

(i) *Mandible* (*Fig. 3*)

Discrimination between strains was comparable with that found by Festing (1972) and in a survey of inbred strains maintained at the MRC Laboratory Animals Centre (Lovell, unpublished data). There was some discrimination between the sexes, but 8·1% of the bones were misclassified by sex. Males had smaller values than females for CVI but there were also larger strain differences for this canonical variate.

Mice with a larger length/height ratio for the mandible had a higher positive value for CVI; the mandibles of females were slightly more slender than those of males. CVII discriminates between strains by the size of the coronoid and condyloid processes: genotypes such as B6D2F_1 with prominent processes have high values, while C3H/HeJ with small processes have low values.

The mandible of one BALB/cJ mouse was excluded from the analysis as the angle was obviously abnormal and the whole bone reduced in size. Seven per cent of the BALB/cJ and 5% of the CBA/J were outside the $P = 0{\cdot}05$ Mahalanobis D^2 criterion, but no other gross abnormality was detected.

(ii) *Os coxae* (*Fig. 4*)

One male (C57BL/6J) from group 1 was excluded after the gross examination showed that the ischium and pubis were twisted relative to the ilium.

A major sex difference was found: 98·2% of bones were classified into the correct strain and sex. Only two bones from females were misclassified as males. In all

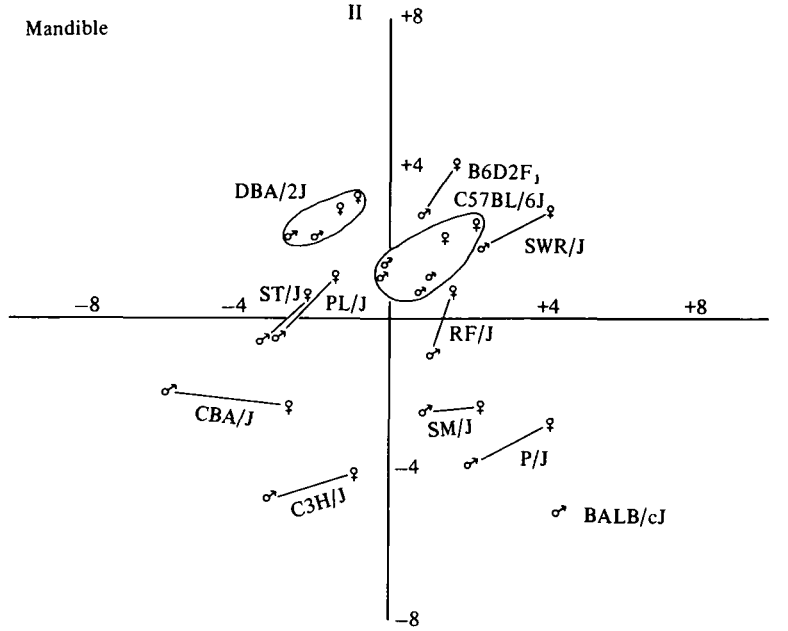


Fig. 3. Graph of CVI against CVII – mandible. Lines have been drawn around the mean values of the C57BL/6J and DBA/2J samples to ease interpretation.

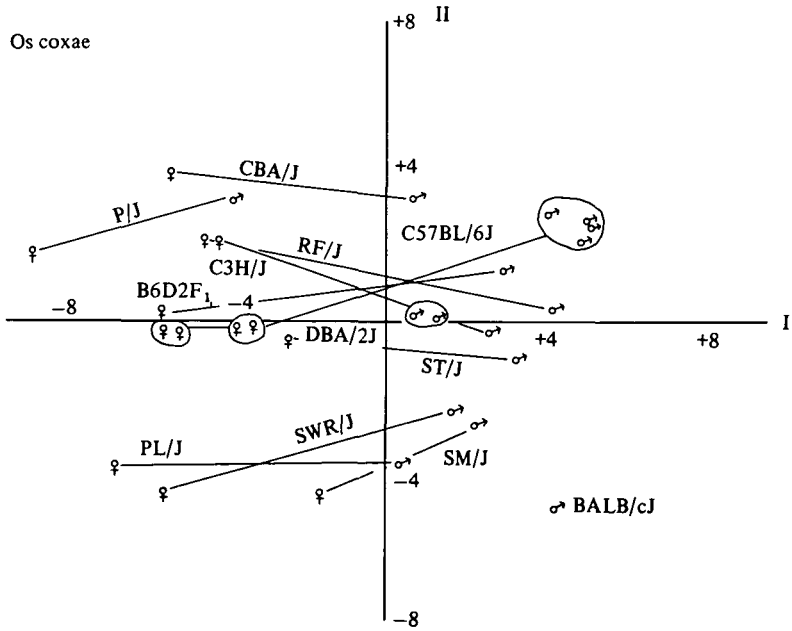


Fig. 4. Graph of CVI against CVII – os coxae.

cases, except strain P/J, males had positive and females negative values for CVI. The first canonical variate gives a large positive value to bones with a small length/height ratio; the os coxae of P/J males are more slender than those of the other genotypes.

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

CVII discriminates between strains by the relative distance between the iliac spine and the acetabulum (measurements 10 and 11) and by the width of the descending ramus (14 and 15). Strains such as CBA/J with high values for CVIII have the iliac spine and acetabulum close together and a wide ramus.

The articular surface of the os coxae with the sacrum was considerably reduced in two male RF/J mice and in one P/J female, which also had a smaller iliac crest.

Female B6D2F$_1$ hybrid mice were highly variable because of differences in the

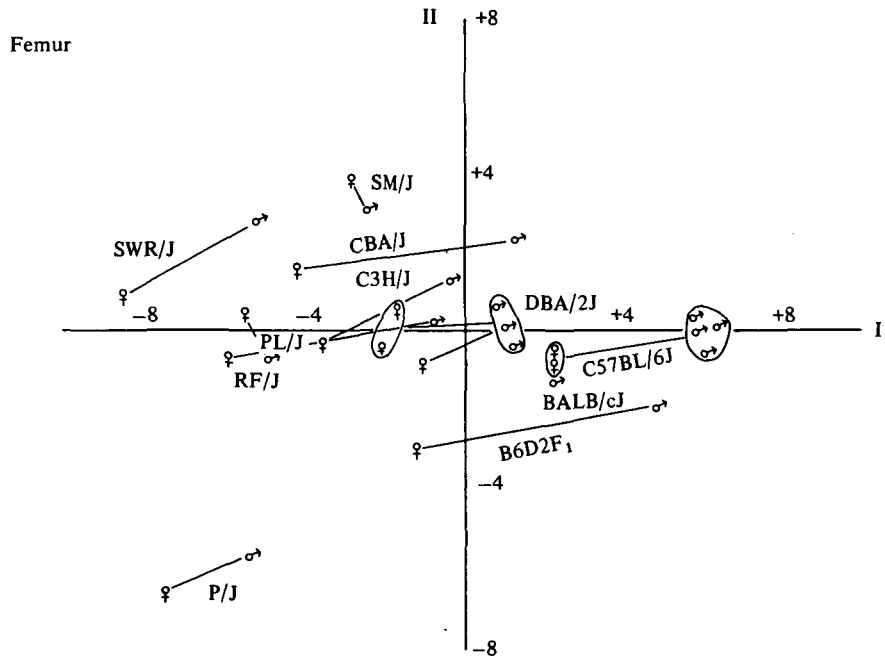


Fig. 5. Graph of CVI against CVII – femur.

width at the pubic symphysis. Some bones were extremely narrow; others had a distinct notch or break at the angle of the pubis. This variation may have resulted from damage during bone preparation but it was only found in female B6D2F$_1$ hybrids. Other possible explanations remain to be investigated. Grüneberg (1952) and Stein (1957) show examples of breaks or dyssymphysis ischio-pubica in the C57BL/Gr strain which are similar to the variants described here.

(iii) *Femur* (*Fig. 5*)

In all 95·4 % of femurs were classified into the correct sex and strain combination. The sex difference was smaller than detected with the os coxae but the CVI values of males were usually larger than those of females. The degree of sexual dimorphism varied among genotypes; strains SM/J and PL/J showed the smallest sex difference and the B6D2F$_1$ hybrid the largest.

Short thick bones have large positive values of CVI. Within a strain, femurs from females are generally thinner and longer. Bones with a large medial condyle and pronounced trochanters have large CVIIs.

Less intra-genotype variation occurred in the femur than in some of the other bones. Only three femurs were outside the Mahalanobis D^2 value for $P = 0{\cdot}001$. One male C57BL/6J had a femur with a large third trochanter, and the femur from a CBA/J male had a large medial condyle and an oddly shaped head. The third bone was from the BALB/c male with the small skeleton. The femurs from the RF/J mice were variable but no distinct pattern of variation was obvious.

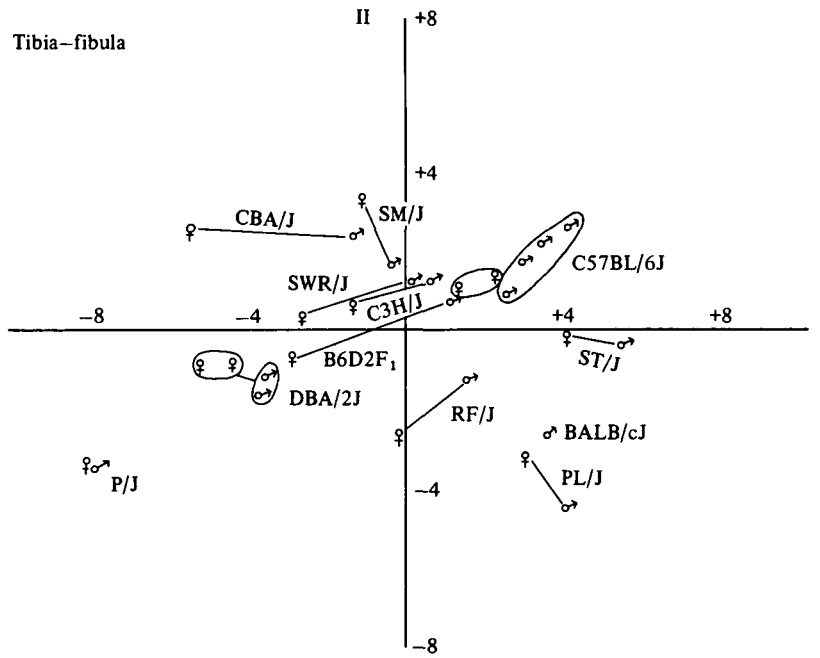


Fig. 6. Graph of CVI against CVII – tibia–fibula.

(iv) *Tibia–fibula* (*Fig. 6*)

One deformed tibia–fibula from a BALB/cJ was excluded from the analysis. Of the remaining bones, 98·4 % were correctly classified by genotype. A sex difference smaller than for the os coxae or the femur was found. The size of the sex difference was dependent on genotype.

Short bones with thick shafts had high positive CVI values. The tibias of males were usually thicker than those of females, resulting in higher CVI values for males. CVII discriminates between strains by the relative curvature of the tibia. A small curvature results in a positive CVII value.

Three strains (BALB/cJ, P/J and RF/J) had a crista tibiae with a small projection towards the head of the fibula. This projection was variable but was not seen in the other genotypes.

Eight bones were detected as outliers using the 0·1 % Mahalanobis D^2 criterion. Four from P/J showed variation in the distance between the head of the fibula and the crista tibiae. The others were from the small BALB/cJ male mentioned earlier, a $B6D2F_1$ male with a large lateral malleus, and two bones (from a CBA/J

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

and a RF/J male) where the fusion of the fibula with the tibia produced a wider angle than normal.

The bones from the BALB/cJ and CBA/J groups were variable because of differences in the size of the lateral and medial mallei and the angle formed by the tibia with the fibula.

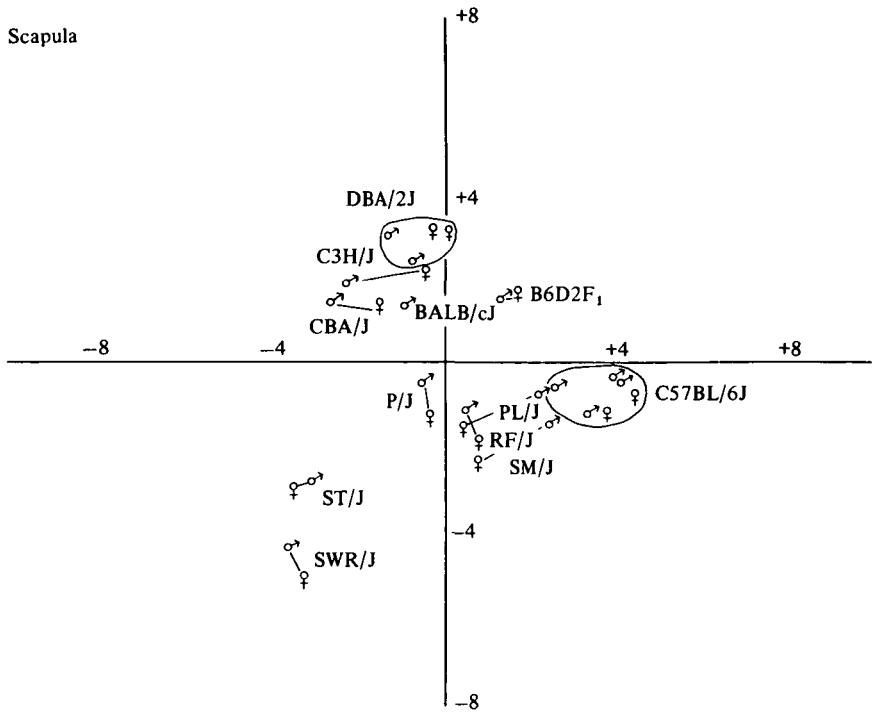


Fig. 7. Graph of CVI against CVII – scapula.

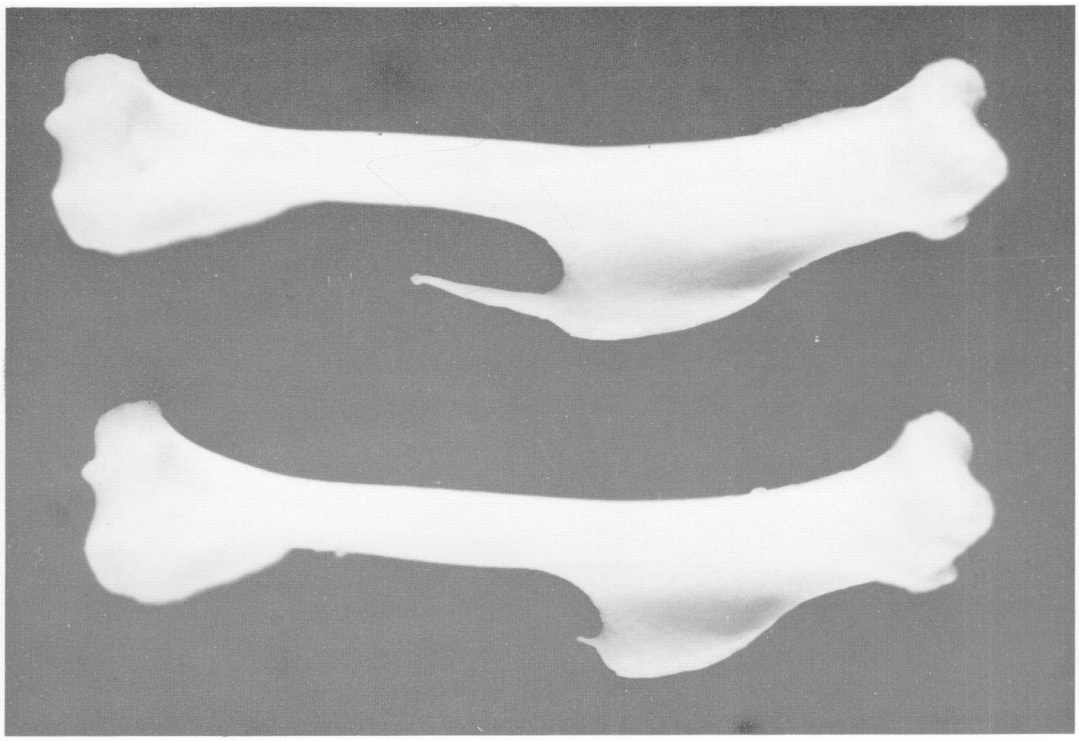
(v) *Scapula* (*Fig. 7*)

The scapula was the poorest of the six bones at discriminating between strains but 87·4 % were classified into the correct genotypes. There was little evidence of any sex difference.

Scapulae with a large height/length ratio had high positive CVI values. CVII discriminates between genotypes by the position of the angulus cervicalis (points 4 and 6 in Fig. 1). Scapulae with a long vertebral margin, which truncates at a distinct angulus cervicalis, have a high CVII.

Some of the genotypes varied in the position of the angulus cervicalis. The vertebral margin in BALB/cJ and RF/J scapulae form a continuous curve with an indistinct angulus cervicalis. A marked angular cervicalis is often found in CBA/J but its position is variable. The size and shape of the acromion in CBA/J is also variable.

Seven bones from males (three BALB/cJ, two RF/J, one CBA/J and one PL/J) were detected as outliers using the 0·1 % Mahalanobis D^2 criterion. All showed variation in the position of the angulus cervicalis. One of the BALB/c males was the small animal mentioned earlier.



Two humeri from BALB/c showing variation in an unusual projection on deltoid tuberosity.

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

(vi) *Humerus* (*Fig. 8*)

A total of 89·3 % humeri were classified into the correct genotype but there was little evidence of a sex difference in shape. Short humeri with a large height/length ratio have a high positive CVI. Genotypes with a prominent deltoid tuberosity have high negative CVIIs. C57BL/6J had large trochleae while P/J and SWR/J had small trochleae.

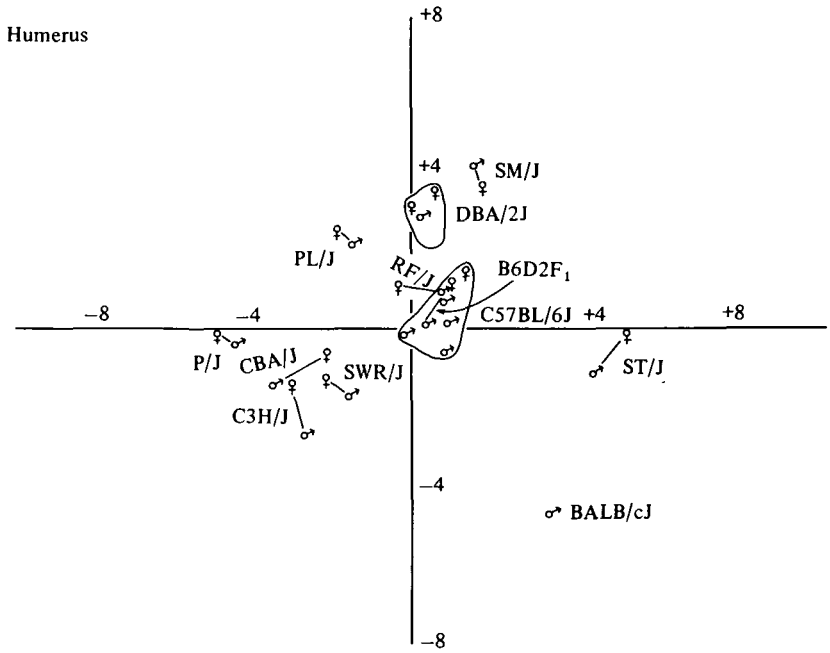


Fig. 8. Graph of CVI against CVII – humerus.

A large proportion of humeri from BALB/c mice had a sharp-pointed projection on the deltoid tuberosity (Plate 1). The projection was variable in size among animals and between sides ranging in length from a distinct 'spike' several millimetres long to a small point on the trochlear edge of the tuberosity. In some BALB/cJ humeri the projection was completely absent. It was not seen in any of the other genotypes. No previous reports of a similar structure were found in the literature.

Six of the eight outliers at the 0·1 % level were BALB/cJ males. Only the small BALB/cJ male of this group did not have the accessory projection. One of the other humeri also had an indentation in the margin of the deltoid tuberosity. The other two variants were a $B6D2F_1$ female with an abnormal head on the humerus and a DBA/2J male with an ill-defined gap between the lesser and greater tubercles.

4. DISCUSSION

Grüneberg (1963) and co-workers have investigated the skeleton of the mouse extensively. Although they found non-metrical variation in many parts of the

https://doi.org/10.1017/S0016672300021637 Published online by Cambridge University Press

skeleton including those bones investigated here, their analyses of quantitative variation were limited. Stein (1957) found considerable variability in the size and shape of long bones of strains A, CBA and C57BL, but did not attempt to quantify the differences between the strains. She writes of the strain differences, 'Like the facial characteristics in man, they are easily recognizable by the trained eye, but they are difficult to measure and it is easier to illustrate the differences by drawings than to describe them in words'. The quantitative methods developed in this study can both measure and describe the variation in shape of a series of bones from a set of genotypes.

Bailey (1956) used quantitative methods to study the genetic and environmental influences on the shape of a single bone, the axis; he extended these methods to an additional three bones in a study of subline divergence within inbred strains of mice (Bailey, 1959). Festing (1972) used a multivariate discriminant analysis to distinguish between inbred strains of mice using the mandible; he also showed that variation in the shape of the mandible could be used to study subline divergence in the C57BL/Gr strain (Festing, 1973). Leamy (1977) and Self & Leamy (1978) have obtained estimates of the heritability of a series of quasi-continuous traits in the skeletons from random-bred mice. Thorpe (1981) has reviewed the use of multivariate methods and morphometrics in the house mouse.

Leamy (1982) applied multivariate methods to analyse the variation in a series of fifteen bone and three body measurements, distinguishing amongst a set of genotypes consisting of inbred strains and F_1 hybrids. The successful discrimination between genotypes obtained with the mandible (Festing, 1972) was repeated in the present study. Comparable levels of discrimination were found with three additional bones, and two others provided moderate separation of genotypes. The variation in bone shape among genotypes is likely to be under genetic control, and represents a rich source of variation for other investigations.

The pattern of discrimination between strains is different for each bone, thus increasing the precision of genetic monitoring methods using the skeleton. Strains which are poorly distinguished by one bone may be separated easily by another. In addition one trait, the accessory spine on the deltoid tuberosity of the humerus, is unique to BALB/cJ mice.

The degree of sexual dimorphism varied among bones. The largest sex difference was found in the os coxae, and large differences were also found in the femur and tibia–fibula. A sex difference was detected in the mandible but not within the humerus and scapula. The sex difference in the shapes of bones is larger in some genotypes than others.

Variation in shape was also found within the strains. Differences in the ages of the animals in the samples may have increased this within-strain variability, although there was no evidence of a systematic effect of age on bone shape after a simple correction had been made for size. The effects of sex and age on the shape of the skeleton are being investigated.

Only a small number of bones were grossly abnormal in shape. Most of the other variant bones were identified by changes in the ratios of their bone measurements. These variants were classified by the Mahalanobis distance (D^2) from the sample mean into one of three groups defined by the D^2 values for the 0·1 %, 1 % and 5 %

probability values. These categories agreed in general with observations on the bone shapes made during measurements. Bones in the first category could be identified as variants during measurement and were defined as abnormal; bones in the second category could be identified during measurement and bones in the third appear to be on the edge of the range of normal values.

Some bones such as the humeri of BALB/cJ and the os coxae of B6D2F$_1$ were particularly variable. Over a quarter of the 1·3 % of bones defined as abnormal by the Mahalanobis D^2 value of $P < 0{\cdot}001$ were from these two samples.

The methods described in this study show that a simple technique is capable of detecting considerable variation in the mouse skeleton, much of which presumably has a strong genetic basis. Stein (1957) also described strain differences in the shape of the ulnae, radii, and clavicles. The approach used here could be extended to these and other bones such as the skull and vertebrae. The inclusion of features not visible in the outline of the bone would detect more variation and further improve strain discrimination.

Taxonomic differences in mice are at present based upon qualitative differences in skull morphology and coat colour (Marshall & Sage, 1981). The investigations of wild mouse populations using the morphometric methods developed in this paper would provide additional information on evolutionary patterns and the relationships between different populations.

Russell (1979) has proposed that the skeleton of the mouse could be used as a system for the detection of chemically induced mutations. Selby (1979) has used the results of his study of γ-radiation-induced skeletal mutations to estimate the genetic risks of radiation to the human populations. The techniques presented here are capable of screening efficiently large numbers of mice for both gross abnormalities and minor variants. An examination of offspring of mice exposed to the potent mutagen ethylnitrosourea is in progress to determine the efficiency of the technique for detecting chemically induced mutations.

The authors would like to thank Debi Leverton and Harriet Burgess for technical assistance, Lorrie Smith and Raye Powell for secretarial help, Lyle Jackson and Julie Foard for preparing the illustrations and Michael Festing for helpful discussions on the data. This work was carried out while one of the authors (David Lovell) was receiving an NIH Visiting Fellowship.

REFERENCES

Bailey, D. W. (1956). A comparison of genetic and environmental principal components of morphogenesis in mice. *Growth* **20**, 63–74.

Bailey, D. W. (1959). Rates of subline divergence in highly inbred strains of mice. *Journal of Heredity* **50**, 26–30.

Berry, R. J., Jakobson, M. E. & Peters, J. (1978). The house mice of the Faroe Islands: A study in microdifferentiation. *Journal of Zoology, London* **185**, 73–92.

Dixon, W. J. & Brown, M. B. (eds) (1979). *BMDP-79 Biomedical Computer Programs P-series.* University of California Press, Berkeley.

Festing, M. F. W. (1972). Mouse strain identification. *Nature* **238**, 351–352.

Festing, M. F. W. (1973). A multi-variate analysis of subline divergence in the shape of the mandible in C57BL/Gr mice. *Genetical Research* **21**, 121–132.

Festing, M. F. W. & Wolff, G. L. (1979). Quantitative characters of potential value in studying mutagenesis. *Genetics* **92**, s173–s179.

Festing, M. F. W. & Lovell, D. P. (1980). Routine genetic monitoring of commercial and other

mouse colonies in the U.K. using mandible shape; five years of experience. 7th ICLAS Symposium Utrecht, 1979, pp. 341–349. Stuttgart: Gustav Fischer Verlag.

GRÜNEBERG, H. (1952). Genetical studies on the skeleton of the mouse. IV. Quasi-continuous variations. *Journal of Genetics* **51**, 95–114.

GRÜNEBERG, H. (1963). *The pathology of development. A Study of Inherited Skeletal Disorders in Animals.* Blackwell Scientific Publications, Oxford.

JOHNSON, F. M., ROBERTS, G. T., SHARMA, R. K., CHASALOW, F., ZWEIDINGER, R., MORGAN, A., HENDREN, R. W. & LEWIS, S. E. (1981). The detection of mutants in mice by electrophoresis: results of a model induction experiment with procarbazine. *Genetics* **97**, 113–124.

JOHNSON, F. M. & LEWIS, S. E. (1981). Electrophoretically detected germinal mutations induced in the mouse by ethylnitrosourea. *Proceedings of the National Academy of Sciences, U.S.A.* **78**, 3138–3141.

KENDALL, M. G. (1975). *Multivariate Analysis.* London: Charles Griffin.

LEAMY, L. (1977). Genetic and environmental correlations of morphometric traits in random bred house mouse. *Evolution* **31**, 357–369.

LEAMY, L. (1982). Morphometric studies in inbred and hybrid house mouse. I. Patterns in the mean values. *Journal of Heredity* **73**, 171–176.

LOVELL, D. P. & FESTING, M. F. W. (1982). Relationships among colonies of the laboratory rat. *Journal of Heredity* **73**, 81–82.

MARSHALL, J. T. & SAGE, R. D. (1981). Taxonomy of the house mouse. *Symposia of the Zoological Society of London* **47**, 15–25.

RUSSELL, W. L. (1979). Comments on mutagenesis risk assessment. *Genetics* **92**, s187–s194.

SELBY, P. B. (1979). Induced skeletal mutations. *Genetics* **92**, s127–s133.

SELBY, P. B. & SELBY, P. R. (1977). Gamma-ray induced dominant mutations that cause skeletal abnormalities in mice. I. Plan, summary of results and discussion. *Mutation Research* **43**, 357–375.

SELF, S. G. & LEAMY, L. (1978). Heritability of quasi-continuous skeletal traits in a random bred population of house mice. *Genetics* **88**, 109–120.

STEIN, K. F. (1957). Genetical studies on the skeleton of the mouse. XXI. The girdles and the long limb bones. *Journal of Genetics* **55**, 313–324.

THORPE, R. S. (1981). The morphometrics of the mouse: a review. *Symposia of the Zoological Society of London* **47**, 85–125.