FLUCTUATING ASYMMETRY IN *Mus musculus* SUBSPECIFIC HYBRIDIZATION

Traditional and Procrustes Comparative Approach

Jean-Christophe Auffray,[1] Paul Alibert,[1] Sabrina Renaud,[1] Annie Orth,[2] and François Bonhomme[2]

[1] Institut des Sciences de l'Evolution, CC064
Université Montpellier II, 34095
Montpellier Cedex, France
[2] Laboratoire Génome et Populations, CC063
Université Montpellier II
34095 Montpellier Cedex, France

ABSTRACT

The traditional approach to fluctuating asymmetry (FA) is compared with an application of the Procrustes superposition method. This comparison was performed on wild-derived and random bred strains of two house mouse subspecies, *Mus musculus domesticus* and *M. m. musculus*, originated from Denmark, and their hybrids in a controlled experiment. Results obtained with the Procrustes method show a decrease of FA for the hybrid sample, which is consistent with what was expected from previous FA studies on wild populations. However, no trend was detectable using the traditional approach in that specific case. Additionally, the observed levels of FA compared with those found in wild populations of the hybrid zone in Denmark suggest that the latter are under higher environmental stress than are laboratory-reared animals.

INTRODUCTION

It has been clearly established that fluctuating asymmetry (FA) which expresses the random difference occurring during development between the right and the left sides of a symmetric bilateral character, increases under environmental or genetic stresses (for a review see Parsons, 1992). This morphological expression is related to reduced developmental homeostasis, suggesting that an intense stress would be sufficient to impair the developmental stability of organisms.

Lerner (1954) formerly hypothesized that heterozygosity may be related to developmental homeostasis and predicted that heterozygosity allows organisms to buffer develop-

Advances in Morphometrics, Edited by L. F. Marcus et al.
Plenum Press, New York, 1996

mental processes (for a review see Mitton and Grant, 1984). Consequently, highly homozygous individuals (e.g., submitted to systematic inbreeding) should exhibit more phenodeviant or asymmetrical characters than do more heterozygous ones. A positive correlation between heterozygosity and developmental stability has often been noted both in strains or natural populations, e.g., in rodents, fishes and lizards (Bader, 1965; Soulé, 1979, Leamy, 1984; Leamy and Atchley, 1985; Leary et al., 1985; Mitton and Grant, 1984). To explain such a correlation, authors have invoked mechanisms of dominance, overdominance or effects due to fortuitous combinations of particular genes (Vrijenhoek and Lerman, 1982; Mitton and Grant, 1984) but, actually, the determinism and mechanism of FA are far from being resolved.

Practically, FA is detectable on meristic or metric characters. FA studies, which are *a fortiori* comparative studies between populations under different levels of environmental or genetic stress, are commonly performed on a set of paired characters. For a single population, each of these characters is treated independently. When combined together, FA levels for all characters give a more or less homogeneous image of FA for the population considered. To test this homogeneity, Soulé (1967) has proposed applying a Kendall test of concordance on FA levels among characters within populations. However, this method remains unsatisfactory because so little is known about the allometric constraints that could mask clear asymmetry patterns.

Bookstein (1991) has proposed a global approach to FA using Procrustes distances between landmark configurations of right and left sides. Using the Procrustes superposition method described by Rohlf and Slice (1990), a single index of FA is obtained per population (instead of one per population per character in the traditional approach), drastically simplifying the statistical synthesis of the FA pattern. The traditional approach to FA may not be performed on scaled material (this depends on the correlation between net asymmetry (*NA*) and the size of the character considered [see Palmer and Strobeck, 1986]) as it is focused on size asymmetry. On the other hand, Bookstein's method clearly measures shape asymmetry by previously scaling all configurations.

The purpose of this paper is to provide an application of the Bookstein Procrustes method and to compare it with the traditional approach. For this study we have chosen a model related to a phenomenon of high evolutionary interest.

According to the current nomenclature of Auffray et al. (1990a), the house mouse (*Mus musculus*) in Europe is subdivided into two subspecies, the Western (*M. m. domesticus*) and Eastern (*M. m. musculus*) house mice. These subspecies have colonized Europe following two different pathways (Auffray et al., 1990b; Auffray and Britton-Davidian, 1992) and have been allopatrically distributed long enough to diverge genetically but only slightly morphologically (Gerasimov et al., 1990; Boursot et al., 1993; Auffray et al., in press). Today, the two subspecies interact along a narrow hybrid zone that crosses all of Europe from Denmark to Bulgaria (Boursot et al., 1984). Although there is no evidence of a reduction in fitness for hybrids in nature, the quasi-absence of introgression for the sex chromosomes (Vanlerberghe et al., 1988; Tucker et al., 1992; Dod et al., 1993) and the higher susceptibility, genetically determined, to parasite infection in hybrid populations (Sage et al., 1986; Moulia et al., 1991, 1993) suggest that hybrid genomes are counter-selected as it is commonly described in narrow hybrid zones (Barton and Hewitt, 1989). However, a morphometrical study across this hybrid zone showed an unexpected reduction of FA towards the center of the hybrid zone in Denmark, suggesting better developmental stability of hybrids than of pure subspecific populations (Alibert et al., 1994). Theoretically, developmental stability in hybrid populations is related to the genetic proximity between hybridizing taxa and should result from a compromise between the stabilizing effect due to increased heterozygosity and the disruptive effect caused by breakdown of genomic coadaptation (Graham, 1992). Such discrepancies between the apparent benefit of hybridization on morphological development and counter-selection of house mouse hybrids could be explained by the decoupling of different biological features (e.g., developmental stability, reproduction and resistance to

parasites). However, due to recurrent crossing between various hybrid combinations, natural hybrid populations are mixtures of complex hybrid recombinants. To evaluate the role of a hybridization between these two subspecies on the F1 hybrid developmental stability, we performed controlled crosses between parental subspecies in the laboratory, hopefully restricting also that way postnatal selective effects on hybrids.

MATERIAL AND METHODS

Mice tested were wild-derived, randombred and maintained for several generations in the laboratory. *Mus musculus domesticus* was represented by the DDO strain, randombred (13th generation) from wild animals of Ødis (Denmark), and *M. m. musculus* by the MDH strain (5th generation) originated from Hov (Denmark). The hybrid sample (F1) was obtained by crossing DDO males with MDH females as well as by the reciprocal crosses. To avoid any parental pair effect, samples were composed of one to three individuals per litter, and one to three litters for nine pairs. We used only males in the three samples to avoid potential sex-related confounding factors. Ages of animals were from 7 to 30 weeks for DDO and MDH, and from 7 to 10 weeks for hybrids.

FA was evaluated on the basis of the lower teeth row. Bader (1965) has already shown that in the house mouse lower molar widths clearly react to strain hybridization through reduction of FA levels. For the traditional approach, four measurements were taken (length and width of M/1 and of M/2, respectively named LM/1, WM/1, LM/2, WM/2); 20 landmarks were determined for the Procrustes method (Fig.1). Sample sizes were respectively 30, 28, and 29 for DDO, MDH and F1.

Data Acquisition

Measurements were taken on a NIKON Measuroscope (1/1000 mm). Landmarks were digitized in two dimensions directly through the microscope using BioScan Optimas version 4.0.

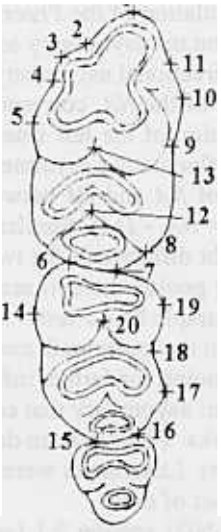

Figure 1. Location of landmarks on the left lower teeth row and on the mirror image of the right

Traditional Approach

The traditional approach to FA is dependent on the type of characters used (meristic character or measurement) and on the sample size. All traditional approaches are exhaustively described in Palmer and Strobeck (1986). In our case, i.e., metric characters with a high sample size (n > 25), the procedure was as follows.

First normality had to be tested for the distribution of the Right - Left (*Ri-Li*) values for each character in the three samples to detect the possibility of antisymmetry (systematic nondirectional deviation from bilateral symmetry). The independence between (|*Ri-Li*|) and the size of the character expressed by (*Ri+Li*) was tested by calculating the coefficient of correlation, *r*, between the two sets of data. An eventual directional asymmetry (systematic, directional deviation from bilateral symmetry) was tested by the application of a mixed-model ANOVA (sides right and left, fixed; genotypes, random). Finally, FA was estimated by the variance of (*Ri-Li*) for each sample.

To detect whether the levels of asymmetry calculated for each parameter are randomly distributed among populations or clearly show a common pattern, it is necessary to apply a Kendall's coefficient of concordance test. Additionally, the main purpose of this study being the comparison between hybrid and parental groups, for any characters for which the parental FA levels were not statistically different, DDO and MDH samples were pooled and compared with the hybrid sample by a *t*-test. Software used for the traditional approach are Statworks version.1.1 and Biomeco version.4.0 (Lebreton et al., 1992).

Procrustes Distances Method

The method is based on the Procrustes superposition (Rohlf, 1990; Rohlf and Slice, 1990), i.e. the best-fitting superposition of several landmark configurations based on Procrustes distances for the calculation of directional and fluctuating asymmetry (Bookstein, 1991).

Briefly, the two sets of landmarks considered here correspond to the left teeth row and the mirror image of the right. The least squares Procrustes superposition method requires that both configurations be previously scaled to unit centroid size. Following the translation and the rotation of one of the sides to a position of best fit to the other, the individual net asymmetry (NA_i) is obtained by the calculation of the Procrustes distance between the two configurations. Afterwards, the population net asymmetry score (*NA*) is given by averaging individual net asymmetries (NA_i). The directional asymmetry (*DA*), which is considered by Bookstein (1991) as being a component of the *NA*, corresponds to the Procrustes distance between the population mean configuration of the left side and that of the right one. The remainder of (*NA-DA*) is the population fluctuating asymmetry (*FA*).

The significance of differences of *NA* and *FA* between populations was tested by one-way ANOVA on NA_i and on FA_i (= NA_i - *DA*). Similarly to the traditional approach, because the means of *FA* and *NA* were not different in the two parental groups, the parental *DA* and *FA* were calculated after having pooled the two samples and were compared with the corresponding values in the hybrid sample by a *t*-test.

As most of the landmarks taken on the lower teeth row of mice belong mainly to type 2 (maxima of curvature) and 3 (extreme point; for further information see Bookstein, 1991), it seemed important to evaluate the part of asymmetry that could be attributed to the lack of accuracy in the determination of landmarks. This has been done by considering only the left sides for one of the populations (hybrids). Landmarks were independently acquired twice, *NA*, *DA* and *FA* being estimated on this set of data.

Generalized Resistant Fit (GRF-ND) version 2.1 (see Slice, "Three-Dimensional" article, this volume) was used for this approach.

RESULTS

Traditional Approach

The independence between (|*Ri-Li*|) and the size of the character estimated by (*Ri+Li*) is shown by the lack of significance of all correlation coefficients calculated for each variable among and within samples (no significant *p*-values with a sequential Bonferroni test [Rice, 1989]). According to Palmer and Strobeck (1986), because there is an independence between (*Ri-Li*) and (*Ri+Li*), no scaling is necessary.

Antisymmetry. The preliminary treatment indicated that all (*Ri-Li*) samples considered here were normally distributed (Lilliefors, sequential Bonferroni test; no significant *p*-values), removing any antisymmetric pattern from our sampling.

Directional Asymmetry. Two-way ANOVAs showed that the means of right and left sides were not significantly different whereas the size of characters differed among samples (Tab. 1). However, because there is no correlation between (|*Ri-Li*|) and (*Ri+Li*), no scaling is required (see above). The non-significant difference of the right and left measurement means expresses the absence of directional asymmetry in our samples.

Fluctuating Asymmetry. According to preliminary analyses, FA may be simply expressed by the variance of (*Ri-Li*) for each population and measurement (Fig. 2). Comparisons of variances, population by population for the four parameters by applying a sequential Bonferroni test per line (pairs of populations compared for all variables) show that only WM/1 exhibits a significant difference between DDO and MDH (Tab. 2). Moreover,

Table 1. Statistical determination of directional asymmetry and size differences between populations by a two-way mixed-model ANOVA (side, fixed; sample, random)

Variable	Sum of squares	df	Mean square	*F*
	0.0007		0.0007	0.58
	0.2686	2	0.1343	108.85**
	0.0003	2	0.0002	0.12
	0.2073	168	0.0012	
	0.0000	1	0.0000	0.040
	0.0442	2	0.0221	26.85**
	0.0001	2	0.0000	0.05
	0.1384	168	0.0008	
	0.0000	1	0.0000	0.01
	0.1264	2	0.0632	60.00**
	0.0003	2	0.0001	0.14
	0.1769	168	0.0011	
	0.0005	1	0.0005	0.54
	0.0155	2	0.0077	8.77**
	0.0003	2	0.0002	0.17
	0.1481	168	0.0009	

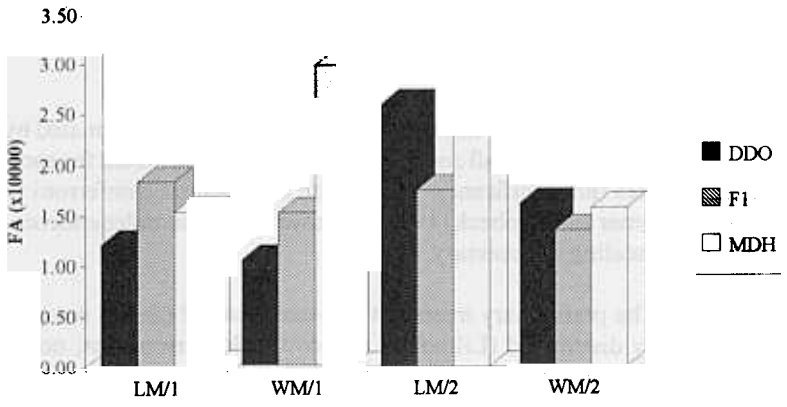

Figure 2. Traditional fluctuating asymmetry (*FA*) levels for the two strains, DDO and MDH, and their F1 hybrids represented for the four measurements considered here (length and width of the two first lower molars M/1 and M/2).

the Kendall test shows independence of rank ($W = 0.344, p > 0.05$), indicating no clear pattern of asymmetry within groups. For all characters except WM/1, a new *FA* value was calculated after having pooled the two parental samples. Comparisons between parental and hybrid *FA* do not provide any significant differences (Table 2).

Although the homogeneous pattern for M/2 indicates a decrease in asymmetry for the hybrid sample, no statistical test could corroborate that result.

Procrustes Superposition

The asymmetry patterns are given in Fig. 3. These results show a lower net asymmetry score for the F1 sample. The lower score also suggests that both *DA* and *FA* are reduced for that sample. ANOVA performed on NA_i distribution within samples shows that the F1 sample presents a reduced net asymmetry ($F = 3.51$, df 2,86; $p = 0.034$). When population *DAs* are respectively subtracted from individual NA_i, the population distributions of the remainders can be considered as the FA_i distribution. In this case, although the p-value is low, there are no significant differences between population means ($F = 2.83$, df 2,86, $p = 0.064$). Both *NA* and *FA* means do not exhibit significant differences between DDO and MDH (*NA*: $t = 0.13$; df = 57; $p = 0.90$; *FA*: $t = 0.042$, df = 57, $p = 0.97$). The two samples were then pooled and *FA* and *NA* recalculated globally for the parental group. Significant differences between hybrid and parental means are shown for *NA* and *FA* (*NA*: $t = 2.7$, df = 85, $p = 0.009$; *FA*:

Table 2. Differences between fluctuating asymmetry (*FA*) levels (i.e., between variances of *Ri-Li*) among populations in the traditional approach

		FAa/FAb		*(FAb/FAa)*	
Groups a-b compared	(Na/Nb)	LM/1	WM/1	LM/2	WM/2
DDO-F1	(30/29)	*1.52*	*1.44*	1.48	1.20
DDO-MDH	(30/28)	*1.27*	*2.82**	*1.24*	1.03
F1-MDH	(29/28)	1.20	*1.95*	*1.83*	*1.17*
<DDO-MDH>-F1	(58/29)	*1.31*	-	1.69	1.24

* $p < 0.05$ sequential Bonferroni test per line

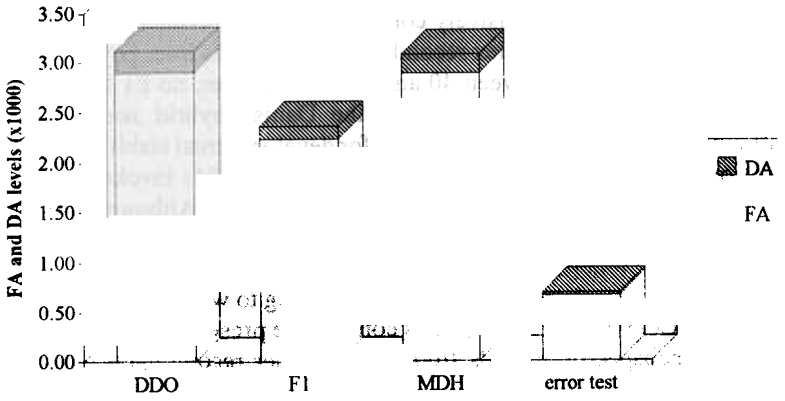

Figure 3. Fluctuating and directional asymmetry (*FA* and *DA*) levels by the Procrustes superposition method for DDO and MDH samples and their F1 hybrids (see text for error sample).

$t = 2.5$, df = 85, $p = 0.013$), clearly expressing a decrease of asymmetry parameters for the hybrid sample as compared with the parental one.

The levels of *NA* and *DA* determined in the error test are relatively important but remain nevertheless low compared with the true asymmetry values.

DISCUSSION

According to the results of Bader (1965) and Alibert et al. (1994) a significant decrease of *FA* was expected for the F1 hybrid sample. In the traditional approach, although not statistically significant, only M/2 measurements suggest this pattern. Using Procrustes superposition, both *NA* and *FA* scores show a significant decrease for the hybrid sample compared with the parental one. Consequently, the Procrustes approach gives results closer to those expected.

Although *DA* is insignificant using a traditional approach, the homologous values in the Procrustes approach are far from negligible; they represent between 5.4 to 7.1% of *NA* values. However, no tests are yet available to evaluate the homogeneity of *DA* among samples.

Practically, in the traditional approach, when four measurements and three populations are considered and compared, 22 tests are, in the simplest case, necessary to perform a statistical treatment for *FA* patterns (four correlations, four normal distributions, 1 two-way ANOVA, 12 variance comparisons and 1 Kendall test). In the Procrustes approach, only two one-way ANOVAs are required to get the same information.

From a biological point of view, the decrease of the *FA* level for hybrids is clearly shown by the application of the Procrustes method. Several experimental studies have already concluded that the developmental stability in strain hybrid mice is increased as compared with that of the parental strains (Leamy, 1984, 1992; Leamy and Atchley, 1985). However, most of these experiments have been performed on inbred strains. A certain heterotic effect in hybrids is usually invoked to explain this pattern, mitigating the destabilizing effect of inbreeding in parental strains. In the present study, the parental samples are randombred and belong to two different subspecies. The higher developmental stability observed in F1 hybrids is similar to the pattern observed in the study by Alibert et al. (1994) on wild

populations of the Danish hybrid zone (see Introduction). The main difference is that the experimental hybrid sample is exclusively composed of F1 individuals whereas the natural hybrid sample is composed of complex recombinant individuals from populations for which the mean hybrid index ranged between 40 and 60%. Moreover, no F1 hybrid between the two pure subspecies has ever been found in the Danish hybrid zone. To explain the discrepancy between the benefit of hybridization for developmental stability and the apparent counter-selection on these natural hybrids, Alibert et al. (1994) invoked a decoupling of consequences of hybridization on different biological functions. Although some of the latter might profit from the heterotic effect of hybridization, others might suffer from the disruption in coadapted genomes. Whereas the disruption of coadapted genomes may not be clearly expressed or detected in F1, there is no evidence according to which heterotic effect may not be expressed in F1. Consequently, our results confirm the presence of heterosis on developmental stability in subspecific hybrids from F1 to further recombinant individuals in the house mouse.

Alibert et al.(1994) performed their study by applying the traditional approach for the calculation of *FA*. *FA* values found in wild populations are higher than those found in the present study (Wilcoxon signed rank test; $Ts = 0$, $n = 12$, $p < 0.001$). However, whereas the decrease of *FA* from wild mice (*M. m. domesticus* and *M. m. musculus*) to their laboratory homologues (DDO and MDH) is respectively of 66.4 and 46%, that decrease from wild hybrids to the F1 sample is only 18%. Bader (1965) did not find any *FA* differences between wild and randombred populations. The lower levels of *FA* found in the laboratory samples compared with those in wild populations may be explained by the environmental stress to which natural populations are subjected. Consequently, the reduction of *FA* due to hybridization is proportionally more important in wild populations than it is for the laboratory-reared animals. This may suggest that the stabilizing effect of heterozygosity is powerful enough to restore the developmental stability of hybrids in nature, despite the apparent environmental stress supported by wild populations.

ACKNOWLEDGMENTS

To Sarah Lenington and Janice Britton-Davidian for stimulating discussions, Guila Ganem for technical assistance and Alfred Zaegel for maintenance of animals. Pub. ISEM N°94-067.

REFERENCES

Alibert, P., S. Renaud, B. Dod, F. Bonhomme, J.-C. Auffray. 1994. Fluctuating asymmetry in the *Mus musculus* hybrid zone: a heterotic effect in disrupted co-adapted genomes. Proceedings of the Royal Society, London, Biological Sciences 258: 53-59.

Auffray, J.-C., P. Alibert, C. Latieule, and B. Dod. Relative warp analysis of skull shape across the hybrid zone of the house mouse (*Mus musculus*) in Denmark. Journal of Zoology, London (in press).

Auffray, J.-C., and J. Britton-Davidian. 1992. When did the house mouse colonize Europe? Biological Journal of the Linnean Society 45:187–190.

Auffray, J.-C., J. T. Marshall, L. Thaler, and F. Bonhomme. 1990a. Focus on the nomenclature of European species of *Mus*. Mouse Genome 88:7–8.

Auffray, J.-C., F. Vanlerberghe, and J. Britton-Davidian. 1990b. The house mouse progression in Eurasia: a palaeontological and archaeozoological approach. Biological Journal of the Linnean Society 41:13–25.

Bader, R. S. 1965. Fluctuating asymmetry in the dentition of the house mouse. Journal of Mammalogy 46:384–388.

Barton, N. H., and G. M. Hewitt. 1989. Adaptation, speciation and hybrid zones. Nature 341:497–503.

Bookstein, F. L. 1991. Morphometric tools for landmark data: geometry and biology. Cambridge University Press: Cambridge.

Boursot, P., J.-C. Auffray, J. Britton-Davidian, and F. Bonhomme. 1993. The evolution of house mice. Annual Review of Ecology and Systematics 24:119–152.

Boursot, P., F. Bonhomme, J. Britton-Davidian, J. Catalan, and H. Yonekawa 1984. Introgression différentielle des génomes nucléaires et mitochondriaux chez deux semi-espèces de souris. Comptes Rendus de l'Académie des Sciences, Paris. 299:365–370.

Dod, B., L. S. Jermiin, P. Boursot, V. M. Chapman, J. T. Nielsen, and F. Bonhomme. 1993. Counterselection on sex chromosomes in the *Mus musculus* European hybrid zone. Journal of Evolutionary Biology 6:529–546.

Gerasimov, S., H. Nikolov, V. Mihailova, J.-C. Auffray, and F. Bonhomme. 1990. Morphometric stepwise discriminant analysis of five genetically determined European taxa of the genus *Mus*. Biological Journal of the Linnean Society 41:47–64.

Graham, J. H. 1992. Genomic coadaptation and developmental stability in hybrid zone. Acta Zoologica Fennica 191:121–131.

Leamy, L. 1984. Morphometric studies in inbred and hybrid mouse. V. Directional and fluctuating asymmetry. American Naturalist 123:579–593.

Leamy, L. 1992. Morphometric studies in inbred and hybrid mouse. VII. heterosis in fluctuating asymmetry at different ages. Acta Zoologica Fennica 191:111–120.

Leamy, L., and W. Atchley. 1985. Directional selection and developmental stability: evidence from fluctuating asymmetry of morphometric characters in rats. Growth 49:8–18.

Leary, R. F., F. W. Allendorf, and R. L. Knudsen. 1985. Inheritance of meristic variation and the evolution of developmental stability in rainbow trout. Evolution 39:308–314.

Lebreton, J.-D., J.-P. Roux, G. Banco, and A.-M. Bakou. 1992. Biomeco (Biometry-Ecology), v. 4.2. Statistical Ecology Software. Centre d'Ecologie Fonctionnelle et Evolutive, CNRS: Montpellier

Lerner, I. M. 1954. Genetic homeostasis. Wiley: New York.

Mitton, J. B. and M. C. Grant. 1984. Associations among protein heterozygosity growth rate, and developmental homeostasis. Annual Review of Ecology and Systematics 15:479–499.

Moulia, C., J.-P. Aussel, F. Bonhomme, P. Boursot, J. T. Nielsen, and F. Renaud. 1991. Wormy mice in a hybrid zone: a genetic control of susceptibility to parasite infection. Journal of Evolutionary Biology 4:679–687.

Moulia, C., N. Le Brun, J. Dallas, A. Orth, and F. Renaud.1993. Experimental evidence of genetic determinism in high susceptibility to intestinal pinworms infection in mice: a hybrid zone model. Parasitology 106:387–393.

Palmer, A. R., and C. Strobeck. 1986. Fluctuating asymmetry: measurement, analysis, patterns. Annual Review of Ecology and Systematics 17:391–421.

Parsons, P. A. 1992. Fluctuating asymmetry: a biological monitor of environmental and genomic stress. Heredity 68:361–364.

Rice, W. R. 1989. Analyzing tables of statistical tests. Evolution 43:223–225.

Rohlf, F. J. 1990. Rotational fit (Procrustes) methods. Pages 227–236 *in* F. J. Rohlf and F. Bookstein, (eds.), Proceedings of the Michigan morphometrics workshop. University of Michigan Museum of Zoology Special Publication 2.

Rohlf, F. J., and D. Slice. 1990. Extensions of the Procrustes method for the optimal superposition of landmarks. Systematic Zoology 39:40–59.

Sage, R. D., D. Heyneman, K. C. Lim, and A. C. Wilson. 1986. Wormy mice in a hybrid zone. Nature 324:60–63.

Soulé, M. E. 1967. Phenetics of natural populations. II. Asymmetry and evolution in a lizard. American Naturalist 101:141–160.

Soulé, M. E. 1979. Heterozygosity and developmental stability: another look. Evolution 33:396–401.

Tucker, P. K., R. D. Sage, J. Warmer, A. C. Wilson, and E. M. Eicher. 1992. Abrupt cline for sex chromosomes in a hybrid zone between species of mice. Evolution 46:1146–1163.

Vanlerberghe, F., P. Boursot, J. T. Nielsen, and F. Bonhomme. 1988. A steep Cline for mitochondrial DNA in Danish mice. Genetical Research, Cambridge 52:185–193.

Vrijenhoek, R. C., and S. Lerman. 1982. Heterozygosity and developmental stability under sexual and asexual breeding systems. Evolution 36:768–776.