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The effects of spontaneous mutation on quantitative traits. II. Dominance of mutations with effects on life-history traits

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Summary

We studied the dominance of the effects of chromosomes carrying unselected mutations on five life-history traits in *Drosophila melanogaster*. Mutations were accumulated on the second chromosome for 44 generations in the absence of natural selection. Traits studied were female fecundity early and late in adult life, male mating ability, and male and female longevity. Homozygous effects were estimated for 50 mutant lines, and heterozygous effects were estimated by crossing these lines in a partial diallel scheme. Direct estimates of dominance showed that the effects of mutants are at least partially recessive. Heterozygotes had higher trait means than homozygotes in all five cases, and these differences were significant for late fecundity and female longevity. For all traits, genetic variance was larger among homozygous crosses than among heterozygous crosses. These results are consistent with those of many other studies that suggest that both unselected mutations and those found segregating in natural populations are partially recessive.

1. Introduction

Most new mutant alleles have deleterious effects on fitness. In random mating populations, the fate of these mutations depends largely on their heterozygous effects on fitness (Simmons & Crow, 1977; Charlesworth & Hughes, 1996), which may be quantified using the dominance parameter, h. If we standardize the performance of the best homozygote to a value of 1, and $1-s$ is the relative fitness of a mutant homozygote, the fitness of the heterozygote may be represented as $1-hs$. When h is 0·5, the mutant acts additively; if $h = 0$, it is recessive. If both h and s are positive, selection will eliminate the mutant from the population. If h is negative, then the wild-type and mutant alleles act overdominantly in combination, and both alleles will persist indefinitely in a large population.

While there is little direct information on the dominance of unselected mutations affecting fitness in any species, many studies have addressed dominance of alleles affecting the important fitness component egg-to-adult viability in *Drosophila melanogaster* (Simmons & Crow, 1977; Charlesworth & Hughes, 1996). Direct estimation of the average dominance of chromosomes bearing new spontaneous mutations (Simmons & Crow, 1977), and of transposon-induced mutations (Mackay *et al.*, 1992), shows that dominance is inversely proportional to the homozygous effects. Lethals are largely, but not entirely recessive, with h averaging about 0·02. Chromosomes which do not carry lethal mutations tend to be more nearly additive in their effects, with h averaging about 0·4 for chromosomes carrying unselected mutations. A wide variety of indirect evidence argues that overdominant mutations are rather rare (Crow, 1993; Charlesworth & Hughes, 1996), although the fact that they would persist for long periods makes it plausible that they may contribute significantly to genetic variation.

Fernández & López-Fanjul (1996) estimated dominance of chromosomes affecting fecundity in a sample of lines which accumulated mutations during 100 generations of brother–sister mating. On the average, chromosomes tested which had significant homozygous effects tended to increase fecundity. The average dominance for these lines was 0·33, but the

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variance in dominance was large, with lines showing underdominant, recessive and dominant effects. There is also a fair amount of information on the dominance of new mutations affecting morphological traits in *D. melanogaster* (Mackay *et al.*, 1992; Santiago *et al.*, 1992; López & López-Fanjul, 1993). While all these studies which have examined the effects of single lines show that on the average mutants tend to have partially recessive effects, they also show considerable variance among chromosomes in their dominance.

The estimates of dominance and average effects for egg-to-adult viability in *D. melanogaster* are widely used in models of the maintenance of genetic variance by mutation–selection balance (Charlesworth & Hughes, 1996). However, since viability probably explains only one-third to one-half of the variance in total fitness (Simmons & Crow, 1977; Mackay, 1986; Charlesworth & Hughes, 1996), there is substantial opportunity for variance in dominance among adult fitness components to alter the overall dominance of alleles for fitness. In this study, we examined the dominance for life-history traits other than egg-to-adult viability of chromosomes carrying spontaneous mutations in *D. melanogaster*. We have previously shown that the mutation-accumulation (MA) lines examined in this study accumulated significant genetic variance in female fecundity and longevity of both sexes (Houle *et al.*, 1994). This provides us with the opportunity to estimate the dominance for unselected mutations affecting these traits.

2. Materials and methods

(i) *Mutation accumulation*

The base population for these experiments, IV, is descended from 21 inversion-free isofemale lines combined in 1977 (Charlesworth & Charlesworth, 1985). Mutations were accumulated on a single second chromosome extracted from this population. The extraction of this chromosome was carried out with the standard balancer combination *SM1, Cy/bw*^{D}, in a background where the X and third chromosomes had been derived from the IV population, and the fourth chromosome was marked with the recessive eye mutation *sparkling-poliert* (*spa*^{pol}) (Houle *et al.*, 1994). Descendant copies of the stem chromosome were independently maintained in heterozygous condition for 44 generations, by backcrossing single male *Cy/+spa*^{pol} flies to the *SM1*, *Cy/bw*^{D}; IV *spa*^{pol} stock. This results in fixation of the mutations in a single generation. Mutations should thus be fixed at very nearly the mutation rate, biased downwards only by the heterozygous effect on viability in non-competitive conditions. Since this is, on average, probably less than the average heterozygous effect on viability in competitive conditions ($< 1\%$, Simmons & Crow, 1977), the discrepancy between the mutation rate and the fixation rate will be small.

Table 1. *Representative diallel crossing scheme, for a hypothetical group of five MA lines*

	Male parents				
Female parents	1	2	3	4	5
1	A, B	**A**			A
2	**B**	**A,B**	**A**		
3		**B**	A, B	A	
4			B	A, B	A
5	B			B	A, B

The two actual diallels performed in this experiment utilized 32 and 18 lines. The letters A and B represent replicate extractions of each line. All homozygous and heterozygous crosses were made within extraction sets. The boldface crosses, all involving MA line 2, represent a group which was dropped during the jackknifing. To jackknife a parameter estimate, all the crosses made with one line were dropped, and the entire analysis performed on the reduced data set. An alternative way of designating jackknife units is represented by the underlined crosses. This jackknifing method proved too liberal in simulations discussed in the Appendix, and was not used on actual data.

Following the accumulation phase, two replicate extractions of each line were rendered homozygous using the balancer. The extractions have a co-ancestry of 0·042 for the third and fourth chromosome, and 0·021 for the X chromosome. Lines which had accumulated a lethal mutation were discarded. Following extraction, lines were maintained for four generations in vials where approximately 30–50 flies were transferred each generation, until these experiments were initiated. Since flies from replicate extractions were always reared together, the extraction effects estimated in subsequent analyses of variance also include effects of parental rearing conditions. Further details of the base population, accumulation procedure and culture conditions are given elsewhere (Houle *et al.*, 1994).

(ii) *Crossing scheme*

We divided the extracted stocks into two groups, which we call sets, with each set containing one extraction from each line. A random sample of 50 mutation accumulation lines from generation 44 were crossed in a partial diallel scheme, as shown in Table 1. Lines were first given arbitrary consecutive numbers, then line 1 was crossed with line 2, line 2 with line 3, etc. The highest-numbered line was also crossed with line 1. Crosses were always made within the same set of extractions. In set A, females from line j and males from line $j+1$ were used as parents of crosses, while in set B line j contributed the male parents, and line $j+1$ the females. Simultaneously, homozygous crosses were also made with the corresponding lines, also by crossing flies from the same extraction. Two diallels were performed, 4 weeks apart, the first involving 32

lines and the second involving 18 lines. Virgin parental flies were crossed when they were between 2 and 6 days post-eclosion, and mated groups were transferred to fresh vials every 3 days to provide sufficient offspring for the phenotypic assays.

(iii) *Phenotypic assays*

We assayed adult longevity, female fecundity and male mating ability. These assays were carried out as previously described (Houle *et al.*, 1994). The following summarizes these procedures. Vials were initiated at a constant density of 4 pairs of flies in each of the two generations prior to the experiment. Offspring were collected for the longevity assay from the first of these vials, and from the third for female fecundity and male mating ability.

Female fecundity was assayed for an individual either at adult age 5 and 6 days, or 27 and 28 days. The sum of day 5 and 6 fecundity for an individual is early fecundity, while the sum of day 27 and 28 fecundity is late fecundity. Females were all mated to males of a standard IV spa^{pol} stock when young, and maintained with these males throughout the assay. Eggs from the first diallel were counted by five different observers, while all eggs from diallel 2 were counted by one of these same observers. Diallel 1 counts were adjusted for counter-effects before data from the data set before analysis.

Male mating was assayed on day 3 post-eclosion. The assay consisted of placing 10 MA and 10 males marked with the X-chromosome recessive mutation *white-apricot* (w^a) in vials with 10 virgin homozygous w^afemales for 2 h. The proportion of mated females which produced wild-type offspring was used as a measure of competitive mating ability.

Longevity of male and female flies was assayed in single-sex groups of 20 virgin flies. Once a week, flies were anaesthetized, and the surviving MA flies counted. Dead flies were replaced with virgin w^a flies to maintain the density of flies at a nearly constant level. The mean survival time of MA flies was used as the index of longevity.

(iv) *Analyses*

Two early fecundity vials and one late fecundity vial were discarded as outliers using Grubb's test (Sokal & Rohlf, 1981). Dominance was estimated as the regression of the outbred phenotype on the sum of the phenotypes of the two corresponding homozygous parental genotypes. This regression was estimated as the ratio of the covariance component between the sum of the two corresponding parental inbred lines and their heterozygous offspring, and the variance of the sum of the parental inbred lines (Mukai & Yamazaki, 1968; Mukai *et al.*, 1972). This estimator results in a weighted average dominance, with the weights consisting of the homozygous genetic effect of each line. It will be unbiased assuming that there is no covariance between the homozygous effect of a chromosome and its average dominance (Mukai & Yamazaki, 1968), and results in estimates biased downwards if, as seems likely, there is a negative covariance between h and s.

Two factors complicate the analyses. First, due to the partial diallel crossing scheme, outbred genotypes were not independent in this experiment. Second, the variance of our estimator of dominance is unclear, as it is the ratio of two variance components. The second problem is amenable to a resampling approach. However, due to the non-independence of heterozygous genotypes in diallel crosses bootstrapping cannot be performed. Resampling would have to be done at the level of lines, and this would require data for crosses which have not been performed. The jackknife method (Sokal & Rohlf, 1981) was therefore adopted to generate estimates of standard errors of inbreeding depression, genetic variance and dominance. To validate this approach, we performed simulations of the experiment and analysis using S-Plus (MathSoft, 1995). These results are shown in the Appendix. On the basis of these results, we chose to jackknife by sequentially removing each homozygous MA line and all the crosses made with it, as shown in Table 1. The simulations suggest that this jackknife method is likely to give accurate to conservative estimates of parameter standard errors, depending on the behaviour of the real parameters.

Estimates of inbreeding depression were calculated from least squares means for inbred and outbred genotypes calculated in the SAS program GLM (SAS Institute, 1990). Variance components were estimated by the MIVQUE0 method in the SAS program Varcomp (SAS Institute, 1990). Covariances were obtained from the variances of the appropriate phenotypic sums. In each analysis, genotypes were nested within diallels, as each genotype only appeared within one diallel.

3. Results

The means and variances for each trait by diallel, and an overall estimate of inbreeding depression are given in Table 2. The results of conventional analyses of variance are summarized in Table 3, and the jackknifed genetic variance components are summarized in Table 4.

For early fecundity there is significant variance among inbred genotypes (see Tables 3 and 4). The difference between homozygous and heterozygous genotypes, especially in diallel 2, is suggestive of heterosis, but is not statistically significant. For late fecundity, heterozygous genotypes had significantly higher fecundities than homozygotes, although the effect of genotype is not significant within either the homozygous or the heterozygous lines alone. For male longevity, there is no evidence for any genotypic

Table 2. *Means* ($\overline{X}$), *sample sizes N and standard deviations by diallel for homozygotes and heterozygotes. The last three columns show the difference between the heterozygous and homozygous population means, along with the probability value for an ANOVA testing for a difference between them, and a standardized estimate of inbreeding depression,* $\delta = (1 - \overline{X}_I/\overline{X}_O)$

		Homozygotes			Heterozygotes			Inbreeding depression		
Phenotype	Diallel	$\overline{X}_I$	N	SD	$\overline{X}_O$	N	SD	$\overline{X}_O - \overline{X}_I$	P	δ
Early fecundity	1	89·4	609	22·179	90·4	600	22·894	4·09	0·15	0·045
	2	82·1	334	24·947	89·9	348	19·388			
Late fecundity	1	46·1	592	20·168	53·2	556	18·453	5·20	0·003	0·105
	2	42·2	302	16·983	45·5	314	16·177			
Male longevity	1	32·5	64	4·753	32·5	64	3·958	0·02	0·98	0·001
	2	29·5	36	4·567	29·5	36	3·754			
Female longevity	1	55·1	64	7·524	57·0	63	5·060	2·00	0·03	0·037
	2	48·7	36	6·702	50·9	35	4·981			
Male mating ability	1	0·712	59	0·144	0·772	63	0·130	0·025	0·42	0·035
	2	0·689	29	0·184	0·672	33	0·172			

Inbreeding depression was tested as the P value for the effect of cross status, in a model including diallel as a main effect, and with genotype as a random effect nested within diallel by cross status.

Table 3. *Analyses of variance for life-history traits*

	Homozygotes			Heterozygotes		
	d.f.	MS	P	d.f.	MS	P
Early fecundity						
Diallel	1	11 254·9	*	1	300·8	
Line	48	2 750·3	**	48	1 533·0	
Extraction/rearing	49	1 225·6	****	48	1 724·6	****
Error	844	377·6		850	347·9	
Late fecundity						
Diallel	1	2 851·6		1	10 677·8	***
Line	48	1 155·2		48	708·9	
Extraction/rearing	48	837·8	****	45	703·0	****
Error	796	288·1		850	265·0	
Male longevity						
Diallel	1	207·43	**	1	201·63	***
Line	48	23·11		48	13·18	
Error	50	20·88		50	16·93	
Female longevity						
Diallel	1	957·11	***	1	802·55	***
Line	48	64·09	†	48	23·15	
Error	50	41·26		48	27·49	
Male longevity						
Diallel	1	0·2714		1	1·7709	**
Line	47	0·2274		48	0·1933	
Error	39	0·1992		46	0·1878	

MS is type III mean square from SAS Proc GLM. In all cases, the analysis was a nested ANOVA, with lines nested in diallels, and extractions within lines. Proc GLM constructs a synthetic denominator mean square for testing purposes, which is not shown. In all cases, the appropriate mean square in the table was close to the synthetic value. For longevity and male mating ability, only a single group of flies was studied for each extraction, so the error term includes extraction/rearing effects. † $0{\cdot}05 < P < 0{\cdot}1$; * $P < 0{\cdot}05$; ** $P < 0{\cdot}01$; *** $P < 0{\cdot}001$; **** $P < 0{\cdot}0001$.

differences at all. For females, heterozygous flies lived significantly longer than homozygotes, while the genetic variance within homozygotes was nearly significant. For male mating, there is also no evidence for a difference between homozygotes and heterozygotes, or of genetic variance. Despite the lack of significant variance for most traits, the homozygous variances from this experiment are all within the 95% confidence limits of estimates from a larger, previous set of experiments (Houle *et al*., 1994).

Examining the overall pattern of results, the difference between heterozygotes and homozygotes is

Table 4. *Genetic variance (V_G) among genotypes, and genetic coefficients of variation ($CV_G = 100\sqrt{V_G}/M$, where M is the trait least-squares mean). Variance estimates were obtained by jackknifing values estimated with the MIVQUE0 method in SAS*

	Among homozygotes			Among heterozygotes		
	V_G	P	CV_G	V_G	P	CV_G
Early fecundity	84·36	0·002	10·70	−12·57	0·61	0
Late fecundity	16·42	0·25	9·14	0·68	0·48	0·91
Male longevity	1·15	0·34	3·46	−1·90	0·81	0
Female longevity	11·33	0·11	6·48	−4·73	0·81	0
Male mating ability	0·0037	0·22	8·82	0·0014	0·37	5·24

Table 5. *Jackknifed estimates of the weighted average dominance of alleles*

		95% confidence limit		
	h	Lower	Upper	d.f.
Early fecundity	−0·03	−0·35	0·29	49
Late fecundity	0·12	−0·52	0·76	47
Male longevity	0·37	−0·82	1·56	49
Female longevity	0·26	−0·10	0·62	49
Male mating ability	−0·07	−1·42	1·28	45
Weighted mean[a]	0·12	−0·17	0·41	

[a] Weighted by the inverse of the jacknife standard error.

always positive, significantly so in two cases. The mean inbreeding depression, δ, is 0·045 over all traits. This suggests that there is heterosis for life-history traits on crossing MA lines. For all five traits, the homozygote genetic variance is higher than the heterozygote variance, and usually this difference is very large. Both these patterns suggest that mutant effects are at least partially recessive.

Estimates of the weighted average dominance of the mutation-accumulation chromosomes (Mukai *et al.*, 1972) are shown in Table 5, along with jackknife confidence limits for these estimates. Overall the results suggest partial recessivity of chromosomal effects. For early fecundity, dominance is significantly less than 0·5. For male mating and male longevity the estimates for the variance of the sum of parental lines are small and near 0, so the dominance values, which use this parental variance in the denominator, have high variance. Assuming that the dominance of mutations is the same for all traits, we calculated the mean dominance, weighted by the inverse of the jackknifed standard errors. This combined estimate of 0·12 suggests that most chromosomes are partially recessive, and the confidence limits rule out additive effects ($h = 0{\cdot}5$). While our estimates never rule out some level of overdominance ($h < 0$), the lack of previous evidence for overdominance (see Section 1) makes it unlikely that the true mean dominance is in this range.

4. Discussion

Our main result is that chromosomes carrying unselected mutations are at least partially recessive in their effects on a suite of life-history traits. Both the average dominance estimate over all traits, and the dominance for early fecundity, are significantly less than the additive value. Our conclusions on dominance are supported both by the tendency for heterozygotes to outperform homozygotes and by the higher genetic variance among homozygotes than heterozygotes.

Previous studies of egg-to-adult viability have estimated that chromosomes carrying new spontaneous or induced mutations with small homozygous effects are partially recessive on average (Simmons & Crow, 1977; Charlesworth & Hughes, 1996). The largest experiments on spontaneous mutations suggest that when lines with large effects are excluded from the analysis, the average dominance is about 0.4 (Mukai & Yamazaki, 1968; Ohnishi, 1977). Our dominance estimates may be somewhat lower because we have not eliminated lines with larger, but non-lethal, homozygous effects, as was done in these studies.

While our direct estimates of dominance reflect solely the impact of unselected mutations, the differences in mean and variance between homozygote and heterozygote populations cannot be unambiguously attributed to new mutations. The homozygous crosses were performed within extractions, where the background on the X, third and fourth chromosomes was somewhat inbred. Extractions were initiated with a single MA male crossed with three virgin balancer females, followed by crossing of approximately 3 male and 3 female offspring. Approximately 6 homozygous wild-type flies were used to initiate the homozygous lines. The autosomal co-ancestry value immediately following these crosses is approximately 1/4, and the X co-ancestry is slightly

higher. On the other hand, our heterozygous crosses necessarily restored heterozygosity in the background as well as the second chromosome. Thus it is possible that the observed heterosis is at least partly due to genetic background. It is important to note that our direct estimates of dominance are not affected by this problem, as these depend only on the genetic variances and covariances.

Despite this, we feel that it is reasonable to suppose that the differences among the homozygous and heterozygous populations mainly reflect the impact of new mutations on the second chromosome. First, we have previously demonstrated significant mutational variance among a subset of these lines for the longevity and fecundity traits (Houle *et al*., 1994). The estimates of homozygous variances here are all within the confidence limits of these older estimates, although most of our new estimates are not significantly different from 0. Therefore, mutations affecting most of these traits were present in this sample of second chromosomes. Second, following the initial crosses, natural selection would reduce the overall co-ancestry of chromosome segments carrying deleterious alleles, as the frequency of these chromosome segments is reduced. There was substantial scope for this reduction in homozygosity, as each extraction was initiated with eight unrelated copies of the third and fourth chromosome, and seven of the X, assuming that all three of the initial females produced offspring. Third, the balancer stock used to extract the MA chromosomes was bottlenecked several times prior to being used to extract these chromosomes, so it probably did not have levels of background variance as high as those in a typical outbred population (Houle *et al*., 1994).

Regardless of the source of the heterosis we observe, our results do help to extend the range of traits for which inbreeding depression has been observed in *Drosophila melanogaster*. Previous studies have tended to focus either on egg-to-adult viability, or on measures of 'total' fitness (Simmons & Crow, 1977; Charlesworth & Charlesworth, 1987). It is clear from studies of total fitness that viability accounts for perhaps only one-third of the total inbreeding depression, and thus that other fitness components must play a major role (Charlesworth & Hughes, 1996). Hughes (1995) has recently summarized data showing that a substantial part of this additional inbreeding depression is due to male traits, including mating ability and male longevity. We have confirmed for the first time that inbreeding depression extends to female longevity. A small number of studies have previously shown inbreeding depression for female fecundity (Simmons & Crow, 1977), consistent with our results.

Appendix. Simulation of jackknifed dominance estimates

To validate our use of jackknife standard errors, we performed a series of simulations of the accumulation process and estimation procedure. We simulated experiments using 20 MA chromosomes. Each chromosome was assigned a mutation number from a Poisson distribution with mean 5. Each mutation was assumed to decrease the phenotype by 2% in the homozygous condition. The dominance of each chromosome was drawn from a normal distribution with mean h and standard deviation σ_h. Phenotypes were then generated by adding a random normal deviate with standard deviation σ_E to the expected phenotype. Chromosomes were crossed in the same partial diallel scheme as used in the experimental study: every chromosome was studied in the homozygous condition, and in crosses with two other chromosomes. Each homozygous and heterozygous cross was represented by two replicate phenotypic values. The range of σ_E values simulated spans a range of cases with high to rather low power to estimate h.

In Table A 1 we show the results of some analyses of these simulated data. We studied average dominance values of 0, 0·2 and 0·4; however, only those for $h = 0{\cdot}2$ are shown in Table A 1. For all parameter combinations, the regression technique estimated h without bias, with the mean estimate over replicates always closely approximating the true value (results not shown). The column labelled $\sigma_{\hat{h}}$ presents the standard deviation of estimates of h over replicate simulations.

Table A 1. *Results of jackknife analyses of 200 sets of simulated diallel data*

σ_h	σ_E	J.M.	$\overline{h}_j$	$\sigma_{\hat{h}}$	σ_{h_j}	$\overline{S.E.}_j$	Type I error rate
0·00	0·33	1	0·200	0·010	0·015	0·016	0·020
		2	0·199	0·010	0·010	0·010	0·080
	1·00	1	0·196	0·031	0·034	0·048	0·015
		2	0·198	0·031	0·031	0·032	0·060
	3·00	1	0·268	0·183	0·283	0·320	0·005
		2	0·105	0·183	1·445	0·260	0·060
0·03	0·33	1	0·198	0·028	0·032	0·037	0·025
		2	0·199	0·028	0·028	0·022	0·095
	1·00	1	0·199	0·039	0·045	0·060	0·015
		2	0·198	0·039	0·040	0·038	0·070
	3·00	1	0·068	0·376	8·341	0·893	0·010
		2	0·429	0·376	8·161	0·578	0·035
0·10	0·33	1	0·198	0·090	0·103	0·110	0·035
		2	0·198	0·090	0·091	0·063	0·130
	1·00	1	0·195	0·093	0·106	0·123	0·030
		2	0·196	0·093	0·094	0·072	0·115
	3·00	1	0·295	0·201	1·595	0·377	0·000
		2	0·082	0·201	1·773	0·308	0·030

J.M. is the jackknife method used. See text for explanation of other symbols.

In jackknifing (Sokal & Rohlf, 1981), one divides the data set into n (usually independent) sets of data. Each set consisting of $1/n$ of the data is then dropped, in turn, from the data set, and the remaining data analysed in its absence. The variation in estimates obtained from these reanalyses is then used to construct an estimate of the standard error of the parameter of interest. As indicated in the text, the non-independence of the data in this case suggest the desirability of comparing estimates of jackknife standard errors with the actual standard error of the estimating process. An additional issue is how to delineate the jackknife sets. Two methods were examined in these simulations, and are shown in Table 1. In method 1, the jackknife unit was the MA line, and both the crosses performed with this line. A unit of this type is shown in Table 1 as the bold-faced crosses. In method 2, the jackknife unit was the MA line, and only one of the two crosses performed with this line. A unit of this type is shown in Table 1 as the underlined crosses. Method 1 is expected to be more appropriate if the variance in dominance among chromosomes is a major source of estimation error. On the other hand, this method removes more than $1/n$th of the data at a time. It may result in standard error estimates which are too large. Method 2 does remove $1/n$th of the data in each set, but does not eliminate all the data involving an MA line. Both methods inevitably leave the jackknifed data sets less balanced than the original one.

Table A 1 gives the mean of the jackknifed dominance estimates, $\overline{h}_j$, the standard deviation of the jackknifed estimates σ_{h_j}, and the mean jackknife standard error over simulations, $\overline{S.E.}_j$. Of these standard errors, $\sigma_{\hat{h}}$ is the underlying quantity we would like to estimate. In comparison with this, σ_{h_j} indicates the amount of additional error which is introduced by using the jackknife technique. $\overline{S.E.}_j$ is the only measure of error which can be estimated from a real experiment. In addition, we would like to know the realized type I error rate associated with using $S.E._j$. This is indicated in the last column as the number of cases where the realized average dominance (which is not exactly h in cases where $\sigma_h > 0$), falls outside the 95% confidence limits, $h_j \pm t_{0{\cdot}05[n-1]} \times S.E._j$. The expected value of h did not affect these error rates, so only results for $h = 0{\cdot}2$ are presented.

When the error variance is less than the maximum value in these simulations, the jackknife methods perform quite well. The mean estimate is always close to the true value, with no indication of bias, and the standard deviation of jackknifed estimates is only slightly higher than the standard deviation of unjackknifed estimates. However, with the largest amount of error variance, both the mean estimate and the variation over simulations behave poorly. Examination of the results of each simulation reveals that this behaviour is due to a small number of cases where the jackknifed estimates are wildly inaccurate. These are cases where the homozygous line variance is quite small, leading to estimates of h with very large absolute values, which are very unstable upon jackknifing. For example, for the parameter combination $\sigma_h = 0$, $\sigma_E = 3$, examination of the raw results shows that two of the 200 cases were outliers. The most extreme of these data sets yielded dominance estimates of 2·1, 18 and -20 for the unjackknifed, method 1 and method 2 estimates respectively. Dropping these two pathological cases results in estimates of $\overline{h}_j = 0{\cdot}17$, $\sigma_h = 0{\cdot}12$, $\sigma_{h_j} = 0{\cdot}12$ and $\overline{S.E.}_j = 0{\cdot}19$. for jackknife method 1. Similar results are obtained by dropping the small number of pathological estimates for other cases where $\sigma_E = 3$.

The results for $\overline{S.E.}_j$ suggest that jackknife method 2 is too liberal in conditions where variation in h among chromosomes is a relatively large source of variance. This is most evident when σ_E is small, and μ_h is large. This is also reflected in the type I error rates. In the cases where σ_E is small, and σ_h is large, method 1 is close to the desired 5% error rate, while method 2 gives rejection rates as high as 13%. Interestingly, the small number of pathological estimates never lead to type I errors, as the standard errors for these cases are always very large. In cases where σ_E is large and σ_h is small, method 1 becomes too conservative and method 2 performs well. Since we do not know the true value of σ_h, and it may be large (see Section 1), we chose jackknife method 1 as the more appropriate.

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