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The population genetic structure of the facultatively sexual parasitic nematode *Strongyloides ratti* in wild rats

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We have investigated the population genetic structure of the parasitic nematode *Strongyloides ratti* in wild rats. In the UK, *S. ratti* reproduces predominantly by mitotic parthenogenesis, with sexual forms present at a rate of less than 1%. *S. ratti* was found to be a prevalent parasite and substantial genetic diversity was detected. Most rats were infected with a genotypic mixture of parasites. A hierarchical analysis of the genetic variation found in *S. ratti* sampled across Britain and Germany showed that 73.3% was explained by variation between parasites within individual hosts and 25.3% by variation between rats within sample sites. Only a small proportion (1.4%) of the total genetic variation was attributable to genetic subdivision between sample sites, suggesting that there is substantial gene flow between these sites. Most parasites sampled were found to exist in Hardy–Weinberg equilibrium and this population genetic structure is discussed in view of the virtual absence of sexual reproduction.

Keywords: *Strongyloides ratti*; nematode; population genetics; genetic variation; recombination; parasite

1. INTRODUCTION

Parasitic helminths exist in an ecologically patchy environment (Price 1980). Hosts are spatially and temporally discrete habitats and parasites are partitioned between hosts. *A priori*, the genetic structure of helminth populations will be dependent on the rate of crossing between helminth genotypes within and between hosts. The rate of crossing will therefore be dependent on the effective rate of migration of helminth genotypes between host patches (Saul 1995). Factors that reduce this movement will favour the genetic subdivision of the helminth population and, conversely, factors that favour movement will prevent genetic subdivision.

The epidemiological distribution of parasitic nematodes, especially those of human and domesticated animals, is well described and understood from empirical and theoretical studies (Anderson & May 1992). In contrast, there is strikingly little information on the genetic structure of such populations (Blouin *et al.* 1995). The epidemiological information is of limited use without a good understanding of the genetic structure of the parasite populations (Anderson & May 1992). This is especially so when attempting to understand how traits, such as genetic resistance to anti-parasitic agents, will arise and spread through the parasite, and hence host, populations. Understanding the genetic variation of parasite populations will also be useful in the theoretical consideration of coevolution of host and parasite genotypes (Lively & Apanius 1995).

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There have been only a small number of studies that have investigated the population structure of parasitic nematodes by comparing the genetic variation of parasites from different sample sites. Studies of *Ascaris suum* in pigs, using randomly amplified polymorphic DNA and isoenzymes, from five sites in the midwestern USA (Nadler *et al.* 1995) found some evidence of inbreeding within sample sites as well as some genetic differentiation between sample sites. A study of mitochondrial DNA (mtDNA) from *Ascaris* in pigs and humans across three sample sites in Guatemala found significant differentiation between sample sites (Anderson *et al.* 1995). Studies of mtDNA diversity across the USA of *Ostertagia ostertagi* and *Haemonchus placei* from cattle, *H. contortus* and *Teladorsagia circumcincta* from sheep, found that these parasites had high levels of genetic diversity with no evidence of genetic subdivision between sample sites. In contrast, a parasite of white-tailed deer, *Mazamastrongylus odocoeli*, was found to be highly genetically subdivided between different sample sites (Blouin *et al.* 1995). High rates of migration of domesticated animals, through human action, compared with the relatively static population of white-tailed deer suggested that the genetic subdivision of the parasite population was a function of host movement. Thus, parasite population subdivision is prevented by host movement (which promotes parasite mixing) and, conversely, subdivision is favoured by less host movement (Blouin *et al.* 1995). These studies revealed little information on the parasite population genetic structure within sampling sites because, with the exception of the study of *Ascaris* in Guatemala (Anderson *et al.* 1995), sampling occurred over large geographical areas with little sampling within sites.

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In this study we measured the distribution of genetic variation between hosts within, and between, sample sites by investigating the population genetic structure of *Strongyloides ratti*. *S. ratti* is a parasitic nematode that is amenable to such studies for a number of reasons. It is an endemic parasite of rats throughout the world and can thus be sampled readily. In addition, the genetic events that occur during its complex life cycle have been experimentally determined. Because of this, it is possible to non-invasively sample larvae passed from hosts, and from this infer directly the genotypic composition of the intestinal parasites without destroying the hosts or the parasitic stages.

Strongyloides ratti has two adult generations. The obligate parasitic generation is female only and reproduces by mitotic parthenogenesis (Viney 1994). The facultative free-living adult generation is dioecious and reproduces by conventional meiosis and syngamy (Viney *et al.* 1993). Eggs that are produced by the parasitic female pass out of the host in the faeces. These eggs can develop by one of two routes, called homogonic and heterogonic. In the former, the larvae moult through two stages into infective third stage larvae (iL3s). In heterogonic development, the eggs produced by the host moult through four larval stages into free-living adult males and females. Their progeny moult through two larval stages into iL3s, as in homogonic development. Heterogonic development is restricted to a single generation. All iL3s are committed to infecting a host, which they do by penetration of the skin. The route by which larvae develop is different between different isolates (Viney *et al.* 1992), is a heritable trait affected by environmental conditions (Viney 1996) and by the immune status of the host (Gemmill *et al.* 1997).

One consequence of this life cycle is that it can be completed with or without the occurrence of sexual reproduction. Thus, parasites that develop solely by the homogonic route reproduce exclusively by mitotic parthenogenesis. Conversely, those that develop by the heterogonic route alternate between sexual and parthenogenetic reproduction. Isofemale lines of isolates of *S. ratti* from the UK develop almost exclusively by the homogonic route and thus only reproduce by mitotic parthenogenesis (Viney *et al.* 1992). One potential consequence of this is that the genotype frequencies of such populations may substantially deviate from those predicted by the Hardy–Weinberg equilibrium. Many parthenogenetic organisms have highly structured populations because of the absence of the homogenizing effect of sexual reproduction. For example, studies on temperate cyclical parthenogenetic populations of *Daphnia pulex* show a range of population structures depending on the frequency of sexual reproduction. In small temporary ponds, sexual reproduction is frequent such that genotypes are in Hardy–Weinberg equilibrium and clonal diversity is high because of the mixing of parental genotypes (Hebert 1974*a*). In permanent ponds, sexual reproduction is infrequent and genotypes deviate from Hardy–Weinberg proportions (Hebert 1974*b*).

Here we investigate the population genetic structure of *S. ratti* in wild rats in relation to the partitioning of parasites (i) within and between hosts; and (ii) within and between different geographical sample sites. In this manner the extent of population subdivision is characterized and the breeding structure measured.

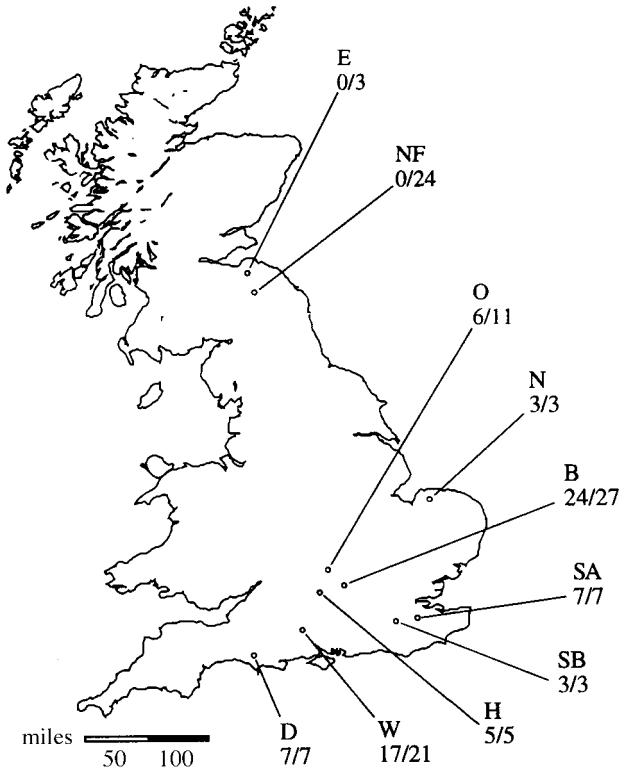

Figure 1. Map of Great Britain showing the location of the sample sites. The number of infected rats/number of rats sampled is shown below the site designation. Locations: B, Berkshire; D, Dorset; E, Edgefield; H, Hedley; N, Norfolk; NF, Nether Fala; O, Oxford; SA, Surrey A; SB, Surrey B; W, Wiltshire. The German sample sites (A, Asbeck; S, Sendenhorst) are not shown.

2. MATERIALS AND METHODS

(a) *Parasite sampling*

Rattus norvegicus were trapped from 11 rural UK farms (figure 1) using live-catch cage traps (Killgerm) between January 1995 and August 1995. Rats were trapped in Germany by Dr H. Pelz (Federal Biological Research Centre, Munster) between February and September 1995. After capture, trapped animals were maintained individually and faecal material collected from each rat over a 12-h period. Faecal cultures were made from 6 g of faecal material and maintained at 19 °C (Viney *et al.* 1993). Infective third stage larvae (iL3s) were harvested from three-day-old cultures, washed twice in distilled water and stored individually in 5 µl of distilled water at −20 °C. A maximum of 20 larvae were collected from each rat. DNA preparations of single iL3s were made as previously described (Viney 1994).

(b) *Genotyping*

All sampled iL3s were genotyped by PCR-restriction fragment length polymorphism (PCR-RFLP) analysis for three polymorphic loci: Actin, BSP-8 and CM-2. BSP-8 and CM-2 are anonymous loci that had RFLPs within a pilot sample of laboratory-maintained UK isolates of *S. ratti* (data not shown). BSP-8 was amplified using primers BSP-8 F: 5′-CCTAGTGGCATTATTCTCG, BSP-8 R: 5′-CACCTAGTGGAAATCCAG with 40 cycles of 95 °C for 1 min, 52 °C for 1 min and 72 °C for 2 min. CM-2 was amplified using nested PCR; the first round primers were CM-2 F: 5′-TGGTGATGTTAACGCATTCG, CM-2 R: 5′-TTATGCATTAGTTTCAGCAGG; second round primers were CM-2 F2: 5′-CAGCAATACGCAATACCTGG,

CM-2 R2: 5′-TGAAATCTCTTGAAGGCAGC. The first round reaction was cycled 30 times through 95 °C for 1 min, 52 °C for 1 min, 72 °C for 2 min, and 1 µl of this reaction was used as the template for the second round reaction, which was cycled 35 times using the conditions from the first round cycle. Actin was amplified as previously described (Viney 1994). All PCR reactions were done in a 50 µl volume in 1X PCR buffer (Cambio) supplemented with magnesium to a final concentration of 1.5 mM, with primers at a final concentration of 100 nM and dNTPs at a final concentration of 75 µM. Following amplification, five units of the appropriate restriction enzyme were added directly to the PCR reaction, which had been supplemented with the supplied restriction enzyme buffer, and incubated at 37 °C. The RFLPs were detected with *Hinf* I, *Hae* III (Promega) and *Mnl* I (New England Biolabs) for BSP-8, CM-2 and Actin, respectively. Digested PCR products were visualized on 2% w/v agarose gels and the genotypes scored. Any ambiguity in genotype was resolved by repeated genotyping.

(c) *Data analyses*

RFLP genotype frequencies were calculated for the iL3s sampled from each rat, for the pooled iL3s from each sample site, and for the pooled iL3s from the total data set. A measure of genetic diversity was calculated by determining the number of unique three-locus genotypes passed by each rat.

Departure from Hardy–Weinberg expectations for each locus for (i) each rat from which 12 or more iL3s had been genotyped, (ii) for each sample site, and (iii) for the pooled population, were performed. Between-locus genotypic linkage disequilibria were estimated. Calculations were done by using GENEPOP v. 1.2 (Raymond & Rousset 1995*b*) and sequential Bonferroni tests to correct for the effects of numerous comparisons as previously described (Rice 1989).

The distribution of genetic variation was assessed by the use of hierarchical *F*-statistics (Wright 1951). The samples collected in this study were considered in a three-level analysis of variance (ANOVA) with the following hierarchies: (i) I—the individual iL3; (ii) R—the individual rats; and (iii) S—the sample sites. *F*-statistics were estimated according to Weir & Cockerham (1984) for $\hat{\theta}_S$ (the genetic variation between sample sites), $\hat{\theta}_R$ (the genetic variation between rats within sample sites) and $\hat{\theta}_I$ (the genetic variation between iL3s within rats) using the Genetic Data Analysis program (Weir 1996). Significance values of $\hat{\theta}$ were determined by permutation tests as described by Excoffier (Excoffier *et al.* 1992). Genetic isolation by distance was tested by correlating pairwise values of $\hat{\theta}_S$ between sample sites with geographical distance, the significance of the correlations being determined by Mantel tests using the statistical package NTSYS (Rohlf 1990). Because of small sample sizes, the German samples were excluded from these calculations.

These analyses (previous paragraph) were done on data obtained from iL3s that were passed from infected rats. Thus, the sample population is the parasites that were destined to contaminate the environment in the next generation rather than the population of parasitic females within the rats *per se*. To estimate the genetic structure of these parasitic females, the data set was recalculated to remove resampling of multiple iL3 progeny of individual parasitic females. This clone-adjusted data set was created by recording only one of each unique genotype detected within one rat. This data set was fully analysed as described in the previous paragraph, with the exception that the between rat-within sample site ($\hat{\theta}_R$) level of analysis was omitted because of reduced sample sizes.

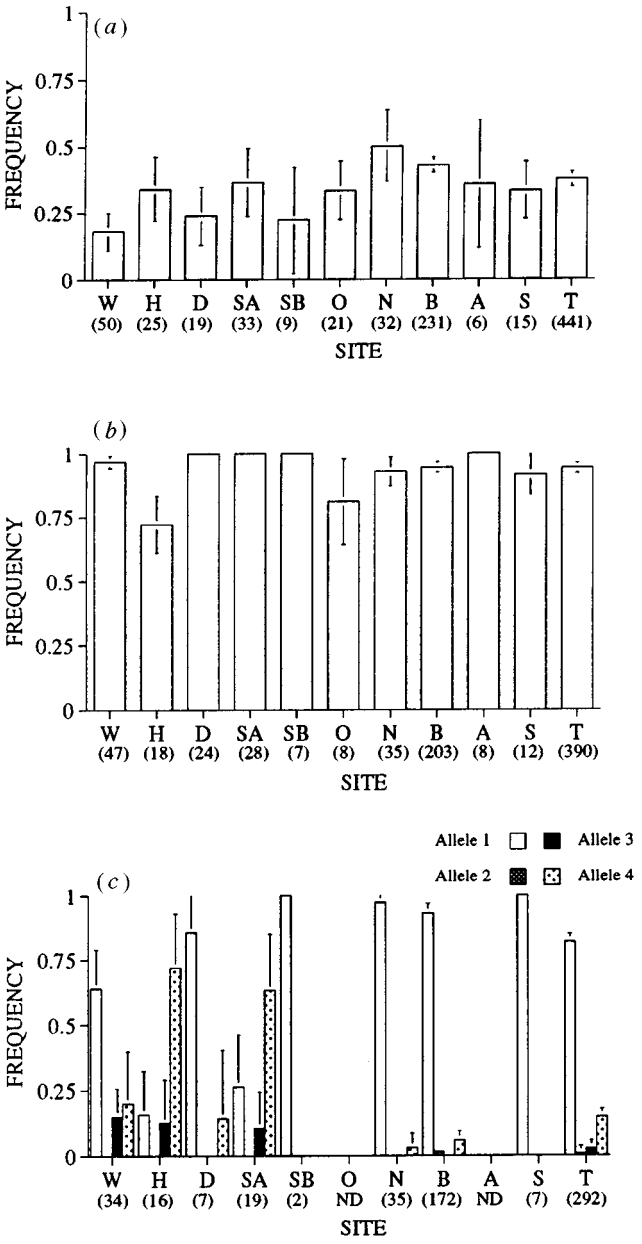

Figure 2. Allele frequency distribution by sample sites. A, Actin allele 2; B, BSP-8 allele 1; C, CM-2 alleles as shown. Error bars are 95% confidence intervals. Sample sizes of the number of iL3s are shown in parentheses under sample site designation. T represents total data set of all sample sites combined. ND represents no data.

3. RESULTS

The number of rats sampled and the number of those infected from each sample site is shown in figure 1. A total of 121 rats from 11 sites were trapped and sampled. The overall prevalence of infection was 62% (s.d.=40). None of the 27 rats sampled in Scotland were infected; among the rats sampled from the south of England the prevalence of infection was 79% (s.d.=26). A total of 1472 iL3s were collected with a mean of 19 iL3s per rat, of which 741 iL3s were successfully genotyped for one or more loci.

The allele frequencies for each locus at each sample site are shown in figure 2. The mean allele frequency for all sample sites combined was 0.374 for allele 1 of Actin,

Table 1. *Observed (H_o) and expected (H_e) heterozygosities for each locus at each sample site*

(Values in parentheses are standard errors. An asterisk signifies that H_o is significantly different from H_e at $p<0.01$, and thus that the genotypes are not found in Hardy–Weinberg proportions. Rules (—) indicates that no data are available.)

		sample site										
		Britain								Germany		
locus		W	H	D	SA	SB	O	N	B	A	S	All sites
Actin	H_o	0.320 (0.063)	0.520 (0.090)	0.474 (0.103)	0.364 (0.070)	0.222 (0.150)	0.476 (0.098)	0.375 (0.080)	0.779* (0.029)	0.714 (0.064)	0.667 (0.045)	0.609* (0.023)
	H_e	0.295	0.440	0.361	0.463	0.346	0.444	0.500	0.490	0.459	0.444	0.468
BSP-8	H_o	0.064 (0.044)	0.556 (0.071)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.375 (0.107)	0.143 (0.051)	0.108 (0.021)	0.000 (0.000)	0.167 (0.071)	0.115 (0.012)
	H_e	0.062	0.401	0.000	0.000	0.000	0.305	0.133	0.103	0.000	0.153	0.109
CM-2	H_o	0.000* (0.000)	0.063* (0.033)	0.000* (0.000)	0.000* (0.000)	0.000 (0.000)	—	0.000 (0.000)	0.023* (0.010)	—	0.000 (0.000)	0.017* (0.008)
	H_e	0.486	0.443	0.245	0.521	0.000	—	0.056	0.131	—	0.000	0.305
all loci	H_o	0.128* (0.060)	0.379* (0.079)	0.158 (0.103)	0.121* (0.070)	0.074 (0.150)	0.284 (0.100)	0.173 (0.070)	0.304* (0.028)	0.238 (0.064)	0.278 (0.045)	0.247* (0.021)
	H_e	0.281	0.431	0.202	0.328	0.115	0.250	0.229	0.241	0.153	0.199	0.294

0.943 for allele 2 of BSP-8 and 0.816, 0.001, 0.010, 0.125, respectively, for alleles 1, 2, 3 and 4 of CM-2. There is little variation in the allele frequencies of the Actin and BSP-8 loci between sample sites (see figure 2). The allele frequencies of the CM-2 locus are more variable between sample sites. In particular, sites H and SA have noticeably high frequencies of allele 4 compared with all other sites. Inspection of the raw data revealed that the high frequency of allele 4 at these sites was, in both cases, almost exclusively owing to one rat at each site (HA 267 and SA 30A). The clone-adjusted data set shows essentially the same distribution for all loci (data not shown). Of 24 possible tests for pairwise locus linkage disequilibria within each sample site, 12 showed no significant linkage disequilibria at $p<0.01$. It was not possible to perform 12 of the tests because of fixed alleles or insufficient sample sizes.

The observed and expected heterozygosities for each locus and each sample site are shown in table 1. The mean heterozygosity for all loci for all sampled sites combined is 0.247 (s.e.m.=0.021), which is significantly different from the expected heterozygosity ($p<0.01$). Analysis of the clone-adjusted data set showed that the same sample sites deviate from Hardy–Weinberg expectations with the exception that site D no longer deviated significantly at the CM-2 locus (data not shown).

The heterozygote deviation (table 1) was owing to the effect of the Actin and CM-2 loci. In the case of Actin, this resulted solely from an excess of heterozygotes at site B. Exclusion of site B from the analysis showed that at the Actin locus, all other sites combined were in Hardy–Weinberg equilibrium. Closer analysis of the Hardy–Weinberg deviation seen at site B on an individual-rat basis is shown in figure 3. This shows that all but four of the 24 infected rats from this sample site contain an excess of heterozygote genotypes, nine of which deviate significantly from Hardy–Weinberg expectations at $p<0.05$.

For the CM-2 locus, five of the sample sites significantly deviated from Hardy–Weinberg expectations (table 1). All of these deviations resulted from a deficit of heterozygotes. Indeed, only 1.75% of the iL3s genotyped at this locus were heterozygotes. Such a pattern at a single locus is suggestive of the existence of a null (non-amplifying) allele (Callen 1993; Pemberton *et al.* 1995) or of selection against heterozygotes. CM-2 could not be amplified from the laboratory isofemale line ED132 Heterogonic (Viney 1996), even though the Actin and BSP-8 loci could be successfully amplified from the same DNA preparations, whereas all three loci could be readily amplified from other laboratory isofemale lines (data not shown). The use of other primers to the CM-2 locus did not allow amplification of CM-2 from isofemale line ED132 Heterogonic (data not shown). This evidence shows that there is a null allele of CM-2 and that this may be owing to the deletion of the locus, rather than point mutations within the sequence of the primer targets. The CM-2 heterozygote deficit seen suggests that this null allele is present at a high frequency within the sampled populations.

The results of the hierarchical ANOVA are shown in table 2. For all loci combined, 73.3% of the total variation is explained by the variation between iL3s within a rat, 25.3% due to variation between rats within a sample site, and 1.4% by variation between sample sites. Thus, there is little geographical genetic subdivision among the worms sampled. The clone-adjusted data set showed that for all loci and sample sites combined the proportion of the total genetic variation explained by variation between sample sites and within sample sites was 9.3% and 90.8%, respectively (significant at $p<0.01$). There was no evidence of genetic isolation by distance ($p>0.05$) for either all loci combined or Actin and BSP-8 combined. This was unsurprising, given the relatively small degree of variation between sites (table 1).

The number of unique genotypes found in individual rats is shown in figure 4. The maximum number of unique genotypes found was five. The mean number of genotypes per rat was 2.34 (s.d.=1.07).

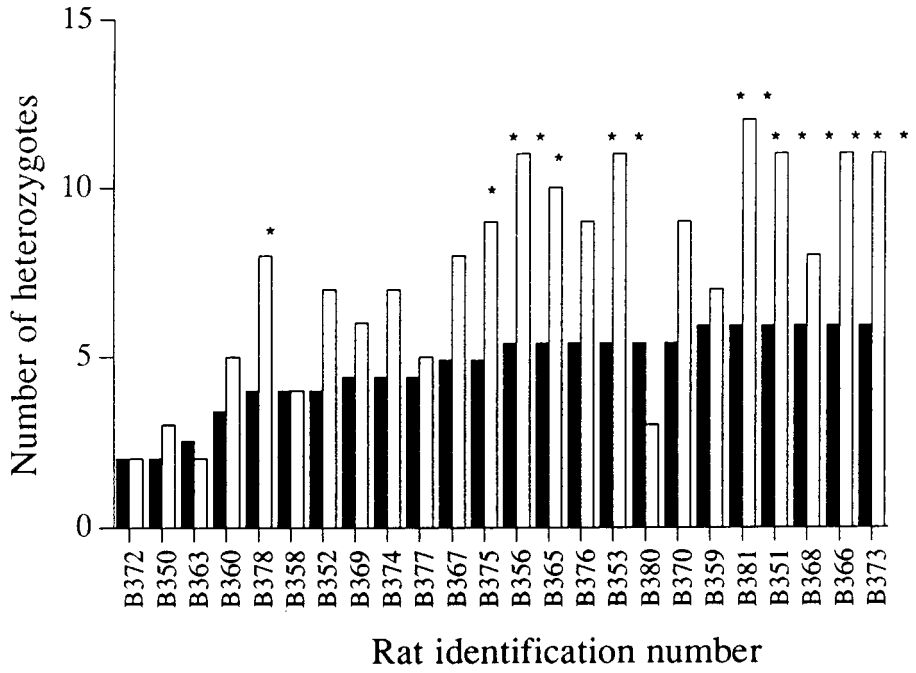

Figure 3. Observed (open bars) and expected (closed bars) numbers of heterozygotes at the Actin locus from each rat sampled at site B. Significant heterozygote excess at $p<0.05$ and $p<0.01$ is shown by * and **, respectively.

Table 2. *ANOVA between iL3 samples from eight sample sites*

(Hierarchy $\hat{\theta}_S$, between sample sites; $\hat{\theta}_R$, between rats within sites; and $\hat{\theta}_I$, between iL3s within rats. Note: d.f., degrees of freedom; variance-mean squares variance at each level of the hierarchy. $^{*}=p<0.05$ and $^{**}=p<0.01$.)

locus	hierarchy	d.f.	variance	% of total variation
Actin	$\hat{\theta}_S$	7	−0.026	−6.04
	$\hat{\theta}_R$	57	0.047	4.69**
	$\hat{\theta}_I$	781	0.611	95.31**
BSP-8	$\hat{\theta}_S$	7	0.005	4.77*
	$\hat{\theta}_R$	49	0.004	8.65**
	$\hat{\theta}_I$	691	0.114	86.58**
CM-2	$\hat{\theta}_S$	6	0.033	12.37**
	$\hat{\theta}_R$	32	0.143	66.10**
	$\hat{\theta}_I$	531	0.017	21.53*
all loci	$\hat{\theta}_S$	7	0.012	1.44*
	$\hat{\theta}_R$	61	0.194	25.30**
	$\hat{\theta}_I$	1091	0.742	73.26**

4. DISCUSSION

S. ratti is a common parasite of rats in the UK. We have been able to detect substantial genetic variation in *S. ratti* at three nuclear loci. Analysis of the distribution of this variation along a geographical range of 300 miles among the three hierarchies of the analysis detected little genetic subdivision between sample sites, but greater genetic subdivision between rats within a sample site. This is consistent with the parasites sampled being composed of one interbreeding population. In view of this it was unsurprising that no genetic isolation by distance could be detected. This pattern of genetic variation is similar to that found for parasites of domesticated animals sampled from across the USA (Blouin *et al.* 1995), although populations of *Ascaris* have more genetic structure than found in this study (Nadler *et al.* 1995; Anderson *et al.* 1995). The absence of any subdivision between *S. ratti* from different sample sites suggests that the effective rate of parasite transfer between sample sites, and hence between rats, is sufficient to prevent the generation of genetic subdivision. Mark–recapture studies of wild rats has found that most rats are recaptured within 20–25 m of the original capture site (Glass 1989). However, there is some indication that juvenile males are ostracized by the colony alpha males, which then disperse (Barnett 1952). These individuals may therefore act as an agent of geographical dispersion, and hence gene flow of *S. ratti*, possibly in addition to other mechanisms of phoretic dispersal. Population genetic theory shows that only low levels of migration are necessary to prevent genetic differentiation within a species (Slatkin 1987).

We have sampled intensively within the sample-site level, to a greater degree than in other studies. This has revealed that there is some genetic differentiation between rats within sample sites (table 1). This is similar to the observations of genetic structuring at the between-host level in *Ascaris* in pigs and humans (Anderson 1995). At site B, all rats share worms of similar genotype, as shown by the distribution of heterozygous Actin genotypes across all rats (figure 3). This is good evidence of cross-infection between individual rats within a sample site which will have the effect of homogenizing the parasite population structure within sample sites.

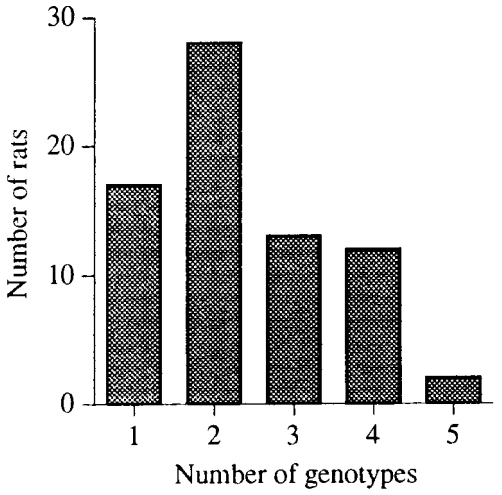

Figure 4. Histogram showing the number of unique three-locus genotypes found in rats.

Most rats contained mixed genotype infections. Parasitic nematodes of vertebrates reproduce sexually in the host's gut, and thus when parasites are partitioned between hosts there is a probability that all the parasites within a host will be of one sex or of one genotype. This scenario clearly does not apply to *S. ratti* because of its unusual life cycle. However, these data show that mixed genotype infections are common which, when extrapolated to other nematodes, suggests that there will be good opportunities for cross-genotype matings.

The parasite population that we have sampled has a genetic structure consistent with it being a single interbreeding population. Clearly, this is not so since parasites sampled from the UK develop almost exclusively by the homogonic route and thus reproduce by mitotic parthenogenesis (Viney *et al.* 1992). Furthermore, 14 parasite isolates from six sample sites used were introduced into the laboratory to measure directly the relative proportions of heterogonic and homogonic development that occurred (M. C. Fisher and A. Gemmill, unpublished observations). This confirmed that 99.4% of the worms develop by the homogonic route, and only 0.6% of the worms were able to undergo sexual reproduction. Therefore, it would appear that this very low level of sexual reproduction, presumably over a sufficient number of generations, is able to generate a population that is in Hardy–Weinberg equilibrium. Theoretical studies have shown that even rare sexual reproduction is sufficient to bring allele frequencies into Hardy–Weinberg equilibrium (Maynard Smith 1989).

The sampling of iL3s passed from hosts is non-invasive and does not destroy the hosts or the parasitic stages. This approach has two advantages over sampling adult parasites artificially purged from hosts. First, repeat samples can be taken from animals over time rendering longitudinal studies possible. Second, the actual sample is the infective stages that will contaminate the environment. Thus, parasites that are not contributing to the next generation are not represented in the sample. However, numerous sampling of genetically identical iL3 progeny of a single parasitic female may occur. To correct for this potential bias a clone-adjusted data set was constructed. Analysis of this showed all the same patterns of population genetic structure as the primary data set. This validates the method of sampling and analysis that we have used.

Site B showed deviation from Hardy–Weinberg equilibrium with a significant excess of heterozygotes. It is probable that in this population insufficient sexual reproduction has occurred to bring the allele frequencies to equilibrium proportions. It is possible to envisage a scenario in which a founding parasite population colonizes a host population. This parasite population would expand predominantly by mitotic parthenogenesis, such that the population genetic structure continues to deviate from equilibrium proportions. The low level of sexual reproduction would, over a number of generations, bring the population into the equilibrium proportions seen at all neighbouring sites. The excess of heterozygotes seen for this locus at site B may also be due to selection for the heterozygote genotype. However, this seems unlikely given that the heterozygote excess was seen only at this site and that *a priori* there is no reason to expect actin genes to be under such selection pressure.

The high frequency of allele 4 of CM-2 at sites H and SA (figure 2) is almost exclusively owing to the parasites sampled from just two rats (H 267 and SA 30A). This clearly distinguishes the parasite of these animals from the other rats in these, and surrounding, sample sites. These parasites may represent the introduction of a new parasite genotype into an existing parasite population. Following on from the scenario described above, this parasite genotype may, by chance, go extinct from these sites or may spread through the host population and, over time, interbreed with the other parasite genotypes. Indeed, that this CM-2 genotype is found in association with all observed Actin and BSP-8 genotypes suggests that such interbreeding has already occurred.

The previously reported population genetic structure of nematode parasites of domesticated animals (Blouin *et al.* 1995; Nadler *et al.* 1995) has been extended here to a parasite of wild rodents. This suggests that this type of genetic structure may be the general structure of all nematode parasites of land vertebrates. Nematode parasites are physically partitioned between host patches and, epidemiologically, all helminth populations are overdispersed so that most of the parasites exist in a minority of the hosts. In spite of this remarkable degree of population structuring, there is essentially no genetic structuring of the parasite populations. These apparently contrasting situations are likely to be a result of the constant flux, by the persistent loss of parasites and the persistent reinfection of hosts, of the parasite population. A practical consequence of this is that any genetic trait, such as resistance to anti-parasitic agents, will spread through the parasite population without hindrance.

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