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Demographic history of a recent invasion of house mice on the isolated Island of Gough

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Abstract

Island populations provide natural laboratories for studying key contributors to evolutionary change, including natural selection, population size and the colonization of new environments. The demographic histories of island populations can be reconstructed from patterns of genetic diversity. House mice (*Mus musculus*) inhabit islands throughout the globe, making them an attractive system for studying island colonization from a genetic perspective. Gough Island, in the central South Atlantic Ocean, is one of the remotest islands in the world. House mice were introduced to Gough Island by sealers during the 19th century and display unusual phenotypes, including exceptionally large body size and carnivorous feeding behaviour. We describe genetic variation in Gough Island mice using mitochondrial sequences, nuclear sequences and microsatellites. Phylogenetic analysis of mitochondrial sequences suggested that Gough Island mice belong to *Mus musculus domesticus*, with the maternal lineage possibly originating in England or France. Cluster analyses of microsatellites revealed genetic membership for Gough Island mice in multiple coastal populations in Western Europe, suggesting admixed ancestry. Gough Island mice showed substantial reductions in mitochondrial and nuclear sequence variation and weak reductions in microsatellite diversity compared with Western European populations, consistent with a population bottleneck. Approximate Bayesian computation (ABC) estimated that mice recently colonized Gough Island (~100 years ago) and experienced a 98% reduction in population size followed by a rapid expansion. Our results indicate that the unusual phenotypes of Gough Island mice evolved rapidly, positioning these mice as useful models for understanding rapid phenotypic evolution.

Keywords: Approximate Bayesian computation, colonization, demography, House mouse, Island, *Mus musculus domesticus*

Introduction

Populations that successfully colonize islands often show rapid divergence in morphology, physiology and behaviour relative to their mainland counterparts (Adler & Levins 1994; Millien 2006; Keller & Taylor 2008; Estoup & Guillemaud 2010). These observations, combined with the fact that island colonizers typically encounter novel environments, have inspired biologists to use them as model systems for understanding

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adaptation (Keller & Taylor 2008; Losos & Ricklefs 2009). Island populations also provide insight into the role of effective population size in evolution because colonization usually involves substantial bottlenecks (Foster 1964; Frankham *et al.* 2002). From a conservation management perspective, studying island colonization reveals the conditions that favour the spread of invasive species (Dlugosch & Parker 2008; Estoup & Guillemaud 2010). Colonization patterns on isolated islands are particularly informative because evolution proceeds without the complicating factor of gene flow from mainland populations.

House mice (*Mus musculus*) are a model system for understanding island colonization, particularly from the perspective of invasive species (Berry *et al.* 1982; Berry 1996). They are listed among the 100 worst invasive species in the world (International Union for Conservation of Nature, Species Survival Commission Invasive Species Specialist Group; http://www.issg.org/worst100_species.html) and are distributed on all continents except Antarctica. Humans are the only mammalian species with a more extensive global distribution than house mice (Angel *et al.* 2009). The commensal behaviour of house mice has facilitated their introduction to islands around the world, providing the opportunity to compare invasion events across a variety of environments (Berry *et al.* 1982; Berry & Scriven 2005; Berry 2009). The association between house mice and humans is consistent enough that phylogeographical studies of island mice have been used to reconstruct the movement history of humans over the last thousand years (Jones *et al.* 2012, 2013). House mice often invade new environments with great success because they reproduce and adapt rapidly (Berry *et al.* 1982; Berry 1996, 2009; Gabriel *et al.* 2010). Mice can negatively impact the flora and fauna on islands, generating significant conservation concerns (Cuthbert & Hilton 2003; Jones *et al.* 2003; Wanless *et al.* 2007; St Clair 2011). A study examining the impacts of house mice on southern oceanic islands determined that mice had the greatest negative impact when they were the only introduced mammal (Wanless *et al.* 2007; Angel *et al.* 2009). House mice feature an expansive genetic toolkit, including a sequenced genome (Waterston *et al.* 2002) and described patterns of sequence diversity across a range of mainland populations (Baines & Harr 2007; Salcedo *et al.* 2007; Geraldes *et al.* 2008, 2011), which provides useful context for reconstructing patterns of island colonization.

Gough Island, belonging to the UK Overseas Territory of Tristan da Cunha, is located in the central South Atlantic Ocean and is one of the most remote islands in the world. It has an area of 65 km^2 and is situated almost halfway between South Africa and South America (40° 19′S and 9° 55′W; Fig. 1). The island was discovered in 1505 by Gonçalo Álvares from Portugal and rediscovered in 1732 by Captain Charles Gough from England (Uhden 1939). Gough is a volcanic island with a temperate climate and habitats that range from bogs to tussock grass and fern bushes (Wace 1961). Animal life on Gough Island includes 22 species of birds, hundreds of invertebrate species and only one land mammal – the house mouse (Holdgate 1965; Rowe-Rowe & Crafford 1992).

The house mice of Gough Island exhibit remarkable phenotypes. They are larger in body size than any other wild house mouse population (Rowe-Rowe & Crafford 1992). In contrast to mainland populations, which are largely commensal with humans and mostly granivorous (but see Slábová & Frynta 2007), Gough Island mice live freely and regularly feed on nesting seabirds, including chicks of the critically endangered Tristan albatross *Diomedea dabbenena* that are over 300 times their mass (Cuthbert & Hilton 2003; Jones *et al.* 2003; Wanless *et al.* 2007). Mice were most likely introduced to Gough Island during visits by sealing or whaling ships that harboured commensal house mice. Colonization is speculated to have occurred approximately 200 years ago (Rowe-Rowe & Crafford 1992) because mice were well established on the island by 1887 (Verrill 1895). Known records of boat landings are sporadic and date from the initial discovery of the island through the early 19th century (Verrill 1895; Heaney & Holdgate 1957; Wace 1961). Currently, only a small number of researchers and maintenance staff inhabit the island.

In this article, we reconstruct the evolutionary history of house mice from Gough Island using genetic data from three different marker types: nuclear microsatellites, nuclear intron sequences and mitochondrial sequences. We show that Gough Island mice belong to the subspecies *Mus musculus domesticus*. We find moderate to low levels of genetic variation within the Gough Island population and estimate genetic distance from mainland populations. Finally, we use approximate Bayesian computation (ABC) to infer a recent colonization of Gough Island by house mice that included a population bottleneck followed by a rapid expansion.

Methods

Genotyping and sequencing

Tissue samples were collected from 52 house mice at several locations across Gough Island (Fig. 1 inlay) and from 50 house mice at nine locations across Western Europe (Fig. 1 & Table S1, Supporting information; Ireland $n = 10$, Scotland $n = 5$, Northern England $n = 5$, Southern England $n = 5$, Northern France $n = 5$,

Fig. 1 Map of global sample locations and Gough Island sample sites and numbers. Black areas indicate *Mus musculus musculus* distribution, medium gray indicates *M. m. domesticus*, light gray indicates *M. m. castaneus* distribution, and white areas are unknown or mixed. Filled circles are regions that were sequenced and genotyped in this study. All other circles indicate locations included in the phylogenetic analysis.

Germany $n = 5$, Eastern Spain $n = 5$, Western Spain $n = 5$, Portugal $n = 5$). Samples were stored in 70%–100% ethanol until processing. Genomic DNA was extracted from Gough Island samples (in the laboratory of BAP) using the Promega Wizard Genomic DNA Kit (Promega Co., Madison, WI, USA) and European samples (in the laboratory of JBS) using the Qiagen Blood and Tissue Kit (Qiagen Inc., Valencia, CA, USA). DNA concentration was adjusted to 5 ng/μL for all samples to ensure consistent PCR amplification and signal strength. Hardy–Weinberg equilibrium, null alleles and genotype peak intensities were evaluated for differences between samples. Patterns for each of these categories were similar across mainland and island samples.

The mitochondrial DNA (mtDNA) d-loop was amplified in all samples (934 bps; Table S2, Supporting information). In a 25-μL reaction mixer, 0.08 mM dNTPs, 0.8 μM of each primer, 1.25 U of EconoTaq with $MgCl_2$ and 2.5 μL of PCR buffer were combined with 10–20 ng of DNA and run on a thermocycler under the following conditions: 95 °C for 2 min; 30 cycles of 94 °C for 30 s, 58 °C for 30 s, and 72 °C for 2 min; and 72 °C for a final extension of 7 min. PCR products were purified using Exonuclease I and Shrimp Alkaline Phosphatase (Amersham Biosciences). PCR products were sequenced using the Big Dye Terminator v3.1 (Applied Biosystems) cycle sequencing kit and run on an Applied Biosystems 3730xl capillary sequencer (Life Technology, Carlsbad, CA, USA). Sequences were visualized and edited using the GENEIOUS software (Biomatters Ltd, Auckland, New Zealand).

We chose 21 dinucleotide microsatellites (Table S2, Supporting information) from two previous studies (Thomas *et al.* 2007; Teschke *et al.* 2008). Microsatellites with high repeat numbers – and presumably high mutation rates – were selected to increase access to recent demographic events. Microsatellites with similar repeat numbers were chosen to minimize interlocus heterogeneity in mutation rate. All loci were unlinked. Microsatellites were pooled by staggering product sizes and fluorescent labels (FAM and HEX). We amplified the loci using the Qiagen Multiplex PCR Kit and M13 labelling protocols (Boutin-Ganache *et al.* 2001). Fragment analysis was performed using Applied Biosystems

3730xl capillary sequencer and scored using the GENEMAPPER software (Life Technology).

Three intronic nuclear loci (*Ncap3*, *Mamdc2* and *Rab21*) were sequenced in Gough Island samples (Table S2, Supporting information), enabling comparisons with previously described patterns of sequence diversity in European house mice (Geraldes *et al.* 2011). These loci were chosen because they reside in high recombination and gene-poor genomic regions and showed high variation as well as nonsignificant skews in the site frequency spectrum in European populations (Geraldes *et al.* 2011). These characteristics suggest minimal effects from selection at linked sites. Loci were amplified following Geraldes *et al.* (2011) and sequenced as described above. Haplotypes were reconstructed statistically using the program PHASE (Stephens & Donnelly 2003), a Bayesian approach that provides pairs of estimated haplotypes for each individual along with their posterior probabilities.

Genetic variation and population structure

Phylogenetic analysis of mitochondrial d-loop sequences was used to identify the species, subspecies and potential source population(s) of Gough Island mice. In addition to sequences from the samples described above (Gough and Western Europe), the analysis included sequences from across much of Europe, Asia, Africa and the Americas. Sequences from *Mus musculus domesticus* ($n = 95$), *M. m. musculus* ($n = 22$) and *M. m. castaneus* ($n = 10$) (Prager *et al.* 1996, 1998; Gündüz *et al.* 2000, 2005; Ihle *et al.* 2006; Geraldes *et al.* 2008; Bonhomme *et al.* 2011) were downloaded from GenBank. Sequences from *M. spicilegus* ($n = 1$), and *M. macedonicus* ($n = 2$) were also downloaded and included as outgroups. We aligned sequences using default parameters in MUSCLE (Edgar 2004). The best fitting model – a general time reversible (GTR) model with gamma-distributed rate variation and a proportion of invariant sites – was selected based upon Akaike's information criterion (Posada & Buckley 2004) using MrModelTest (Nylander 2004). Four Markov chains (two simultaneous runs) were run for 2 000 000 generations in MrBayes 3.2.1 (Huelsenbeck & Ronquist 2001; Ronquist & Huelsenbeck 2003). The initial 25% of trees were discarded as burn-in.

To identify population structure in Western Europe and Gough Island and search for source populations for Gough Island mice, we analysed microsatellite data using principal coordinate analysis (PCo; GenAlEx; Peakall & Smouse 2006) and STRUCTURE (Pritchard *et al.* 2000; Falush *et al.* 2007; Hubisz *et al.* 2009). PCo was performed on a pairwise genetic distance matrix of squared differences between all individuals (Goldstein *et al.* 1995a). In STRUCTURE, Western European mice and Gough Island mice were first analysed separately to explore population structure within each of these sample sets. We ran the admixture model with correlated allele frequencies for a burn-in period of 50 000 generations and 10^6 generations thereafter. To estimate the number of populations, we ran ten replicate analyses for values of K (number of populations) ranging from 1 to 10. Resulting likelihoods were compared using the method described in Evanno *et al.* (2005) to estimate the number of populations. Two approaches were used to examine the relationship between Gough Island mice and the European populations (Falush *et al.* 2007; Hubisz *et al.* 2009). First, we performed the analysis outlined above on the combined data set. Second, the populations determined from the analysis of European samples alone were set as 'known' by activating the USEPOPINFO flag, and the Gough Island samples were included as unknown. This approach forced Gough Island samples to cluster with the populations identified in the European sample set.

Summary statistics were calculated from microsatellite data using MSA (Dieringer & Schlotterer 2003) and ARLSUMSTAT (Excoffier & Lischer 2010) (Table S3, Supporting information). Statistics were first calculated separately for each of the European countries and Gough Island. These same measures were then calculated in the ABC analysis for the two populations, Europe and Gough Island (simulated and observed). The observed European data set included the combined samples of Ireland, England, France, Spain and Portugal only (more details below). Microsatellite measures included mean and standard deviation across loci for the number of alleles (k), expected heterozygosity (H; Nei 1987), Garza-Williamson's statistic (GW & NGW; Garza & Williamson 2001; Excoffier *et al.* 2005), range in allele size (r) and variance in allele size ($\mathrm{Var_{AS}}$). For the ABC analysis, these values were calculated within and among the two populations (Europe and Gough Island), and ratios of k, H, r, GW and NGW were calculated between the two populations. In addition, we calculated R_{ST} (Slatkin 1995), D_{mu} (Goldstein *et al.* 1995b) and F statistics (Weir & Cockerham 1984) as measures of population differentiation.

Under a given demographic scenario, we expect summary statistics of polymorphism to behave in predictable ways. A significant reduction in population size, an expected outcome of a founding event, will amplify genetic drift. At microsatellite loci, the population should experience reductions in the number of alleles, heterozygosity, range in allele size and variance in allele size (Goldstein & Pollock 1997; Williamson-Natesan 2005; Hoffman *et al.* 2011). Because the loss of alleles is not related to allele size, the number of alleles decreases more quickly than the range of alleles (Garza

& Williamson 2001). Similarly, the number of alleles is reduced faster than heterozygosity, leaving an excess of heterozygosity (Cornuet & Luikart 1996).

Summary statistics for sequence data were calculated using ARLSUMSTAT (Table S3, Supporting information). As with the microsatellite measures, we first calculated the statistics separately for each of the European countries and Gough Island, and then the same statistics were calculated in the ABC analysis for the European and Gough Island populations (simulated and observed). As above, the observed European data set included the combined samples of Ireland, England, France, Spain and Portugal only (more details below). Haplotype pairs for individuals were taken to be those with the highest posterior probabilities in an analysis using PHASE (Stephens & Donnelly 2003). Sequence polymorphism measures included mean and standard deviation across loci for the number of haplotypes (k), heterozygosity/gene diversity (H; Nei 1987), number of segregating sites (S) and the average number of pairwise differences (π_{intra}). The number of private segregating sites (prS) was also calculated for mtDNA. These values were calculated within and among the European and Gough Island populations for mtDNA and within Gough Island for nuclear DNA. Ratios between the two populations for k, H, S and prS were also calculated for mtDNA. Further ratios of k, H, S and π_{intra} between mtDNA and nuclear DNA for Gough Island were calculated. Additional sequence measures within populations included Tajima's D (Tajima 1989), Fu's F_S (Fu 1997), sum of squared haplotype frequencies (HH) and θ_w (Watterson 1975) for mtDNA and nuclear loci; we also calculated F_{ST} (AMOVA, Jukes/Cantor), and the average number of pairwise differences between populations (π_{inter}) for mtDNA in the ABC analysis.

As with microsatellites, we expect summary statistics of sequence data to behave in predictable ways under certain demographic scenarios. In sequenced regions, a reduction in population size will decrease overall genetic diversity. This will be exhibited by reductions in the number of segregating sites, the number of haplotypes and nucleotide diversity (Thornton & Andolfatto 2006; Lohmueller *et al.* 2009; Gattepaille *et al.* 2013). Measures of the frequency spectrum will show a skew towards intermediate frequency alleles in a bottlenecked population (positive Tajima's D and Fu's F_S) and a skew towards rare alleles in an expanding population (negative D and F_S; Gattepaille *et al.* 2013).

Approximate Bayesian computation analysis

Approximate Bayesian computation (ABC) was used to reconstruct the demographic history of Gough Island mice. ABC is a powerful and flexible framework that compares simulated data to observed data to estimate parameters of interest (Beaumont *et al.* 2002; Bertorelle *et al.* 2010). In this study, we focused on estimating parameters associated with island colonization, including colonization time, bottleneck magnitude and current population size. We used ABCtoolbox (Wegmann *et al.* 2010), a program that can incorporate data from multiple classes of molecular markers and enables consideration of a range of demographic models by interacting with external programs to generate simulations and compute summary statistics.

The models, assumptions and prior distributions used in this study were established based on all available knowledge of the study system, species and molecular marker characteristics. However, there is no commonly accepted method for the construction of ABC models and priors, which leaves experience and prior knowledge from previous studies as the only guide; however, even flat and uninformative priors can still give reasonable informative results (Sunnåker *et al.* 2013).

Our main model featured a colonization event from a single mainland population (Western Europe) with the potential for a bottleneck followed by exponential growth in the colonizing population (Fig. 2A). Estimated parameters included current effective population sizes of the island (N1) and the structured European (N2) population, island effective population size at the time of colonization (N3), island colonization time (T1), growth rate following island colonization (g, where $N2 = N3\ \exp^{-gT1}$), mutation rates of molecular markers (u) and mitochondrial ratio (r_{mt}, where $2r_{mt}$ = fraction of females in the populations). To test whether our estimates were robust to departures from model assumptions, we examined two variations of the basic model. One variation (variation 1) allowed an ancestral bottleneck,

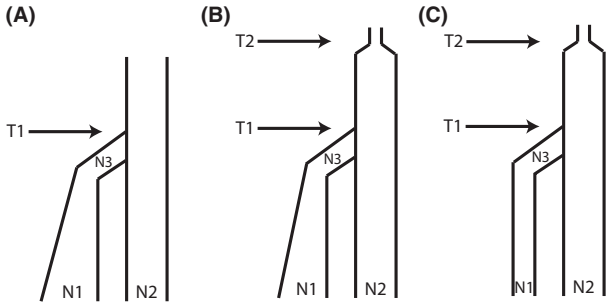

Fig. 2 Schematic representation of demographic history modelled for Gough Island house mice. (A) Main model of island colonization at time T1 of size N3 followed by exponential growth to the current island population size of N1 and mainland population size of N2. (B) Variation 1 that includes ancestral bottleneck in the mainland population. (C) Variation 2 that restricts the population size of Gough Island by removing exponential growth after colonization.

intended to represent the initial colonization of Western Europe. The second model variation (variation 2) assumed only a population split with a constant effective population size on the island after colonization (i.e. no population growth).

The prior distributions were established based on available knowledge of the Gough Island mice and similar house mouse populations and previous studies using ABC methods. Prior distributions were either uniform or uniform on a $\log_{10}$ scale when ranges spanned orders of magnitude (Table 1). Density estimates of Gough Island mice are 224 mice per hectare, which suggests the census population size is >1 million (Rowe-Rowe & Crafford 1992). However, effective population sizes of wild populations can be small fractions of census populations (Palstra & Ruzzante 2008); thus, we set the current effective population size prior of Gough Island mice to vary between 400 and 50 000. Estimates for the mainland populations were taken from Geraldes *et al.* (2008). They used the isolation-migration analytical framework (Hey & Nielsen 2004) to estimate the long-term mutation–drift equilibrium population size. Our choice of colonization time priors was guided by known shipping records and island geological activity (Verrill 1895; Heaney & Holdgate 1957; Wace 1961). The average generation time of Gough Island mice was found to be 1 year based on a study of Gough Island mouse diet and reproductive activity (Jones *et al.* 2003). The average microsatellite mutation rate prior was set to range from 10^{-3} to 10^{-5} on a log-uniform scale. Twenty-one unlinked microsatellite loci were simulated according to the stepwise-mutation model (Ohta & Kimura 1973). Sequence mutation rate ranges were based on previous studies in mice of these and similar marker sets (Geraldes *et al.* 2008, 2011) for mitochondrial (10^{-7} to 10^{-9}) and nuclear (10^{-7} to 10^{-10}) DNA. Recombination in the nuclear loci was set according to values presented in (Geraldes *et al.* 2011), where these same loci were sequenced in other house mouse populations.

We used MarkSim (Haasl & Payseur 2011) to generate simulated data according to the assumed prior distributions. The adjustable pipeline in ABCtoolbox (Wegmann *et al.* 2010) was used to store and manage 1 million simulated data sets for each model. A total of 120 summary statistics (Table S3, Supporting information) that describe patterns of variation within and between populations were calculated in ARLSUMSTAT across the three marker types (microsatellites, mitochondrial sequences and nuclear sequences). A partial least squares (PLS) analysis was performed to reduce the dimensionality of the summary statistics, and each PLS component was weighted according to the variance explained (Wegmann *et al.* 2009). The optimal number of PLS components was chosen by performing a root

Table 1 Prior and posterior distribution characteristics for inference under the main ABC model

	Priors				Posterior distribution characteristics*					
Parameter	Distribution	Scale	Min	Max	Mode	Mean	Median	q50_lower	q50_upper	q90_lower	q90_upper
N1 - Gough N_e	Uniform	Log	2.6	4.7	20 398	11 344	12 855	6053	23 600	2078	41 266
N2 - Mainland N_e	Uniform	Log	4	5.7	51 173	62 749	58 730	31 917	116 912	16 352	288 935
N3 - Colonization N_e	Uniform	Log	0.3	4.3	941	549	620	155	2164	22	8674
T1 - Colonization time†	Uniform	Log	1.6	3.7	110	223	193	95	463	51	1487
Mitochondria ratio	Uniform	Linear	0.05	0.5	0.143	0.257	0.247	0.152	0.358	0.077	0.459
Mitochondrial mutation	Uniform	Linear	5	9	6.085	6.151	6.145	5.804	6.487	5.402	6.949
Microsatellite mutation	Uniform	Linear	3	5	3.573	3.705	3.673	3.402	3.975	3.121	4.397
Nuclear mutation L1	Uniform	Linear	7	10	7.874	8.008	7.980	7.648	8.342	7.256	8.839
Nuclear mutation L2	Uniform	Linear	7	10	8.809	8.798	8.809	8.417	9.201	7.859	9.683
Nuclear mutation L3	Uniform	Linear	7	10	8.583	8.627	8.628	8.221	9.035	7.678	9.563

These distributions are for the main model, a colonization event followed by exponential growth.
*All values on a Log_{10} scale are transformed from Log_{10}.
†In years, assuming one generation per year.

mean squared error (RMSE) analysis and determining the minimum set containing the largest amount of information about the model parameters. Specifically, PLS components were examined to determine whether including more components greatly reduced the prediction error, an approach that gauges how precisely parameters can be inferred. We subsequently used rejection sampling to retain the 5000 (0.5%) simulations that best fit the observed data. A post-sampling regression adjustment was performed on the final data set using the general linear model (GLM) as presented in Leuenberger and Wegmann (2010) and implemented in ABCtoolbox.

STRUCTURE analysis suggested that our mainland sample was composed primarily of three populations (Ireland, England/France, Spain/Portugal); when treated as a single population, this data set exhibited higher levels of F_{IS} because of a Wahlund effect (Wahlund 1928). This effect can generate a false signal of a bottleneck (Nielsen & Beaumont 2009; Peter *et al.* 2010). To account for this effect in our simulations (which ignored population structure within western Europe), we replicated the same level of substructure by randomly making the European individuals homozygous at a locus with probability F_{IS} (Wegmann & Excoffier 2010). This procedure was performed after simulations but prior to the calculation of summary statistics.

We used several posterior predictive tests to confirm that the model and parameter estimates were reasonable fits to the observed data. The retained simulations were used as proxies for the posterior samples. First, we confirmed that the observed data fell within the distribution of the summary statistics simulated with parameter values drawn from the posterior distribution. However, as the large number of summary statistics created a high-dimensional space, it was difficult to judge fit from marginal distributions alone. Therefore, we also examined pairwise scatter plots of summary statistics and verified the observed data fell within the simulated data cloud. Moreover, ABCtoolbox gives an error message if any observed statistics fall outside of the marginal density distribution. Finally, we took an even more holistic approach by comparing the marginal density of the observed data with marginal densities obtained from the retained simulations to compute a *P*-value, which measured the ability of the model to reproduce the data (Wegmann *et al.* 2010).

To detect potential biases in our posterior distributions empirically, we generated pseudo-observed data by picking 5000 parameter combinations from the prior distribution under a given model and used our ABC pipeline to infer marginal posterior distributions. We then recorded the positions of the true parameter values in the cumulative posterior distributions and the cumulative highest posterior density (HPD) interval. If the posterior distributions are unbiased, the positions should be distributed uniformly and deviations would be informative about the type of bias present (Wegmann & Excoffier 2010; Wegmann *et al.* 2010). These distributions were compared to a uniform distribution using a Kolmogorov–Smirnov test.

Results

Genetic variation within populations

Gough Island mice showed low nucleotide variation in the mitochondrial d-loop, with fewer segregating sites than most European populations despite the much larger number of individuals sampled (Table 2). Most mice carried one haplotype, while two additional haplotypes occurred at low frequencies, leading to high haplotype homozygosity (HH). The diversity reduction was apparent in values of π and $\theta_{w,}$ two estimators of $2N_e\mu$ (where N_e is the effective population size and μ is the per-site mutation rate; Table 2), which were at least an order of magnitude lower in Gough Island mice than the European populations. In further contrast to the European populations, Gough Island mice exhibited a strongly negative Tajima's *D*. Fu's F_s was also negative for Gough Island mice (and for Ireland and France). These negative values indicate a skew towards rare alleles in the site frequency spectrum of the Gough Island population, consistent with a recent population expansion.

Intronic sequences from three nuclear loci revealed reduced nucleotide diversity in Gough Island mice compared with published values for the same loci in 27 *M. m. domesticus* mice from Western Europe (Geraldes *et al.* 2011; Table 3): π_{intra} = 0.303% in Gough Island vs. 0.388% in Western Europe (*Ncapd3*), 0.168% vs. 0.300% (*Mamdc2*), and 0.048% vs. 0.224% (*Rab21*), respectively. In contrast to mitochondrial d-loop variation, site frequency spectra for *Ncapd3* and *Mamdc2* showed a significant skew towards intermediate frequency alleles in either Tajima's *D* or Fu's F_S for the Gough Island populations (Table 3). *Rab21* did not show a skew in the allele frequency spectrum but had a severe reduction in diversity, indicating that all three nuclear loci exhibited signs of a population bottleneck. Haplotype reconstruction was well supported: average posterior probabilities for the most likely haplotype pairs were 0.998 for *Rab21*, 0.979 for *Mamdc2*, and 1.00 for *Ncap3*.

Patterns of variation at the 21 microsatellites exhibited weaker evidence of a bottleneck. Overall, the Gough Island population harboured appreciable diversity, broadly similar to that observed in European

Table 2 Summary statistics of sequence variation at the mitochondrial d-loop (936 bp)

	n	S (S_{sam})	S_{pr}	π_{intra}	θ_w	D	F_S	K (K_{sam})	HH
Scotland	2	2	1	0.2137	0.2137	—	0.693 (0.633)	2	0.500
Ireland	10	16 (12.7)	7	0.6766	0.6042	0.555 (0.251)	−2.843 (0.949)	9 (4.8)	0.120
England	10	3 (2.0)	1	0.1021	0.1133	−0.356 (0.676)	0.390 (0.514)	3 (2.5)	0.420
France	5	5	1	0.2564	0.2564	0.000 (0.39)	−2.680 (0.99)	5	0.200
Spain	8	16 (13.1)	9	0.6792	0.6593	0.155 (0.435)	−1.368 (0.835)	7 (4.6)	0.156
Portugal	5	0	0	—	—	—	—	—	—
Germany	5	0	0	—	—	—	—	—	—
Gough	52	2 (0.3)	2	0.0122	0.0473	−1.313 (0.927)	−2.369 (0.993)	3 (1.3)	0.890

n, number of mitochondrial chromosomes sampled (=number of individuals); S, number of segregating sites; S_{sam}, average number of segregating sites in 1000 resampled sets of 10 chromosomes; S_{pr}, number of private segregating sites; π_{intra}, number of pairwise differences per nucleotide (percentage); θ_w, Watterson's theta (percentage); D, Tajima's D (P-value); F_s, Fu's F_s (P-value); K, number of haplotypes; K_{sam}, average number of haplotypes in 1000 resampled sets of 10 chromosomes; HH, sum of squared frequency of haplotypes.

Table 3 Summary statistics of sequence variation at three nuclear loci for the Gough Island population

Gene	Chr	bp	n	S	π_{intra}	θ_w	D	F_S	K	HH
Ncap3	9	1987	46	13	0.3027	0.1489	3.144 (0.011)	10.888 (0.000)	4	0.394
Mamdc2	19	2053	46	22	0.1681	0.2438	−1.014 (0.885)	8.136 (0.005)	3	0.803
Rab21	10	1163	46	2	0.0479	0.0391	0.406 (0.374)	0.554 (0.391)	3	0.584

Chr, chromosome on which the locus resides; bp, number of base pairs sequenced; n, number of chromosomes sampled; S, number of segregating sites; π_{intra}, number of pairwise differences per nucleotide (percentage); θ_w, Watterson's theta (percentage); D, Tajima's D (P-value); F_s, Fu's F_s (P-value); K, number of haplotypes; HH, sum of squared frequency of haplotypes.

Table 4 Summary statistics of variation at 21 dinucleotide microsatellites

	n	A	A_{sam}	R	Var_{AS}	H_e	GW
Scotland	10	4.1 (1.22)	—	7.33 (4.48)	9.90	0.7 (0.19)	0.58 (0.23)
Ireland	20	7.95 (2.44)	5.58	11.24 (5.33)	12.93	0.82 (0.10)	0.71 (0.18)
England	20	6.76 (2.19)	4.72	11.9 (10.32)	21.54	0.76 (0.15)	0.63 (0.21)
France	10	5.71 (1.42)	—	10.81 (5.68)	18.74	0.85 (0.07)	0.57 (0.23)
Spain	20	8.24 (2.00)	5.89	10.33 (3.34)	9.55	0.87 (0.04)	0.76 (0.16)
Portugal	10	5.43 (1.36)	—	8.38 (4.28)	10.82	0.81 (0.12)	0.65 (0.21)
Germany	10	3.1 (1.00)	—	6.62 (5.44)	10.44	0.55 (0.18)	0.57 (0.28)
Gough	104	7.86 (3.05)	4.15	13.38 (11.12)	15.64	0.7 (0.18)	0.64 (0.21)

n, number of chromosomes sampled; A, number of alleles; A_{sam}, average number of alleles in 1000 resampled sets of 10 chromosomes; r, range of allele sizes; Var_{AS}, average variance in allele sizes; H_e, expected heterozygosity; GW, Garza–Williamson statistics. Values in parentheses are standard deviations.

populations (Table 4). An average of 7.9 alleles per locus put Gough Island mice at the upper end of the European distribution; however, subsampling showed that this relatively high diversity was explained by the larger sample size (Table 4). Depending on the European population chosen for comparison, the average expected heterozygosity in Gough Island mice (0.7) suggested a weak reduction in diversity, but no reduction was seen using average variance in allele size. Two loci exhibited minor deviations from Hardy–Weinberg equilibrium in Gough Island mice, while one locus showed a significant deviation ($P < 0.001$). The latter outlier locus had a large number of alleles, several of which were at low frequency perhaps due to rare genotyping errors or incomplete sampling of the island (Table S4, Supporting information). Other European populations had a few loci that were marginally out of Hardy–Weinberg equilibrium; however, this was likely

due to data being analysed by country vs. closed populations. Furthermore, the average value of the Garza–Williamson statistic was consistent with a bottleneck in the Gough Island population (and in European populations), which is indicated by values <0.68 (Garza & Williamson 2001). Summary statistics and allele frequency spectra for individual microsatellites are presented in Supporting information Tables S4 & S5, respectively.

Genetic variation between populations

Phylogenetic analysis of mitochondrial d-loop sequences recovered two subspecies of house mice, *M. musculus domesticus* and *M. m. musculus*, as monophyletic groups with high posterior probabilities, whereas *M. m. castaneus* was paraphyletic (Fig. S1, Supporting information; Rajabi-Maham *et al.* 2012). Gough Island mice clustered within the *M. m. domesticus* clade. The phylogeny did not clearly group Gough Island mice with a specific geographical region within *M. m. domesticus*, leaving the source population uncertain. However, the high-frequency haplotype from the Gough Island population was identical to sequences of some mice from England, France and Cameroon, and the resulting clade was strongly supported (posterior probability = 0.92). Alternatively, Gough Island mice were most similar to mice from Portugal and Spain when genetic distances were calculated from microsatellites (Table 5). These combined results suggest the source population may lie within Western Europe. Therefore, we focused on *M. m. domesticus* samples from this region (England, France, Ireland, Scotland, Spain, Portugal and Germany) in subsequent analysis.

Overall, principal coordinate analysis (PCo) revealed no close association between Gough Island mice and any one Western European population (Fig. S2, Supporting information). Along the first axis of variation (explaining 37.7%), we observed two distinct clusters: one containing the European samples and the other containing samples from Gough Island. Germany formed a cluster distinct from the other European populations along the second axis, which explained an additional 17.7% of the variation. Additional principal coordinates showed slight separation of the remaining European populations.

STRUCTURE analyses combining Gough Island and European microsatellite genotypes also suggested the presence of two populations. The highest Delta *K* value was *K* = 2 (Evanno *et al.* 2005). This pattern was consistent with the PCo results in that the greatest separation fell between Gough Island and Europe. No clear source population was identified for Gough Island mice (Fig. 3). Even when *K* = 10, Gough Island was completely differentiated from the rest of the samples. Thus, we took a different approach in STRUCTURE with the microsatellite data to find potential source populations (see Hubisz *et al.* 2009). First, we confirmed that Gough Island house mice showed no evidence of population structure, with equal membership across all groups despite the number of *K* specified. This was true despite reasonable levels of genetic variation. Next, we identified distinct genetic groups within the European sample: *K* = 5 yielded the highest Delta *K* value (Evanno *et al.* 2005). These five groups were dominantly characterized as (i) Ireland, (ii) England and France, (iii) Spain and Portugal, (iv) Scotland and (v) Germany (Fig. 3; Table S6, Supporting information). When Gough Island mice were subsequently added, they clustered with multiple groups, including 37% genetic membership in Ireland, 30% in England/France and 19% in Spain/Portugal (Fig. 3; Table S7, Supporting information). This pattern suggests that Gough Island mice either have mixed ancestry, the data set lacks power for source population assignment, or the true source population(s) has not been sampled. We note this analysis does force the Gough Island mice to have mixed ancestry because it is unlikely for them to match any of the European locations exactly. However, this approach is commonly used to determine the origins of 'unknown' samples,

Table 5 Genetic distances between populations based on microsatellites

$R_{ST}\backslash D_{mu}$	Scotland	Ireland	England	France	Spain	Portugal	Germany	Gough
Scotland	—	3.874	3.040	4.680	2.723	5.193	10.488	6.401
Ireland	0.080	—	7.277	5.092	3.827	7.051	8.195	5.625
England	0.010	0.139	—	4.766	5.226	9.148	17.453	9.146
France	0.060	0.088	0.039	—	5.879	8.329	9.097	6.039
Spain	0.062	0.107	0.106	0.138	—	4.485	9.767	4.692
Portugal	0.131	0.175	0.151	0.154	0.131	—	15.531	4.910
Germany	0.294	0.208	0.291	0.175	0.297	0.387	—	12.643
Gough	0.135	0.134	0.198	0.119	0.115	0.096	0.265	—

Above the diagonal are Delta mu values and below the diagonal are R_{ST} values.

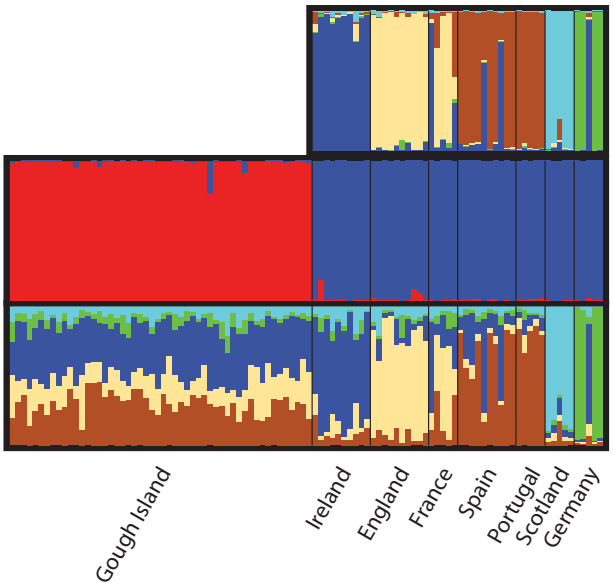

Fig. 3 Results of STRUCTURE analyses. Each individual is represented by a vertical line. Lines are broken into colour segments with lengths proportion to group membership. The number of colours is set based on the number of defined *K* groups. Top panel: European samples only result with no population priors specified. $K = 5$ data shown. Middle panel: All samples run together with no population prior specified. $K = 2$ data shown. Bottom panel: Gough and European samples run together with European population set as known (shown in top panel).

especially when the samples are more closely related to each other than to any other group (STRUCTURE manual v2.3, Hubisz *et al.* 2009), which we do observed in the PCo results. We used the combined sample of these three European populations (Ireland, England/France, Spain/Portugal) as the structured mainland observed data in the ABC analysis.

Approximate Bayesian computation

We used ABC to reconstruct the demographic history of Gough Island mice. Posterior distributions of the parameters in the main model (Figs 2A & S3, Supporting information) generated from 10^6 simulations are summarized in Table 1. Modes of the estimated parameters suggested a colonization time (T1) of 110 years (90th quantile range (q90th): 51–1487 years; assuming one generation per year) and a bottleneck effective population size (N3) of 941 individuals (q90th: 22–8674). Modes of posterior distributions of current effective population sizes were 19 429 individuals (q90th: 2078–41 266) for Gough Island mice (N1) and 50 176 (q90th: 16 352–288 935) for the structured European source population (N3). In general, these numbers suggest a severe colonization bottleneck event, with a colonization population size 2% of the mainland population size and 5% of the current island population size. Modes of nuclear mutation rate distributions were similar to values reported in Geraldes *et al.* (2011) for the same loci. Modes of mtDNA mutation rate distributions were slightly higher than values reported in Geraldes *et al.* (2008). The mode of the average microsatellite mutation rate was similar to values reported in Teschke *et al.* (2008).

Based on the root mean squared error (RMSE) plots, we used seven partial least square (PLS) components (Fig. S4, Supporting information). Analyses performed with different numbers of PLS components (ranging from 5 to 10) produced similar posterior distributions. Prediction error in the RMSE plots suggested high precision in estimates of all parameters except N1. Summary statistics calculated from microsatellites were the most heavily weighted across PLS components, suggesting strong contributions from these loci to parameter inference (Table S3, Supporting information). This finding is consistent with a previous study in chimpanzees, which used both microsatellite and sequence data in an ABC analysis of demographic history (Wegmann & Excoffier 2010).

Suitable coverage of the marginal posterior density distribution was verified by random validation across 5000 pseudo-observed data sets. Most marginal distributions failed to reject the expected uniform distribution; exceptions included N2, N3 and mutation rates at two of the nuclear loci. These parameters showed minor deviations from uniform (Fig. S5, Supporting information), but the level of departure would cause only a slight overestimation on average. Moreover, we used pairwise scatter plots of the summary statistics to verify that the simulations captured the observed data (data not shown). Lastly, we observed the *P*-value estimated under the GLM to be a value of 1.00. Therefore, we can be confident that the posterior distributions are not biased and our model is capable of recreating the observed data.

To test the robustness of our main model, we made comparisons with results when two key characteristics were altered. One variation added a mainland (European) bottleneck (variation 1). The second variation removed the possibility of growth after colonization (variation 2). Variation 1 yielded a similar N2 (19 907 individuals, q90th:2346–41 266), a similar N3 (898 individuals, q90th:35–8674), a similar T1 (128 years; q90th:51–1349) and a larger N3 (92 327; q90th:21 117–318 809; Fig. S6 & Table S8, Supporting information). We conclude variation in European demographic characteristics had little effect on parameter estimates for Gough Island. Modelling a population with no growth after colonization (variation 2) produced a drastic

decrease in the current N1 (2129; q90th:533–7174) and an increased T1 (1317 years; q90th:155–3654; Fig. S7 & Table S8, Supporting information). The resulting decrease in the N2 is needed to be consistent with the observed reduction in genetic diversity. Overall, the plurality of our results supports a bottleneck occurring as a result of colonization followed by an expansion.

Discussion

Reconstructing the demographic history of a population is an essential step in characterizing an island colonization event. Our results support a Western European origin for Gough Island mice, consistent with shipping records indicating that the most frequent and earliest visits to Gough Island came from this geographical region (Verrill 1895; Uhden 1939). Although coastal populations are the most likely ancestral populations, the primary source of Gough Island mice remains unresolved. Microsatellite data suggested shared ancestry between Gough Island mice and multiple coastal populations of Western Europe, including Ireland, England, France, Portugal and Spain. The combination of few haplotypes (despite a reasonable number of segregating sites) and appreciable π_{intra} at nuclear loci is consistent with multiple founding lineages with little time for recombination. Most Gough Island mice shared identical mitochondrial sequence haplotypes with individuals from England, France, and Cameroon, suggesting that the maternal lineage could have originated in these countries. The affinity with Cameroon likely reflects colonization of West Africa by Western European house mice in the 19th century (Bonhomme *et al.* 2011).

Although our results raise the possibility of multiple source populations, this interpretation should be viewed with caution. When an invasive population shows membership in multiple populations from its native range, there are several possible explanations (Estoup & Guillemaud 2010), including missed sampling of the true source population, genetic drift in the invading population during or after colonization, insufficient historical information in molecular markers, multiple invasion events and/or admixture in the source population. In this study, we sampled mice from a wide range of localities to increase the probability of including the source population (Fig. S1, Supporting information). PCo analysis displayed strong differentiation between Gough Island mice and European mice – likely as a result of genetic drift – but Gough Island mice still shared microsatellite alleles with multiple mainland populations. Although we employed a larger number and variety of markers than is typical for studies of island colonization, our data may lack power to identify and accurately measure the genetic contributions of source populations. Minimal structure within Europe was indicated by shared mitochondrial haplotypes and by shared population membership in STRUCTURE analyses of microsatellites, suggesting that additional informative markers may be necessary to identify the source population(s). This finding agrees with other studies reporting regional differentiation but minimal fine-scale differentiation between house mouse populations (Britton-Davidian 1990; Bonhomme *et al.* 2011; Jones *et al.* 2011b). Alternatively, a history of admixture is consistent with our results, especially in the light of the propensity for long-distance dispersal among house mice (Berry *et al.* 1982; Gabriel *et al.* 2010), their tight commensalism with humans (Jones *et al.* 2012, 2013) and their tendency to stow away in cargo (Caldwell 1964; Berry *et al.* 1982).

Other island populations of house mice have mixed ancestries (Berry 2009; Searle *et al.* 2009; Jones *et al.* 2011a), with mitochondrial and nuclear loci showing different patterns. New Zealand house mice were inferred to be a 'melting pot' of the three subspecies (*M. m. domesticus*, *M. m. musculus*, and *M. m. castaneus*). Mitochondrial haplotypes were found to be *M. m. domesticus* and *M. m. castaneus* in origin and nuclear DNA showed mixed ancestry from interbreeding of all three founding subspecies (Searle *et al.* 2009). Madeira Island house mice had mtDNA haplotypes consistent with a Northern European origin and nuclear DNA consistent with a Portuguese origin (Britton-Davidian *et al.* 2007). On the Kerguelen archipelago, the main island was initially colonized by house mice from Western Europe, and the small satellite islands were colonized secondarily by related Western European populations and nearby oceanic island populations (Hardouin *et al.* 2010). On the Faroe Islands, researchers found that the better connected and closer the island was to the mainland the more likely it was to have mixed ancestry from both *M. m. domesticus* and *M. m. musculus*, whereas the most remote islands were only derived from *M. m. domesticus* (Jones *et al.* 2011a).

Although many researchers have investigated the recent demographic histories of mainland and island populations, obtaining accurate parameter estimates remains a challenge. Some investigators have suggested that it is only possible under restricted conditions (Palsboll *et al.* 2013). The reliability of demographic parameter estimates is often limited by focusing on one genomic compartment (*e.g.* mtDNA) or class of molecular marker, using a limited number of population genetic summary statistics, failing to account for temporal fluctuations in population size, or failing to account for unsampled influential populations. We used several approaches in an attempt to overcome these limitations. We employed multiple markers and marker types to

increase the precision and robustness of our estimates (Cornuet *et al.* 2010; Wegmann & Excoffier 2010). We used ABC analysis with priors guided by previous studies and known aspects of population and island history, allowing us to estimate demographic parameters under a realistic model. Furthermore, we focused on an unusually isolated island to reduce the likelihood of random migrants. Finally, we sampled a large mainland data set to include possible influential populations.

The combination of population genetic patterns at all three marker sets (mitochondrial d-loop sequences, 21 microsatellites and three nuclear sequence loci) support a population bottleneck followed by an expansion during the history of Gough Island mice. Contrasting frequency spectra in the mitochondrial d-loop (skew towards rare alleles) and the three nuclear sequence loci (skew towards intermediate frequency alleles) likely reflect sensitivities to demographic events occurring on different timescales. Specifically, mtDNA features a comparatively smaller effective population size (especially after island colonization) (Hardouin & Tautz 2013), mutates faster, and is maternally inherited (Ballard & Whitlock 2004; Mourier *et al.* 2012). The single dominant mtDNA haplotype was likely present in the founding individuals, and the two lower frequency haplotypes may have been the result of mutations that occurred on the island as the population expanded. Compared with mtDNA, nuclear sequence variation is affected by a higher effective population size, a lower mutation rate and recombination. The small number of haplotypes at nuclear sequences despite many segregating sites (*e.g. Mamcd2*) suggests that there has been little time for recombination since the most recent common ancestor of the Gough Island mouse sample. The relatively smaller reduction in microsatellite diversity suggests that the higher mutation rates of these markers produced a faster recovery from the bottleneck and shifts in the frequency spectrum as the population expanded (Slatkin & Hudson 1991; Hoffman *et al.* 2011). Collectively, these loci capture a range of demographic events on various timescales, providing clues into the complex demographic history of Gough Island mice.

Because the number of potential scenarios would increase rapidly with the number of source populations, we elected to focus on the time and population size of colonization instead of the frequency of invasions and the number of source populations. Consequently, our results cannot discriminate between a single large colonization event and several small introductions from the same native population(s). The estimated colonization time of approximately 100 years ago is consistent with shipping records, human exploration and literature stating that mice were already present on the island in 1887 (Verrill 1895). The remote location of Gough Island suggests that house mice would not have had an opportunity to colonize it prior to human seafaring.

The point estimate of the colonization effective population size (N3 = 941) is large and biologically unrealistic. Several factors should be considered when interpreting this value. First, this point estimate is based on the mode; the posterior distribution includes smaller numbers, with a 50% probability that N3 is <549 (the median) and a 25% probability that N3 is <155. Second, the small deviation in the random validations (Fig. S4, Supporting information) suggests that N3 was overestimated. Third, N3 is an effective population size, which corresponds to the number of breeding individuals in an idealized panmictic population that fits the diversity observed (Wright 1931). An effective population size can take on values larger than the census size in structured populations or when variance in reproductive success is low (Wakeley 2001). Fourth, evidence of a bottleneck (including reduced genetic diversity) can be masked by the effects of an expansion when bottlenecks are very short (Amos & Harwood 1998; Hoffman *et al.* 2011). Fifth, the inflated N3 estimate could reflect multiple colonization events, which are not captured by our model. Finally, the samples from potential source populations featured some shortcomings, including small sample sizes, and combined data from these populations showed a Wahlund effect in the ABC analysis.

To explore how issues with source populations and multiple colonizations affected our inferences, we conducted additional coalescent simulations (results not shown). First, we generated 10 sets of microsatellite data for each combination of parameters mimicking the model presented in Fig. 2A and our sampling regime. We varied θ_w (2, 4, 10), founding population size (10 & 100) and time since colonization (200 & 2000). The resulting polymorphism data were analysed with STRUCTURE, following the procedures outlined in the Methods. We found that with increasing θ_w, N3 or T1, the simulated island population showed increasing genetic affiliation with incorrect source populations. Second, we conducted preliminary ABC analysis on simulations following the scenario in Fig. 2A but with two founders (Ireland, Spain/Portugal) instead of one. Our estimates of N1, N2 and N3 were similar to those described above, but the T1 was pushed further into the past. Lastly, we conducted a preliminary ABC analysis following Fig. 2A, but using only the Ireland samples as the observed source population data instead of the combined European sample. Again, similar estimates for N3 were recovered. Overall, these exploratory simulations underscore the difficulty of identifying a source population for a recent colonization event from an array of closely related populations. The results also suggest that our N3 estimate may be robust to some assumptions of

our model. Nonetheless, it is clear that additional markers, samples and analysis are needed to define the source population and N3.

Some of our parameter estimates have wide credibility intervals, as is typical of population genetic studies (including those relying on ABC). One reason is that the reconstruction of population history is inherently complex. For example, as mentioned previously, rapid expansion following a very short bottleneck could mask the bottleneck signal by increasing genetic diversity (Amos & Harwood 1998; Hoffman *et al.* 2011). Second, variance in the posterior distribution is contributed by the use of summary statistics, which provides an incomplete view of patterns of variation and inflates credible intervals under any model (Sunnåker *et al.* 2013). Despite this shortcoming, population genetic inference typically relies on summary statistics because model-fitting that uses the entire data set tends to be computationally prohibitive. Third, our analyses assume that microsatellites follow the stepwise-mutation model: mutations increase or decrease allele size by one repeat with equal probability. Our parameter estimates therefore ignore the likely possibilities of some multiple-step mutations and expansion/contraction biases. Finally, it is possible that our models may have missed a key component of population history.

Although modelling methods such as approximate Bayesian computation have a number of advantages over the simpler population genetic statistics with the ability to study complex histories, they still yield a degree of uncertainty around the parameter inferences. In this study, we were able to generate estimates of demographic parameters, yet we still had some level of ambiguity in our results (i.e. source population). Furthermore, many demographic studies use only one locus type, microsatellite markers or mitochondrial DNA, compared with our three marker set, which would only increase the level of ambiguity. This suggests that although these methods are popular and provide great advantages, they do not yet provide a complete and definitive picture of a population's demographic history.

Similar to the Gough Island mice, it is common for populations that successfully colonize or invade new habitats to undergo a bottleneck followed by population growth. Examples include the silvereye birds of the southwest Pacific Islands (Clegg *et al.* 2002), macaques of the Mauritius Island (Bonhomme *et al.* 2008) and the invasive Ladybird of Eastern North America (Lombaert *et al.* 2011). The details of the colonization event do vary with some populations exhibiting admixed ancestry vs. a single source population, some exhibiting rapid expansion which obscured the bottleneck signal, and all reveal a variety of dates of the initial colonization.

Our results reveal aggressive population growth from approximately 900 individuals during the bottleneck to its current N1 of 20 000 (census size of 1–2 million; Rowe-Rowe & Crafford 1992) within a 100-year time frame (exponential growth $r = 3.1$ per 100 years). The rapid expansion was likely enabled by the lack of predators and competitors on the island. Furthermore, Gough Island mice have increased fecundity, population density and litter sizes – all potential accelerators of population growth (Rowe-Rowe & Crafford 1992; Cuthbert & Hilton 2003; Jones *et al.* 2003). Gough Island is one of the world's most important refuges and breeding grounds for seabirds, such as petrels, albatross, and endemic moorhens and buntings (Wanless *et al.* 2007, 2009, 2012). The rapid decline of some of these species has been directly linked to predation by house mice (Cuthbert & Hilton 2003; Jones *et al.* 2003; Wanless *et al.* 2007). The adaptability and reproductive rate of these mice suggest that land managers need to act quickly and thoroughly in eradicating the island mouse population. Even a small number of individuals could repopulate the island in a short time span.

The recent colonization of Gough Island suggests that the exceptional body size, carnivorous behaviour and other phenotypes that characterize this population of house mice evolved rapidly. The characteristics of species that successfully invade and establish populations in new environments are an area of intense investigation (Keller & Taylor 2008; Estoup & Guillemaud 2010; Lombaert *et al.* 2011; St Clair 2011). By shedding light on the demographic history of this invasive population, we set the stage for genetic and ecological studies of these traits and their role in successful invasions.

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References

Adler GH, Levins R (1994) The island syndrome in rodent populations. *Quarterly Review of Biology*, **69**, 473–490.

Amos W, Harwood J (1998) Factors affecting levels of genetic diversity in natural populations. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, **353**, 177–186.

Angel A, Wanless RM, Cooper J (2009) Review of impacts of the introduced house mouse on islands in the Southern Ocean: are mice equivalent to rats? *Biological Invasions*, **11**, 1743–1754.

Baines JF, Harr B (2007) Reduced X-linked diversity in derived populations of house mice. *Genetics*, **175**, 1911–1921.

Ballard JWO, Whitlock MC (2004) The incomplete natural history of mitochondria. *Molecular Ecology*, **13**, 729–744.

Beaumont MA, Zhang WY, Balding DJ (2002) Approximate Bayesian Computation in population genetics. *Genetics*, **162**, 2025–2035.

Berry RJ (1996) Small mammal differentiation on islands. *Philosophical Transactions of the Royal Society of London Series B*, **351**, 753–764.

Berry RJ (2009) Evolution rampant: house mice on Madeira. *Molecular Ecology*, **18**, 4344–4346.

Berry RJ, Scriven PN (2005) The house mouse: a model and motor for evolutionary understanding. *Biological Journal of the Linnean Society*, **84**, 335–347.

Berry RJ, Cuthbert A, Peters J (1982) Colonization by house mice - an experiment. *Journal of Zoology*, **198**, 329–336.

Bertorelle G, Benazzo A, Mona S (2010) ABC as a flexible framework to estimate demography over space and time: some cons, many pros. *Molecular Ecology*, **19**, 2609–2625.

Bonhomme M, Blancher A, Cuartero S, Chikhi L, Crouau-Roy B (2008) Origin and number of founders in an introduced insular primate: estimation from nuclear genetic data. *Molecular Ecology*, **17**, 1009–1019.

Bonhomme F, Orth A, Cucchi T *et al.* (2011) Genetic differentiation of the house mouse around the Mediterranean basin: matrilineal footprints of early and late colonization. *Proceedings of the Royal Society B*, **278**, 1034–1043.

Boutin-Ganache I, Raposo M, Raymond M, Deschepper CF (2001) M13-tailed primers improve the reliability and usability of microsatellite analyses performed with two different allele sizing methods. *Biotechniques*, **31**, 24–26.

Britton-Davidian J (1990) Genic differentiation in *M. m. domesticus* populations from Europe, the Middle-East and North-Africa - geographic patterns and colonization events. *Biological Journal of the Linnean Society*, **41**, 27–45.

Britton-Davidian J, Catalan J, Lopez J *et al.* (2007) Patterns of genic diversity and structure in a species undergoing rapid chromosomal radiation: an allozyme analysis of house mice from the Madeira archipelago. *Heredity*, **99**, 432–442.

Caldwell LD (1964) An investigation of competition in natural populations of mice. *Journal of Mammalogy*, **45**, 12–30.

Clegg SM, Degnan SM, Kikkawa J *et al.* (2002) Genetic consequences of sequential founder events by an island-colonizing bird. *Proceedings of the National Academy of Sciences, USA*, **99**, 8127–8132.

Cornuet JM, Luikart G (1996) Description and power analysis of two tests for detecting recent population bottlenecks from allele frequency data. *Genetics*, **144**, 2001–2014.

Cornuet J-M, Ravigne V, Estoup A (2010) Inference on population history and model checking using DNA sequence and microsatellite data with the software DIYABC (v1.0). *BMC Bioinformatics*, **11**, 401.

Cuthbert R, Hilton G (2003) Introduced house mice *Mus musculus*: a significant predator of threatened and endemic birds on Gough Island, South Atlantic Ocean? *Biological Conservation*, **117**, 483–489.

Dieringer D, Schlotterer C (2003) Microsatellite analyser (MSA): a platform independent analysis tool for large microsatellite data sets. *Molecular Ecology Notes*, **3**, 167–169.

Dlugosch KM, Parker IM (2008) Founding events in species invasions: genetic variation, adaptive evolution, and the role of multiple introductions. *Molecular Ecology*, **17**, 431–449.

Edgar RC (2004) Muscle: a multiple sequence alignment method with reduced time and space complexity. *BMC Bioinformatics*, **5**, 1–19.

Estoup A, Guillemaud T (2010) Reconstructing routes of invasion using genetic data: why, how and so what? *Molecular Ecology*, **19**, 4113–4130.

Evanno G, Regnaut S, Goudet J (2005) Detecting the number of clusters of individuals using the software STRUCTURE: a simulation study. *Molecular Ecology*, **14**, 2611–2620.

Excoffier L, Lischer HEL (2010) Arlequin suite ver 3.5: a new series of programs to perform population genetics analyses under Linux and Windows. *Molecular Ecology Resources*, **10**, 564–567.

Excoffier L, Estoup A, Cornuet JM (2005) Bayesian analysis of an admixture model with mutations and arbitrarily linked markers. *Genetics*, **147**, 915–925.

Falush D, Stephens M, Pritchard JK (2007) Inference of population structure using multilocus genotype data: dominant markers and null alleles. *Molecular Ecology Notes*, **7**, 574–578.

Foster JB (1964) The evolution of mammals on islands. *Nature*, **202**, 234–235.

Frankham R, Ballou JD, Briscoe DA (2002) *Introduction to Conservation Genetics*. Cambridge University Press, Cambridge, UK.

Fu YX (1997) Statistical tests of neutrality of mutations against population growth, hitchhiking and background selection. *Genetics*, **147**, 915–925.

Gabriel SI, Jóhannesdóttir F, Jones EP, Searle JB (2010) Colonization, mouse-style. *BMC Biology*, **8**, 131.

Garza JC, Williamson EG (2001) Detection of reduction in population size using data from microsatellite loci. *Molecular Ecology*, **10**, 305–318.

Gattepaille LM, Jakobsson M, Blum MGB (2013) Inferring population size changes with sequence and SNP data: lessons from human bottlenecks. *Heredity*, **110**, 409–419.

Geraldes A, Basset P, Gibson B *et al.* (2008) Inferring the history of speciation in house mice from autosomal, X-linked, Y-linked and mitochondrial genes. *Molecular Ecology*, **17**, 5349–5363.

Geraldes A, Basset P, Smith KL, Nachman MW (2011) Higher differentiation among subspecies of the house mouse (*Mus musculus*) in genomic regions with low recombination. *Molecular Ecology*, **20**, 4722–4736.

Goldstein DB, Pollock DD (1997) Launching microsatellites: A review of mutation processes and methods of phylogenetic inference. *Journal of Heredity*, **88**, 335–342.

Goldstein DB, Linares AR, Cavallisforza LL, Feldman MW (1995a) An evaluation of genetic distances for use with microsatellite loci. *Genetics*, **139**, 463–471.

Goldstein DB, Linares AR, Cavallisforza LL, Feldman MW (1995b) Genetic absolute dating based on microsatellites and

the origin of modern humans. *Proceedings of the National Academy of Sciences, USA*, **92**, 6723–6727.
Gündüz I, Tez C, Malikov V *et al.* (2000) Mitochondrial DNA and chromosomal studies of wild mice (Mus) from Turkey and Iran. *Heredity*, **84**, 458–467.
Gündüz I, Rambau RV, Tez C, Searle JB (2005) Mitochondrial DNA variation in the western house mouse (*Mus musculus domesticus*) close to its site of origin: studies in Turkey. *Biological Journal of the Linnean Society*, **84**, 473–485.
Haasl RJ, Payseur BA (2011) Multi-locus inference of population structure: a comparison between single nucleotide polymorphisms and microsatellites. *Heredity*, **106**, 158–171.
Hardouin EA, Tautz D (2013) Increased mitochondrial mutation frequency after an island colonization: positive selection or accumulation of slightly deleterious mutations? *Biology Letters*, **9**, 20121123.
Hardouin EA, Chapuis JL, Stevens MI *et al.* (2010) House mouse colonization patterns on the sub-Antarctic Kerguelen Archipelago suggest singular primary invasions and resilience against re-invasion. *BMC Evolutionary Biology*, **10**, 325.
Heaney JT, Holdgate MW (1957) The Gough Island scientific survey. *Geographical Journal*, **123**, 20–31.
Hey J, Nielsen R (2004) Multilocus methods for estimating population sizes, migration rates and divergence time, with applications to the divergence of *Drosophila pseudoobscura* and D-persimilis. *Genetics*, **167**, 747–760.
Hoffman JI, Grant SM, Forcada J, Phillips CD (2011) Bayesian inference of a historical bottleneck in a heavily exploited marine mammal. *Molecular Ecology*, **20**, 3989–4008.
Holdgate MW (1965) Part 3. The fauna of the Tristan da Cunha Islands. *Philosophical Transactions of the Royal Society B*, **249**, 361–402.
Hubisz MJ, Falush D, Stephens M, Pritchard JK (2009) Inferring weak population structure with the assistance of sample group information. *Molecular Ecology Resources*, **9**, 1322–1332.
Huelsenbeck JP, Ronquist F (2001) MRBAYES: Bayesian inference of phylogenetic trees. *Bioinformatics*, **17**, 754–755.
Ihle S, Ravaoarimanana I, Thomas M, Tautz D (2006) An analysis of signatures of selective sweeps in natural populations of the house mouse. *Molecular Biology and Evolution*, **23**, 790–797.
Jones AG, Chown SL, Gaston KJ (2003) Introduced house mice as a conservation concern on Gough Island. *Biodiversity and Conservation*, **12**, 2107–2119.
Jones EP, Jensen JK, Magnussen E *et al.* (2011a) A molecular characterization of the charismatic Faroe house mouse. *Biological Journal of the Linnean Society*, **102**, 471–482.
Jones EP, Jóhannesdóttir F, Gündüz I, Richards MB, Searle JB (2011b) The expansion of the house mouse into north-western Europe. *Journal of Zoology*, **283**, 257–268.
Jones EP, Skirnisson K, McGovern TH *et al.* (2012) Fellow travellers: a concordance of colonization patterns between mice and men in the North Atlantic region. *BMC Evolutionary Biology*, **12**, 35.
Jones EP, Eager HM, Gabriel SI, Jóhannesdóttir F, Searle JB (2013) Genetic tracking of mice and other bioproxies to infer human history. *Trends in Genetics*, **29**, 298–303.
Keller SR, Taylor DR (2008) History, chance and adaptation during biological invasion: separating stochastic phenotypic evolution from response to selection. *Ecology Letters*, **11**, 852–866.
Leuenberger C, Wegmann D (2010) Bayesian computation and model selection without likelihoods. *Genetics*, **184**, 243–252.
Lohmueller KE, Bustamante CD, Clark AG (2009) Methods for human demographic inference using haplotype patterns from genomewide single-nucleotide polymorphism data. *Genetics*, **182**, 217–231.
Lombaert E, Guillemaud T, Thomas CE *et al.* (2011) Inferring the origin of populations introduced from a genetically structured native range by approximate Bayesian computation: case study of the invasive ladybird *Harmonia axyridis*. *Molecular Ecology*, **20**, 4654–4670.
Losos JB, Ricklefs RE (2009) Adaptation and diversification on islands. *Nature*, **457**, 830–836.
Millien V (2006) Morphological evolution is accelerated among island mammals. *PLoS Biology*, **4**, 1863–1868.
Mourier T, Ho SYW, Gilbert MTP, Willerslev E, Orlando L (2012) Statistical guidelines for detecting past population shifts using ancient DNA. *Molecular Biology and Evolution*, **29**, 2241–2251.
Nei M (1987) *Molecular Evolutionary Genetics*. Columbia University Press, New York, NY, USA.
Nielsen R, Beaumont MA (2009) Statistical inferences in phylogeography. *Molecular Ecology*, **18**, 1034–1047.
Nylander JAA (2004) *MrModelTest v2* (http://www.abc.se/~nylander/mrmodeltest2/mrmodeltest2.html) Evolutionary Biology Centre, Uppsala University, Sweden.
Ohta T, Kimura M (1973) A model of mutation appropriate to estimate the number of electrophoretically detectable alleles in a finite population. *Genetical Research*, **22**, 201–204.
Palsboll PJ, Peery MZ, Olsen MT, Beissinger SR, Berube M (2013) Inferring recent historic abundance from current genetic diversity. *Molecular Ecology*, **22**, 22–40.
Palstra FP, Ruzzante DE (2008) Genetic estimates of contemporary effective population size: what can they tell us about the importance of genetic stochasticity for wild population persistence? *Molecular Ecology*, **17**, 3428–3447.
Peakall R, Smouse PE (2006) GENALEX 6: genetic analysis in Excel. Population genetic software for teaching and research. *Molecular Ecology Notes*, **6**, 288–295.
Peter BM, Wegmann D, Excoffier L (2010) Distinguishing between population bottleneck and population subdivision by a Bayesian model choice procedure. *Molecular Ecology*, **19**, 4648–4660.
Posada D, Buckley TR (2004) Model selection and model averaging in phylogenetics: advantages of Akaike information criterion and Bayesian approaches over likelihood ratio tests. *Systematic Biology*, **53**, 793–808.
Prager EM, Tichy H, Sage RD (1996) Mitochondrial DNA sequence variation in the eastern house mouse, *Mus musculus*: comparison with other house mice and report of a 75-bp tandem repeat. *Genetics*, **143**, 427–446.
Prager EM, Orrego C, Sage RD (1998) Genetic variation and phylogeography of central Asian and other house mice, including a major new mitochondrial lineage in Yemen. *Genetics*, **150**, 835–861.
Pritchard JK, Stephens M, Donnelly P (2000) Inference of population structure using multilocus genotype data. *Genetics*, **155**, 945–959.
Rajabi-Maham H, Orth A, Siahsarvie R *et al.* (2012) The southeastern house mouse *Mus musculus castaneus* (Rodentia:

Muridae) is a polytypic subspecies. *Biological Journal of the Linnean Society*, **107**, 295–306.
Ronquist F, Huelsenbeck JP (2003) MRBAYES 3: Bayesian phylogenetic inference under mixed models. *Bioinformatics*, **19**, 1572–1574.
Rowe-Rowe DT, Crafford JE (1992) Density, body size, and reproduction of feral house mice on Gough Island. *South African Journal of Zoology*, **27**, 1–5.
Salcedo T, Geraldes A, Nachman MW (2007) Nucleotide variation in wild and inbred mice. *Genetics*, **177**, 2277–2291.
Searle JB, Jamieson PM, Gündüz I *et al.* (2009) The diverse origins of New Zealand house mice. *Proceedings of the Royal Society B*, **276**, 209–217.
Slábová M, Frynta D (2007) Morphometric variation in nearly unstudied populations of the most studied mammal: the non-commensal house mouse (*Mus musculus domesticus*) in the Near East and Northern Africa. *Zoologischer Anzeiger - A Journal of Comparative Zoology*, **246**, 91–101.
Slatkin M (1995) A measure of population subdivision based on microsatellite allele frequencies. *Genetics*, **139**, 457–462.
Slatkin M, Hudson RR (1991) Pairwise comparison of mitochondrial DNA sequences in stable and exponentially growing populations. *Genetics*, **129**, 555–562.
St Clair JJH (2011) The impacts of invasive rodents on island invertebrates. *Biological Conservation*, **144**, 68–81.
Stephens M, Donnelly P (2003) A comparison of Bayesian methods for haplotype reconstruction from population genotype data. *American Journal of Human Genetics*, **73**, 1162–1169.
Sunnåker M, Busetto AG, Numminen E *et al.* (2013) Approximate Bayesian Computation. *PLoS Computational Biology*, **9**, e1002803.
Tajima F (1989) Statistical-method for testing the neutral mutation hypothesis by DNA polymorphism. *Genetics*, **123**, 585–595.
Teschke M, Mukabayire O, Wiehe T, Tautz D (2008) Identification of selective sweeps in closely related populations of the house mouse based on microsatellite scans. *Genetics*, **180**, 1537–1545.
Thomas M, Moller F, Wiehe T, Tautz D (2007) A pooling approach to detect signatures of selective sweeps in genome scans using microsatellites. *Molecular Ecology Notes*, **7**, 400–403.
Thornton K, Andolfatto P (2006) Approximate Bayesian inference reveals evidence for a recent, severe bottleneck in a Netherlands population of *Drosophila melanogaster*. *Genetics*, **172**, 1607–1619.
Uhden R (1939) Oldest Portugese original chart of the Indian Ocean. *Imago Mundi*, **3**, 7–11.
Verrill GE (1895) Notes on birds and eggs from the islands of Gough, Kerguelen, and South Georgia. *Transactions of the Connecticut Academy*, **11**, 429–480.
Wace NM (1961) Vegetation of Gough Island. *Ecological Monographs*, **31**, 337–367.
Wahlund S (1928) Zusammensetzung von Population und Korrelationserscheinung vom Standpunkt der Vererbungslehre aus betrachtet. *Hereditas*, **11**, 65–106.
Wakeley J (2001) The coalescent in an island model of population subdivision with variation among demes. *Theoretical Population Biology*, **59**, 133–144.
Wanless RM, Angel A, Cuthbert RJ, Hilton GM, Ryan PG (2007) Can predation by invasive mice drive seabird extinctions? *Biology Letters*, **3**, 241–244.
Wanless RM, Ryan PG, Altwegg R *et al.* (2009) From both sides: dire demographic consequences of carnivorous mice and longlining for the critically endangered Tristan albatrosses on Gough Island. *Biological Conservation*, **142**, 1710–1718.
Wanless R, Ratcliffe N, Angel A *et al.* (2012) Predation of Atlantic Petrel chicks by house mice on Gough Island. *Animal Conservation*, **15**, 472–479.
Waterston RH, Lindblad-Toh K, Birney E *et al.* (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature*, **420**, 520–562.
Watterson G (1975) On the number of segregating sites in genetical models without recombination. *Theoretical Population Biology*, **7**, 256–276.
Wegmann D, Excoffier L (2010) Bayesian inference of the demographic history of chimpanzees. *Molecular Biology and Evolution*, **27**, 1425–1435.
Wegmann D, Leuenberger C, Excoffier L (2009) Efficient approximate Bayesian computation coupled with Markov chain Monte Carlo without likelihood. *Genetics*, **182**, 1207–1218.
Wegmann D, Leuenberger C, Neuenschwander S, Excoffier L (2010) ABCtoolbox: a versatile toolkit for approximate Bayesian computations. *BMC Bioinformatics*, **11**, 116.
Weir BS, Cockerham CC (1984) Estimating F-statistics for the analysis of population-structure. *Evolution*, **38**, 1358–1370.
Williamson-Natesan EG (2005) Comparison of methods for detecting bottlenecks from microsatellite loci. *Conservation Genetics*, **6**, 551–562.
Wright S (1931) Evolution in Mendelian populations. *Genetics*, **16**, 97–159.

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Data accessibility

Raw microsatellite data, sequence files, sample accessions and simulation parameter files are available at Dryad Digital Repository doi:10.5061/dryad.tv492.

Supporting information

Additional supporting information may be found in the online version of this article.

Fig. S1 Bayesian phylogenetic tree constructed in Mr. Bayes based on mtDNA d-loop sequence.

Fig. S2 Principal coordinate analysis of 21 microsatellite loci.

Fig. S3 Posterior density distributions of the main model.

Fig. S4 Root mean squared error (RMSE) plots of partial least

squared components for each parameter inferred in the main demographic model.

Fig. S5 Distributions of the posterior quantiles for the parameters inferred in the main model of the ABC analysis.

Fig. S6 Posterior density distributions of variation 1 model.

Fig. S7 Posterior density distributions of variation 2 model.

Table S1 European samples included in the study.

Table S2 Genetic marker characteristics, primers, and reference sequence location.

Table S3 Summary statistics and partial least squared components calculated in the approximate Bayesian computation analysis.

Table S4 Microsatellite population genetic measures per locus per population.

Table S5 Microsatellite allele frequencies per locus per country.

Table S6 STRUCTURE group membership of European populations for $K = 5$.

Table S7 STRUCTURE group membership of Gough Island with European populations set as known.

Table S8 Posterior distribution characteristics for model variations in the ABC analysis.