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Genetic rescue in an inbred Arctic fox (*Vulpes lagopus*) population

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Isolation of small populations can reduce fitness through inbreeding depression and impede population growth. Outcrossing with only a few unrelated individuals can increase demographic and genetic viability substantially, but few studies have documented such genetic rescue in natural mammal populations. We investigate the effects of immigration in a subpopulation of the endangered Scandinavian arctic fox (*Vulpes lagopus*), founded by six individuals and isolated for 9 years at an extremely small population size. Based on a long-term pedigree (105 litters, 543 individuals) combined with individual fitness traits, we found evidence for genetic rescue. Natural immigration and gene flow of three outbred males in 2010 resulted in a reduction in population average inbreeding coefficient (f), from 0.14 to 0.08 within 5 years. Genetic rescue was further supported by 1.9 times higher juvenile survival and 1.3 times higher breeding success in immigrant first-generation offspring compared with inbred offspring. Five years after immigration, the population had more than doubled in size and allelic richness increased by 41%. This is one of few studies that has documented genetic rescue in a natural mammal population suffering from inbreeding depression and contributes to a growing body of data demonstrating the vital connection between genetics and individual fitness.

1. Introduction

Long-term isolation at small population size can reduce individual fitness through inbreeding depression and has been demonstrated as a major threat to the viability of small populations [1–4]. The phenomenon of heterosis (i.e. higher fitness in outbred offspring) was described in the eighteenth century [5,6], but Darwin was the first scientist to systematically investigate inbreeding depression and heterosis [7]. The outcrossing with unrelated individuals can prevent a small inbred population from genetic deterioration by increasing population size and influencing reproduction and survival [8,9]. Outcrossing can mitigate inbreeding depression by masking recessive deleterious alleles and increasing heterozygosity at loci with overdominance (i.e. genetic rescue [10–12]). Gene flow from only a few outbred individuals can have a positive impact on individual fitness and/or population growth [13–20].

It is challenging to investigate the occurrence of genetic rescue in natural populations as it requires replicate populations to control for effects of gene flow [21] and/or detailed individual monitoring, keeping record of genotypes and construction of pedigrees across several generations [22,23]. First, inbreeding depression must be established as the underlying mechanism for lowered fitness. Second, events of immigration and subsequent gene flow must be documented and, third, the effects of gene flow on fitness need to be verified. Despite the long-standing scientific interest, inbreeding depression and genetic rescue have mainly been documented in captivity and only in approximately 20 wild populations so far [24,25]. In mammals, genetic rescue has been documented on a few, rare occasions. In Florida panthers (*Puma concolor* [26]) and bighorn sheep (*Ovis canadensis* [27]) offspring with higher frequency of

immigrant alleles had higher survival compared with inbred offspring. In the severely inbred Scandinavian wolf (*Canis lupus* [28]), natural immigration by two males resulted in immigrant offspring with higher pairing and breeding success compared with inbred individuals [17]. Translocation of outbred individuals into a population of mountain pygmy possums (*Burramys parvus*) resulted in hybrid females producing more juveniles compared with non-hybrids [20]. Many studies on genetic rescue are based on indirect evidence, such as positive changes in population demography coinciding with outcrossing, which could have both demographic, environmental and genetic explanations [13,29,30].

The dramatic decline of the Scandinavian arctic fox (*Vulpes lagopus*) population provides a rare opportunity to study genetic rescue under natural conditions. At the end of the nineteenth century, the population experienced a major demographic and genetic bottleneck due to intensive hunting and fur trade [31]. The population was reduced from more than 10 000 to only a couple of hundred individuals persisting in a highly fragmented distribution [32–34]. In 1928, the arctic fox became protected by Swedish law. Norway followed in 1930, and Finland in 1940, but despite protection, the population continued to decline. Small population size in itself with its inherent demographic and genetic factors, such as Allee effects [35] and inbreeding depression [36], may prevent small population recovery. In addition, increased competition with red fox (*Vulpes vulpes*) [37,38] and irregularity in small rodent cycles [38] are well-documented threats to the arctic fox.

A near-complete pedigree of the southernmost Swedish arctic fox population revealed that it was founded by only seven individuals (of which six are represented in the population) and remained isolated for 9 years [36] with high relatedness and kin encounter rates as a result [39]. The population exhibited a 10-fold increase in inbreeding levels and in 2008 the population average inbreeding coefficient corresponded to that of progeny from half-sibling matings ($f = 0.125$). The population also suffered from inbreeding depression through lower juvenile survival and lower reproduction [36]. However, from 2010 to 2011, three male foxes released from the Norwegian captive breeding programme [40] immigrated into the study population. The immigrant foxes established at three vacant den sites and shortly thereafter all three started to reproduce. This was documented by the introduction of a blue colour morph in a population that previously only consisted of white foxes.

This background, combined with life-history traits and a genetically verified pedigree, provides a suitable dataset to test for effects of genetic rescue under natural conditions. We investigated (i) how rapid immigrant ancestry spread, (ii) how the demography developed the years following the immigration events, and (iii) whether immigration increased genetic variation and individual fitness.

2. Material and methods

(a) Study system

The Scandinavian arctic fox resides in the mountain tundra where its main food source consists of cyclic populations of voles (*Microtus* spp.) and lemmings (*Lemmus lemmus*). The fox population subsequently fluctuates in response to the rodent cycle [32,41,42]. Dalén *et al.* [33] documented three geographically isolated arctic fox subpopulations in Fennoscandia. This study

focuses on the southernmost subpopulation in Sweden, which resides in an area of 3400 km^2 in Helagsfjällen, Jämtland County (62° N, 12° E). Intensive monitoring and management actions have been performed in the area since year 2000 [38]. During summer inventories, all known arctic fox den sites are visited to document survival and reproduction. When litters are present, juveniles are ear-tagged with individual unique colour combinations. During 2001–2013, 68% of the total population were captured and ear-tagged [42] and during 2014–2015, approximately 60% were ear-tagged.

(b) Colour morphs

Arctic foxes appear in two different colour morphs: blue, which is expressed by a dominant allele, and white, which is recessively inherited [43]. Two of the immigrants were siblings belonging to the blue colour morph and the third one was an unrelated white male. The immigrants originated from foxes released from the captive breeding programme in Norway, released with the purpose to re-establish and strengthen arctic fox populations in mountain fragments in Norway, thereby restoring connectivity in the Scandinavian arctic fox population [40]. The parents of the white immigrant originated from Reisa Nord and Saltfjellet, in northern Norway. The parents of the blue immigrants were born within the captive breeding programme, and were descendants of individuals originating from five different subpopulations from Blåfjellet in mid-Scandinavia to the northeastern population at Varangerhalvøya in eastern Finnmark. The three males were released in September 2009 in Snøhetta, Dovre (62° N, 9° E). By spring 2010, they had reached the Helags arctic fox population in Sweden, covering a distance of approximately 250 km.

(c) Fitness measures

We used data on fundamental fitness traits (first-year survival and reproduction) for each individual. Survival was defined as whether an individual survived its first year (i.e. 0 or 1) based on visual observation and genetic assignment. Without visual observations of an individual for a full rodent cycle (i.e. 3–4 years), the individual was assumed to be dead. Reproduction was estimated as breeding success (i.e. the number of litters divided by age of the breeding adult). As survival and reproduction are strongly connected to the rodent cycle [42,44], which phase in the cycle an individual was born during was also considered [36]. The data covered five rodent cycles and the rodent densities were inferred based on indices of abundance from snap trapping [45].

(d) Genetic analyses

We assembled data on 11 polymorphic and autosomal loci from a total of 678 individuals that were ear-tagged during 2001–2015. The dataset included previously published microsatellite data on 247 individuals (2001–2009) [36] and recently analysed microsatellite data on 431 individuals (2010–2015). DNA storage, extraction and PCR amplification were conducted in accordance with Norén *et al.* [36] with the exception that locus CPH15 [46] was replaced with locus 606 [47]. Gene fragments (microsatellite alleles) were size-determined using LIZ-500 size standard (Thermo Fisher Scientific, Waltham, MA, USA) on an ABI3730 capillary sequencer (Applied Biosystems, Foster City, CA, USA). Previously published data were analysed on a Beckman-Coulter CEQ8000 capillary sequencer (Beckman-Coulter Life Sciences, Brea, CA, USA). Possible differences in allele sizes were therefore accounted for by parallel analysis of five samples.

(e) Pedigree construction

We constructed a pedigree comprising the foxes born and tagged during 2010–2015. To test for effects of genetic rescue, this was
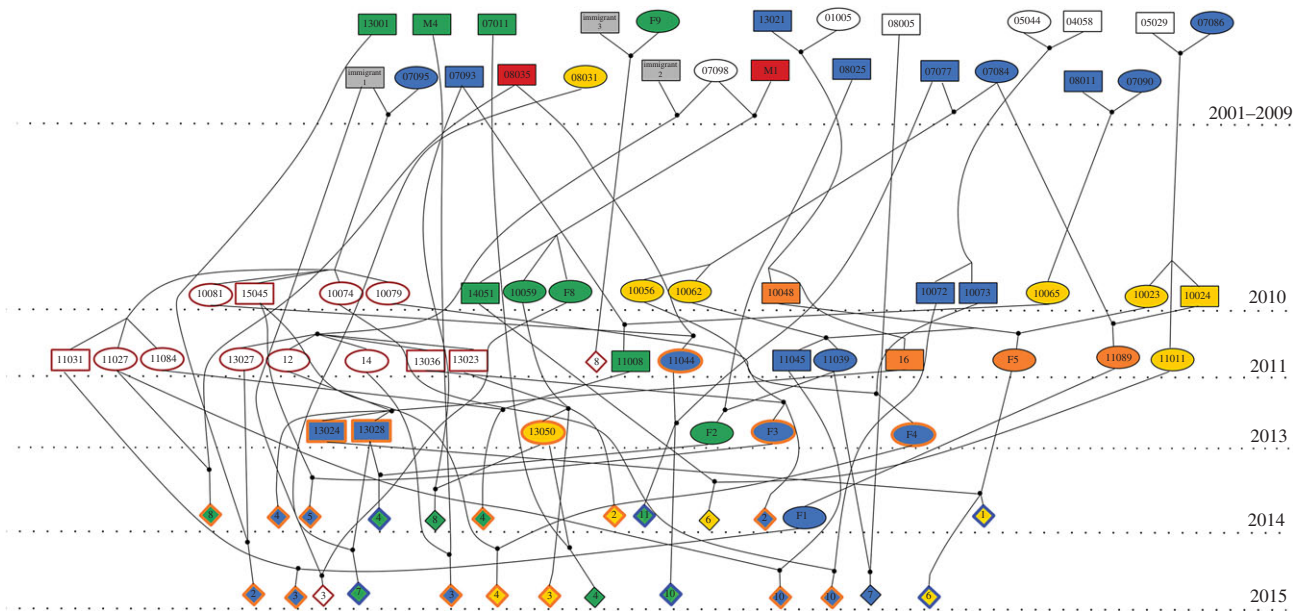
Figure 1. Reduced version of a genetically verified pedigree of a Swedish arctic fox population depicting individuals born during 2010–2015 and their parents. Ellipses represent females, rectangles represent males and diamonds are individuals that have not reproduced. Immigrants are represented as grey symbols. The remaining fill colours represent inbreeding categories (blue: $0.02 < f < 0.07$, green: $0.074 < f \leq 0.125$, yellow: $0.15 < f < 0.18$, orange: $0.1875 \leq f < 0.22$, red: 0.25). The outline colours of the symbols represent the generation of immigrant descendants (red = F_1, orange = F_2, blue = F_3). All individuals with unknown inbreeding coefficients as well as all non-reproducing individuals born before the two last years of the study period were excluded for simplicity. The full pedigree can be found in the electronic supplementary material. (Online version in colour.)

combined with a previously published pedigree (2001–2009) [36]. Three approaches were used: the exclusion method [36], parental assignment in the software COLONY v. 2.0 [48] and manual re-construction of parental genotypes for litters with only one assigned parent. Reconstructed genotypes were also run in COLONY and the genotypes of 12 additional parents could be identified. Finally, we uploaded all inferred relationships to PEDIGRAPH v. 2.2 [49] where a pedigree was drawn and individual inbreeding coefficients (f) were calculated.

(f) Statistical analyses

The population size for each year was approximated as the number of breeding adults (i.e. the number of litters multiplied by two). We calculated number of alleles per locus, as well as expected and observed heterozygosity for 10 microsatellite loci before immigration and for 11 loci after immigration, using the software GENALEX v. 6.5 [50]. We also calculated genetic distance for all individuals with known ancestry and performed a principal coordinate analysis with standardized covariance in the same software. We calculated allelic richness in the software FSTAT v. 2.9.3.2 [51]. Multilocus heterozygosity (MLH), for each individual, was calculated according to Hansson and Westerberg (i.e. number of heterozygous loci divided by number of loci genotyped [52]). We estimated the number of founder genome equivalents remaining at the last year of the study period by performing 10 000 gene drop simulations in the software PEDSCOPE v. 2.4.01.

We performed a non-parametric Mann–Whitney U-test to test whether immigrant offspring had higher MLH than inbred ones and Wilcoxon signed-rank tests to find out whether expected heterozygosity and allelic richness differed between the pre- and post-immigration populations. First-year survival was compared between immigrant first-generation offspring and native offspring through a generalized linear mixed-effect model with binomial distribution and logit links. In addition, we performed the same test on immigrant second- and third-generation offspring compared with native ones. Sex and phase of the rodent cycle, when an individual was born, were used as fixed effects, and natal den was used as a random effect. We performed a linear mixed-effect model controlling for the same confounding variables to compare

the difference in breeding success. All tests were performed in R-studio v. 3.3.3 using package lme4.

3. Results

(a) Pedigree, gene flow and inbreeding

DNA was sampled from 90 litters and 431 individuals between 2010 and 2015. For 14 of those litters (77 foxes), it was not possible to resolve the parentage and they were therefore excluded from further analyses. For 4 litters (28 foxes), grandparents could not be assigned and they were hence also excluded, giving a remaining sample size of 326. An additional 27 individuals born before 2010 were assigned as parents in 30 litters and were therefore included in the pedigree. Furthermore, the genotypes of 12 additional parents were manually reconstructed and included in the pedigree. The final pedigree between 2010 and 2015 thus comprised 72 litters and 365 individuals (figure 1). This was combined with a previous pedigree between 2001 and 2009 consisting of 33 litters and 205 individuals, giving a final pedigree comprising 105 litters and 543 individuals (electronic supplementary material, figure S1). The probability of identity was estimated to 1.0×10^{-8} for unrelated individuals and 3.0×10^{-4} for full-sibs.

In 2010, 10% of the litters with known parentage (one out of 10 litters) were the offspring of immigrants and in 2015, 89% of the litters (17 out of 19) were related to the three immigrants (figure 2a). Furthermore, the ancestry of the immigrants (i.e. the expected proportion of genes from a given individual carried by its descendants [53]) constituted 5% in 2010 and 22% in 2015 (figure 2b). The two blue immigrants were particularly successful: in 2015, they were related to 84% of the population and their ancestry constituted 21% of the population. Descendants from the white individual, on the other hand, could only be found in 5% of the litters (one out of 20) and his ancestry constituted 1% of the population in 2015 (table 1).
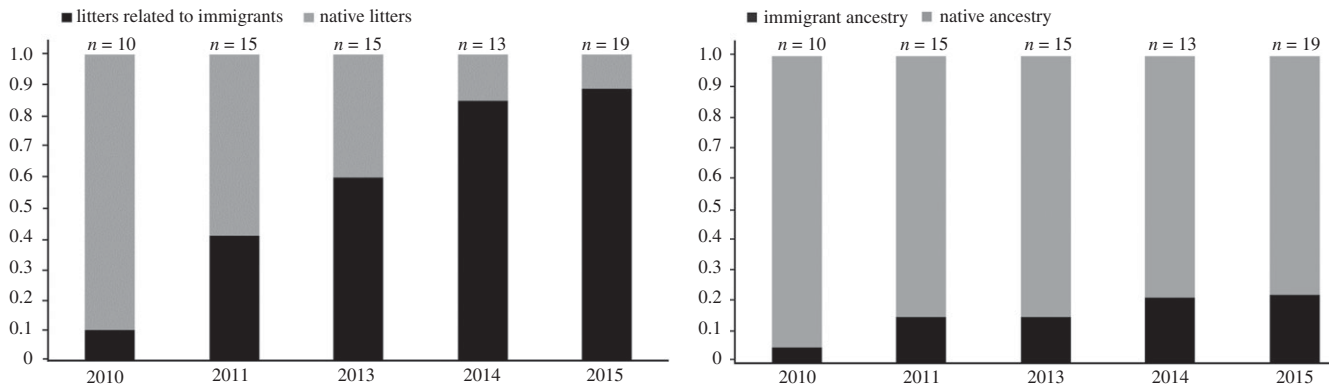
Figure 2. Proportion of litters descending from three immigrants (*a*) and proportion of ancestry from the immigrants (*b*) since the first event of immigration (2010) in a Swedish arctic fox population (*n* = 72).

At the start of the study (2010), the population average inbreeding coefficient (*f*) was 0.14 and by 2015, it had decreased to $f = 0.08$. During the same period of time, the population more than doubled (26 breeding individuals in 2010 and 58 breeding individuals in 2015; figure 3). The individual inbreeding coefficients ranged from $f = 0$ to 0.250 and the smallest non-zero inbreeding coefficient was $f = 0.027$. During 2010–2015, there were 41 individuals (12.5%) that were fully outbred ($f = 0$), all of them first-generation offspring of the three immigrants. Two litters (eight individuals, 2.4%) were produced from full sibling matings ($f = 0.25$; figure 4). It was primarily three of the six founders that caused the inbreeding. Between 2010 and 2015, their contribution to the inbreeding varied between 78 and 93%. The immigrant siblings contributed to the inbreeding in two litters (one in 2014 and one in 2015; electronic supplementary material, figure S2).

(b) Immigration and genetic variation

Before immigration, average expected heterozygosity was 0.61 (± 0.12) and average number of alleles per locus was 3.7 (± 0.82). There was a heterozygote excess in six out of 10 loci (electronic supplementary material, table S1). After immigration, average expected heterozygosity was 0.63 (± 0.08) and average number of alleles per locus was 5.36 (± 1.29). Heterozygote excess was recorded in one out of 11 loci, whereas a heterozygote deficiency was found in five loci (electronic supplementary material, table S1). There was no difference in expected heterozygosity before and after immigration (Wilcoxon signed-rank, $p = 0.34$), but a weak trend for higher MLH in immigrant first-generation offspring (0.67 ± 0.19) compared with native ones born between 2010 and 2015 (0.61 ± 0.17; Mann–Whitney, $n = 183$, $p = 0.09$). Furthermore, there was a higher allelic richness after immigration ($p = 0.0224$; electronic supplementary material, table S1). The immigrants brought in 13 novel alleles into the population (electronic supplementary material, table S2). The principal coordinate analysis based on genetic distance revealed that native individuals and individuals with immigrant ancestry largely overlapped but varied slightly from each other as descendants of immigrants had a smaller spread (figure 5). Analysis of founder allele retention yielded 6.19 founder genome equivalents remaining in the population.

(c) Immigration and fitness

During 2010–2015, the three immigrants produced a total of 51 first-generation offspring in six litters ($f = 0$). DNA samples were collected from 41 of them. Fitness traits were compared with 109 native offspring ($f = 0.05$–0.25) born during the same years.

According to the linear mixed-effect model, first-generation immigrant offspring (F_1) had higher first-year survival compared with inbred offspring ($Z = 2.24$, $p = 0.025$, $n = 150$). Survival was lower during phases with low rodent densities (21% survival of individuals born during low densities and 40% survival of those born during high densities; $Z = -2.42$, $p = 0.016$). There was no correlation between survival and sex (28% survival of males and 27% survival of females; $Z = 0.36$, $p = 0.72$). In a generalized linear model, results were concordant with the mixed-effect model but showed a clearer difference between survival of outbred versus inbred foxes ($Z = 2.58$, $p = 0.01$) and an even more pronounced negative effect of low food abundance on survival ($Z = -2.67$, $p = 0.008$). Sex remained uncorrelated with survival ($Z = 0.3$, $p = 0.77$). In summary, 41% of immigrant offspring survived their first year, whereas 22% of inbred offspring survived their first year (figure 6a). More distant descendants (i.e. immigrant second- and third-generation offspring, in this paper termed F_2 and F_3, which were the result of immigrant offspring which in most cases backcrossed with native individuals) did not have higher survival compared with native offspring ($Z = -1.3$, $p = 0.19$, $n = 277$).

Breeding success (i.e. number of litters divided by the age of breeding adults) was calculated for the first-year survivors of immigrant first-generation offspring and native offspring born during the same years (16 F_1 and 24 native foxes). A linear mixed-effect model showed that F_1 offspring had higher breeding success compared with inbred offspring ($t = 2.18$, $p = 0.029$, $n = 40$). The average breeding success was 0.5 (± 0.16) for immigrant offspring and 0.39 (± 0.17; figure 6b) for native inbred offspring. There was no relationship between breeding success and phase of the rodent cycle ($t = -0.65$, $p = 0.51$) or sex ($t = -0.61$, $p = 0.54$).

4. Discussion

Although genetic rescue has been of scientific interest for centuries and is theoretically well established, few studies have explored how gene flow affects wild mammal populations suffering from inbreeding depression under natural conditions [24,25]. We had the rare opportunity to investigate genetic rescue effects in a small and isolated subpopulation of arctic foxes in Scandinavia, exploring how rapidly the ancestry of

Table 1. Proportion of genetic contribution of each immigrant and the six founders during 2010–2015 in all litters with known parentage in a Swedish arctic fox population. Immigrant 1 and 2 are siblings belonging to the blue colour morph and immigrant 3 to the white colour morph.

year	ancestry of immigrant 1 (blue)		ancestry of immigrant 2 (blue)		ancestry of immigrant 3 (white)		ancestry of founders		no. litters with known ancestry
	genetic contribution	proportion	genetic contribution	proportion	genetic contribution	proportion	genetic contribution	proportion	
2010	0.5	0.05	—	—	—	—	9.5	0.95	10
2011	1.25	0.084	0.5	0.033	0.5	0.033	12.75	0.85	15
2013	0.5	0.033	1.75	0.117	—	—	12.75	0.85	15
2014	1.125	0.087	1.625	0.125	—	—	10.25	0.788	13
2015	2	0.105	2	0.105	0.25	0.013	14.75	0.777	19

three immigrants spread and if any effects on demography, genetic variation and individual fitness could be connected to immigration and outbreeding.

Immigration and subsequent reproduction (gene flow) into an inbred population generally reduces population inbreeding levels. Since the first event of immigration (2010), the average inbreeding coefficient decreased to the lowest level the population has experienced since 2006 (figure 3). This 43% reduction is even more pronounced than the reduction the Scandinavian wolf population recently experienced (20%) as a result of two immigration events [17]. This is probably due to the lower number of reproducing arctic foxes over a smaller geographical distribution compared with the Scandinavian wolves at the immigration events, facilitating a more rapid spread of immigrant ancestry. Furthermore, wolves use fairly stable food sources, whereas the highly fluctuating food availability of the arctic foxes might give outbred foxes a strong selective advantage when food is scarce.

Immigration of unrelated individuals into small inbred populations is predicted to increase the genetic variation and decrease the proportion of individuals that are homozygous for alleles identical by descent [54]. In an inbred population of pumas (*Puma concolor*), expected heterozygosity and allelic richness based on 44 microsatellite loci increased substantially 7 years after the immigration of a single male [55]. However, it is also well known that the level of heterozygosity responds slowly to demographic changes [56,57]. A short time interval since the immigration events occurred in combination with a limited number of loci used probably prevented the detection of genome-wide variation in heterozygosity in this study (e.g. [58–62]). Nevertheless, the immigrants have increased the allelic richness (electronic supplementary material, table S1), resulting in higher fitness and improved potential for adaptation to environmental changes. Before immigration, there was a heterozygote excess in six loci, whereas after immigration a deficiency was found in five loci (electronic supplementary material, table S1). This is counterintuitive as heterozygosity is expected to decrease during isolation and increase in response to gene flow. Heterozygote excess despite extended periods of isolation has been found in previous studies [13,63] and could arise by chance due to small effective population size [64] but could also be caused by inbreeding avoidance, which was recently discovered in this population [65]. The heterozygote deficiency found after immigration is likely an artefact of appeared subpopulation structure arising from the admixture event [66].

Perhaps the most important criterion for genetic rescue is that gene flow increases individual fitness [12]. Five years after the first immigration event, 89% of the litters descended from the three immigrants and their ancestry constituted 22% (figure 2). This rapid spread of immigrant ancestry can be explained by the higher first-year survival and breeding success in offspring to immigrants compared with native offspring (figure 6a,b). In two isolated populations of South Island robins (*Petroica australis*), offspring to immigrants had higher juvenile survival and breeding success [15] and in the severely inbred Swedish wolf population, immigrant offspring had higher reproductive success compared with native offspring [17]. Our results are in line with these studies, and strengthen the evidence that gene flow from a limited number of individuals can have large impacts in inbred populations.

Another important component of genetic rescue is that gene flow is accompanied by an increase in population
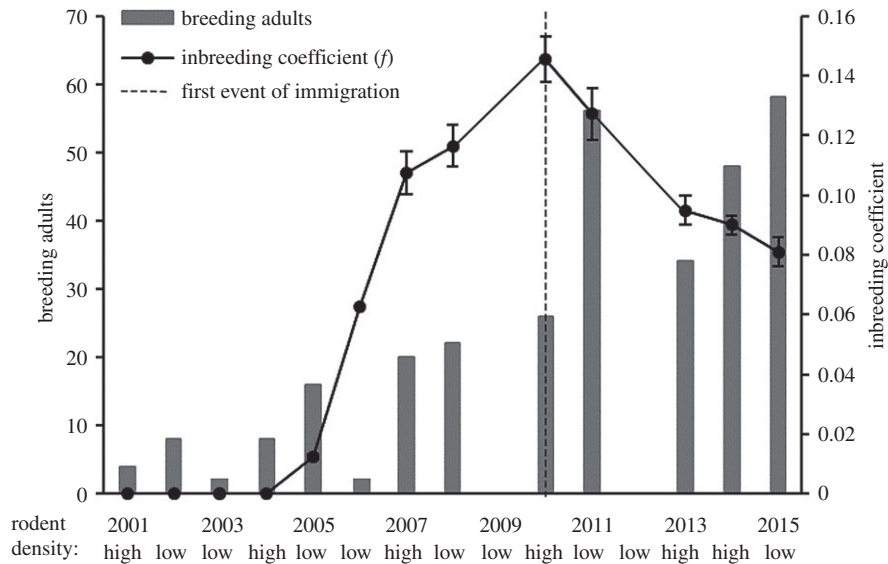
Figure 3. Average inbreeding coefficient (f) with variance (line with bars), and population dynamics approximated as number of breeding adults (bars) during 2001–2015 in a Swedish arctic fox population. Rodent density is specified for each year. The dashed vertical line shows immigration of three male foxes from the Norwegian captive breeding programme.
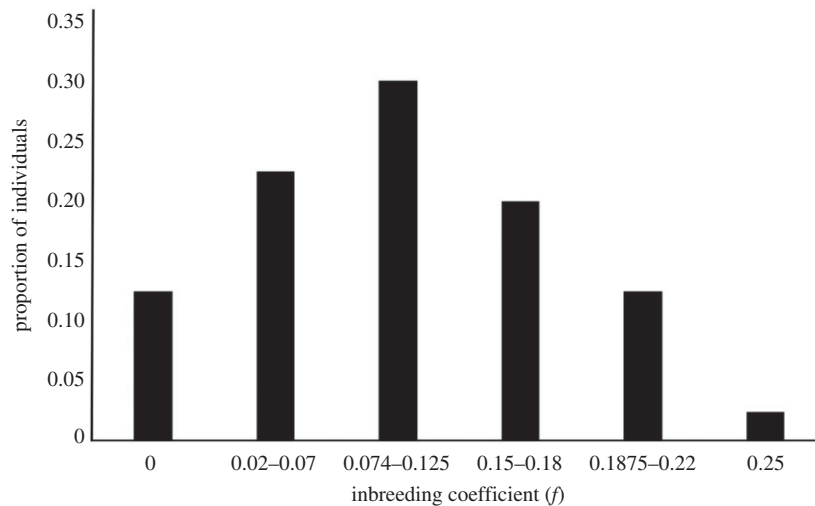

Figure 4. Proportion of different inbreeding levels for individuals born during 2010–2015 in a Swedish arctic fox population ($n = 326$).
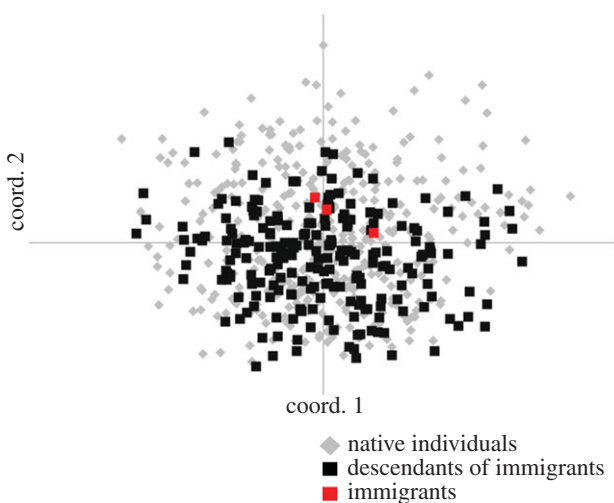
Figure 5. Principal coordinate analysis of genetic distance for native individuals ($n = 360$) and individuals with immigrant ancestry ($n = 225$) in a Swedish arctic fox population. Red data points represent three male immigrants. (Online version in colour.)

growth [50]. Since the immigration events, the population has more than doubled (figure 3). This is partly due to the extensive conservation efforts such as supplementary feeding and red fox culling, together with recurring small rodent dynamics, which all have contributed to the population growth [35,38]. Furthermore, increased population size is often followed by a positive feedback caused by facilitation of finding a mate and by reduced *per capita* risk of natural enemies [8]. However, in several other studies, immigration has been followed by an increased population growth rate [13,17,18,20,67], and it is likely that the immigration events in this population have contributed to the increase in population size, due to higher fitness in immigrant offspring (figure 6). Although the effect of immigration is hard to distinguish from other beneficial factors, the conservation efforts have been implemented at a constant intensity since 2000 [38], and yet has the population size experienced a more substantial increase after immigration (2010–2015) compared with before (2000–2010; figure 3). This implies that the conservation efforts are not the only drivers of the population growth.
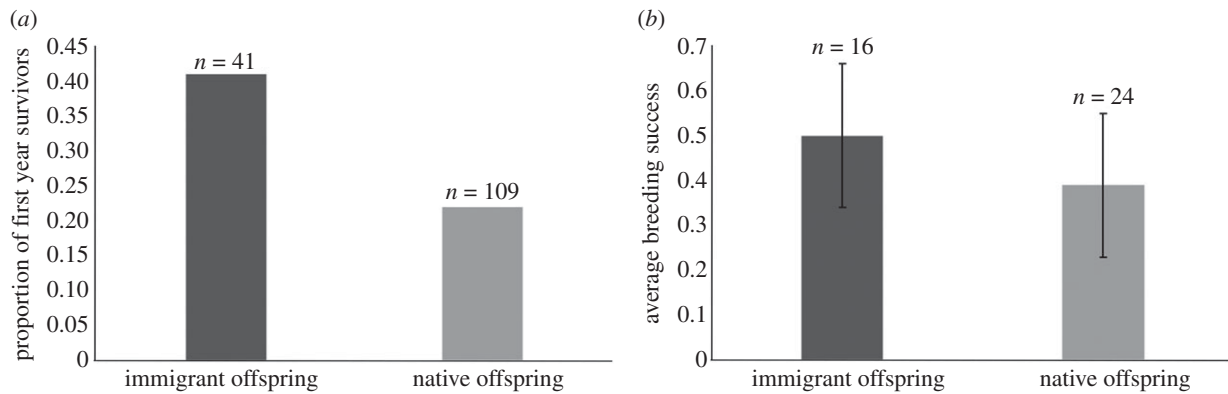
Figure 6. (a) Proportion of immigrant first-generation offspring (0.41) and native offspring (0.22) that survived their first year ($n = 150$) and (b) average breeding success for immigrant first-generation offspring (0.5, standard deviation ± 0.16) and native offspring (0.39, standard deviation ± 0.17; $n = 40$) in a Swedish arctic fox population.

The increased fitness was not apparent in more distant descendants of the immigrants (F_2 and F_3 offspring). In contradiction to this, results from a meta-analysis [16] revealed that benefits of genetic rescue generally persisted to at least the third-generation offspring of immigrants. It is possible that immigrant second- and third-generation offspring in this population also have elevated fitness, although not detectable in this study because many individuals were born at the end of the study period and their survival may thus be underestimated. However, without additional gene flow in the near future, the genetic rescue is not likely to be persistent because the inbreeding levels will soon increase again, probably with lowered fitness as a result. However, there is a risk that a second event of immigration from the same source would be less successful, because detrimental alleles at specific loci might already be reduced in frequency from the first immigration event, but additional immigrants may not carry non-detrimental alleles for remaining loci [68]. Although the immigrants carried ancestry from several subpopulations in Norway, the Scandinavian arctic fox population generally has rather low genetic variation [33]. Even if a second event of immigration may not be as successful in decreasing the expression of detrimental alleles, it could still improve the evolutionary potential [69].

At an initial stage, the immigration of three males has resulted in genetic rescue, documented as increased population size and higher fitness in immigrant first-generation offspring compared with native ones. It is more challenging to predict future effects of the immigration events. If immigration is too overwhelming, a large part of the population could be replaced by immigrant ancestry and eliminate local variation [68]. In the wolf population on Isle Royale, immigration of a single male caused inbreeding levels to drop by 89% in only 4 years. By that time, the immigrant was related to every individual and his ancestry constituted 56%. Inbreeding increased again rapidly and a large part of the native gene pool was replaced with that of the immigrant [70]. There could be a similar outcome from the immigration in the arctic fox population, although not as dramatic. The genetic structure has shifted slightly (figure 5), but the immigrant ancestry has not spread as rapidly as in the wolf population. Only two recorded litters have been produced by inbreeding between descendants of immigrants. Moreover, unlike that of the wolves, immigration has been accompanied by population growth, allowing inbreeding levels to decrease steadily. Nevertheless, most ancestors of the immigrants are from the full siblings (21 of 22%), so in fact more than one-fifth of the gene pool descends

from only 1.5 individuals. It is probably inevitable that inbreeding between immigrant descendants will increase during coming years. If immigrant ancestry becomes very high in future generations, the effective population size will decrease and neutral genetic variation that may play a potential role in future adaptation could be lost [68].

The specific genes connected to higher survival and breeding success in outbred arctic foxes remain unknown. The higher fitness in immigrant offspring is likely to be due to lower expression of deleterious alleles (i.e. the dominance hypothesis), but also a general heterozygote advantage could be involved. Phenotypically, the higher survival in immigrant offspring could be explained by higher birth weight and/or pathogen resistance [11], whereas the higher breeding success may be due to social dominance [70], higher dispersal capacity [71] or inbreeding avoidance [62]. It is possible to detect specific genomic regions and traits that contribute to inbreeding depression by identifying chromosomal regions with unusually low frequency of runs of homozygosity and test for phenotypic effects in these regions [72].

5. Conclusions and future directions

Our results show clear evidence for genetic rescue through substantial selective advantage for immigrant offspring. This is one of few studies to document genetic rescue at both individual and population level in a natural mammal population suffering from inbreeding depression. To improve our understanding about the underlying mechanisms of genetic rescue, future studies should be directed at exploring the relationship between functional genes and inbreeding depression, which could be achieved with high-resolution genomic data [56,73]. This would provide a deeper understanding of specific fitness effects linked to inbreeding and broaden our perspective on evolutionary processes in small populations [60].

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