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Original Article

Temporal genomic change in the Scandinavian Arctic fox (*Vulpes lagopus*)

Johanna von Seth[1,2,3,4,*], Petter Larsson[2], Malin Hasselgren[4], Nicolas Dussex[2,4,5], Liliana Farelo[6,7], Johan Wallén[4,5], Verena E. Kutschera[8], Nina E. Eide[9], Arild Landa[10], Anders Angerbjörn[4], Øystein Flagstad[9], José Melo-Ferreira[6,7,11], Karin Norén[4], Love Dalén[2,3,4,*]

[1]Department of Organismal Biology, Evolutionsbiologiskt Centrum EBC, Uppsala University, Norbyvägen 18 A, 752 36 Uppsala, Sweden
[2]Centre for Palaeogenetics, Svante Arrhenius väg 20C, Stockholm, SE-10691, Sweden
[3]Department of Bioinformatics and Genetics, Swedish Museum of Natural History, Box 50007, Stockholm, SE-10405, Sweden
[4]Department of Zoology, Stockholm University, Stockholm, SE-10691, Sweden
[5]Department of Population Analysis and Monitoring, Swedish Museum of Natural History, Box 50007, Stockholm, SE-10405, Sweden
[6]InBIO Laboratório Associado, CIBIO, Centro de Investigação em Biodiversidade e Recursos Genéticos, Universidade do Porto, Campus de Vairão, 4485-661 Vairão, Portugal
[7]BIOPOLIS Program in Genomics, Biodiversity and Land Planning, CIBIO, Campus de Vairão, 4485-661 Vairão, Portugal
[8]Department of Biochemistry and Biophysics, National Bioinformatics Infrastructure Sweden, Science for Life Laboratory, Stockholm University, SE-171 65 Solna, Sweden
[9]Land and biodiversity, Norwegian Institute for Nature Research, Trondheim, NO-7485, Norway
[10]NINA-Bergen, Norwegian Institute for Nature Research, Thormøhlensgate 55, Bergen, NO-5006, Norway
[11]Department of Biology, Faculty of Sciences, University of Porto, Rua Campo Alegre s/n, 4169-007 Porto, Portugal

*Corresponding authors. Johanna von Seth, Department of Organismal Biology, Evolutionsbiologiskt Centrum EBC, Uppsala University, Norbyvägen 18 A, 752 36 Uppsala, Sweden. E-mail: johanna.n.vonseth@gmail.com; Love Dalén, Centre for Palaeogenetics, Svante Arrhenius väg 20C, SE-10691 Stockholm, Sweden. E-mail: love.dalen@zoologi.su.se

ABSTRACT

Demographic declines have important consequences for population viability, since they can lead to losses in genome diversity, as well as increased inbreeding and expression of deleterious mutations. Scandinavia was colonized by the Arctic fox (*Vulpes lagopus*) at the Pleistocene/Holocene transition, and the population has since been on the periphery of the global distribution. The Scandinavian population became even more fragmented in the early 1900s due to human persecution, and experienced an additional decline in the 1980s. We generated high-coverage genomes from pre-bottleneck, as well as modern Scandinavian and Russian specimens, and found that genome-wide diversity was lower and inbreeding higher in Scandinavia compared to the Siberian population, even prior to the historical bottleneck, most likely reflecting the long-term partial isolation and recent postglacial origin of the Scandinavian population. The southern subpopulation has the highest inbreeding levels, likely due to having been recently founded and highly isolated. Our results also show that although inbreeding increased substantially over the past century, the amount of total genetic load did not change. Overall, these findings illustrate the utility of a temporal approach to disentangle the genomic consequences of recent declines from ancient biogeographic processes.

Keywords: Arctic fox; conservation; degraded DNA; gene flow; genetic load; genomic diversity; inbreeding; population decline; Scandinavia; small populations

INTRODUCTION

Anthropogenic threats to the viability of natural populations have increased globally in recent centuries, driven both by the intensification of long-established drivers for extinction (e.g. habitat destruction and overexploitation) and by the emergence of new stressors (e.g. climate disruptions and introduced pathogens; Dirzo *et al.* 2014). As a consequence, many species have recently gone through dramatic demographic declines (Dirzo *et al.* 2014, Murphy and Romanuk 2014). Studies from the past decade using whole genomes from endangered populations have shown that

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such declines have had an impact on genome diversity, inbreeding, and genetic load (Xue *et al.* 2015, Feng *et al.* 2019, Robinson *et al.* 2019, van der Valk *et al.* 2019, Grossen *et al.* 2020, Dussex *et al.* 2021, Sánchez-Barreiro *et al.* 2021, von Seth *et al.* 2021). Fragmented and small populations thus face an increased risk of extirpation due to not only demographic and environmental change, but also genetic stochasticity (Caughley 1994), where population decline leads to increased genetic drift. Population decline leads to increased genetic drift and inbreeding, and can cause an accumulation of genetic load that can hamper population viability (Frankham 2005). However, genetic load can also be purged from a population that is experiencing inbreeding depression, implying that population viability can recover if the population manages to avoid extirpation (reviewed in Hedrick and Garcia-Dorado 2016, Dussex *et al.* 2023).

Arctic species are also under increasing pressure from ongoing climate change. From a climate perspective, increasing global temperatures cause temperate zones and boreal species to expand northwards, and upwards along altitudinal gradients, leading to decreasing availability of suitable habitats as well as fragmentation of Arctic populations (Hersteinsson and MacDonald 1992, Callaghan *et al.* 2004, Elmhagen *et al.* 2015). Moreover, many Arctic species depend on yearly sea ice for dispersal and foraging. The current decline in sea ice extent and thickness, as well as the shortening of the period during which the sea is covered by ice, has led to reduced population connectivity, thus increasing the rate of genetic drift and inbreeding within populations (Stirling and Parkinson 2006, Geffen *et al.* 2007, Barber *et al.* 2009, Post *et al.* 2013).

The Arctic fox (*Vulpes lagopus* Linnaeus, 1758) is a mesopredator distributed across high-latitude regions of the Northern Hemisphere and is capable of migrating long distances, including across sea ice, as was exemplified by a young female that in 2018 travelled a cumulative distance of 3506 km from Svalbard, Norway to Ellesmere Island, Nunavut, Canada over the course of 76 days (Pamperin *et al.* 2008, Gagnon and Berteaux 2009, Tarroux *et al.* 2010, Lai *et al.* 2015, Norén *et al.* 2017, Fuglei and Tarroux 2019). Thus, areas with only temporal sea ice harbour relatively more isolated populations with higher genetic differentiation in comparison to populations connected by yearly sea ice, which almost resemble one homogeneous population (Dalén *et al.* 2004, Geffen *et al.* 2007, Norén *et al.* 2011, 2017). One such isolated area is the Scandinavian Peninsula, where the local Arctic fox population has remained connected to the global distribution only via Finland and the Kola Peninsula (Dalén *et al.* 2006). The fur trade almost caused a local extinction of the species in Scandinavia in the early 20th century, when the population declined from *c.* 10 000 to *c.* 100 individuals (Lönnberg 1927, Tannerfeldt 1997). Although hunting of Arctic foxes was completely banned in Fennoscandia by 1940, the population did not recover. Instead, the Scandinavian Arctic fox population experienced an additional decline in the 1980s and 1990s due to disruptions in small rodent cycles and increased interspecific competition, as the red fox (*Vulpes vulpes* Linnaeus, 1758) population expanded (Angerbjörn *et al.* 1995, 2013). These factors have also been proposed as the primary causes behind a lack of population recovery during the past 100 years, but loss of genetic variation and inbreeding depression may also have played a role (Hersteinsson *et al.* 1989, Elmhagen *et al.* 2000, Tannerfeldt *et al.* 2002, Herfindal *et al.* 2010, Norén *et al.* 2016, Hasselgren *et al.* 2018, 2021).

The demographic decline that took place in the past 100 years caused a fragmentation of the Scandinavian population into several small and isolated subpopulations (Dalén *et al.* 2006, Herfindal *et al.* 2010, Cockerill *et al.* 2022). Previous work has suggested that the Scandinavian Arctic fox population has lost 25% of its microsatellite variation and at least half of its mitochondrial DNA haplotypes since the decline in the early 1900s (Nyström *et al.* 2006, Larsson *et al.* 2019). It is not until the last decade that positive demographic trends have been reported, largely due to extensive conservation actions (Hemphill *et al.* 2020), where approximately 560 adult individuals were estimated to have been occupying the mountain tundra in Scandinavia and Finland between the years of 2021 and 2023 (Wallén *et al.* 2023a). In the well-studied southernmost subpopulation, the situation has been especially dire (Fig. 1A). It became functionally extinct in the 1980s, was re-founded in the early 2000s by only seven individuals of unknown origin and relatedness, but remained isolated until 2010 (Norén *et al.* 2016).

In this study, we aimed to further investigate to what extent long-term as well as more recent demographic processes have affected the genomic state of the Scandinavian Arctic fox population. By extending from previous studies on nuclear and mitochondrial markers to whole genomes (five *c.* 100-year-old Scandinavian specimens, and 29 modern samples from both Scandinavia and Russia), we tested whether the past *c.* 100 years of population decline has led to a decrease in genome-wide diversity, and if the fragmentation of the Scandinavian population has caused an increase in inbreeding within the remaining isolated subpopulations. Lastly, we estimated levels of genetic load to investigate whether the ensuing isolation of the subpopulations caused changes in the amount of potentially detrimental genetic variation.

MATERIALS AND METHODS

Genome re-sequencing preparation

Museum specimens

We extracted total DNA following Ersmark *et al.* (2015) from 33 museum specimens collected between 1832 and 1927 that were provided by the Natural History Museum (NHM), Oslo; the Swedish Museum of Natural Histroy (NRM), Stockholm; and Gothenburg Natural History Museum (GNM), Gothenburg (Supporting Information, Table S1), and used the approach of Meyer and Kircher (2010) to build double-stranded libraries with halved reaction volumes and the following modifications: (i) during blunt-end repair, 20 µl of DNA extract was incubated with both the blunt-end repair reaction mix and with 3U of USER enzyme (New England Biolabs) for 3 hours at 37°C to remove uracils that had been introduced as a consequence of post-mortem damage (Briggs *et al.* 2010, Kircher *et al.* 2012), (ii) all reaction clean-up steps with Solid Phase Reversible Immobilization (SPRI) beads were replaced with spin column purification using MinElute PCR columns (Qiagen), and (iii) a heat-kill step of incubation at 80°C for 20 minutes replaced the last reaction clean-up step. After having shotgun sequenced all libraries at the Science for Life Laboratories (SciLifeLab) in Stockholm for an initial screening of endogenous DNA content (i.e. the proportion of sequenced bases successfully mapped to the Arctic fox

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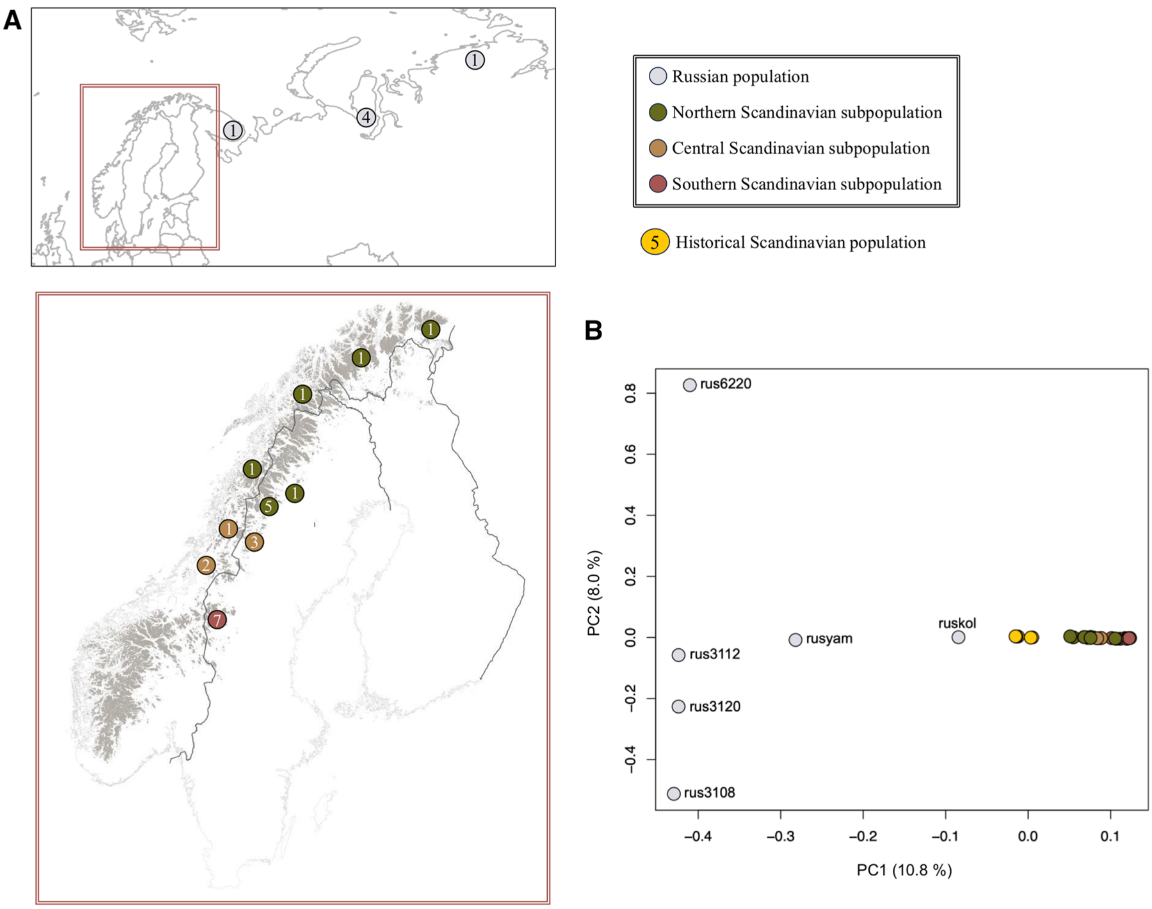

Figure 1. Approximate sampling locations and population structure of historical and modern Arctic fox (*Vulpes lagopus*) samples from Scandinavia and Russia. Colour of points indicate population or subpopulation affinity, where yellow = historical Scandinavian population, red = southern modern Scandinavian subpopulation, beige = central modern Scandinavian subpopulation, green = northern modern Scandinavian subpopulation, and grey = Russian modern population. A, Geographic origin of all modern Arctic fox samples shown with coloured circles. Numbers within coloured circles indicate the number of samples from the corresponding location. All historical specimens originate from Norway or Sweden, but exact sampling locations are unknown. The historical Scandinavian Arctic foxes were distributed across the entire Scandinavian mountain tundra (depicted in grey). B, Principal Component Analysis (PCA) based on 1 674 379 SNPs. Sample ID ruskol corresponds to the sample from the Kola Peninsula, rus6220 to the sample from Taimyr, while rus3112, rus1320, rus3108, and rusyam correspond to samples from Yamal.

reference genome; see Data processing), we selected five samples with an estimated endogenous DNA content above 74% (Supporting Information, Table S1). Libraries from these were amplified with 5–6 different indices to increase library complexity, and shotgun sequenced further ('Deep sequenced' in Supporting Information, Table S1) to reach an average coverage of approximately 10X at SciLifeLab Stockholm and Uppsala using an Illumina HiSeq X platform, with a paired-end 2 × 150 bp set-up and Illumina v.2.5 sequencing chemistry.

Modern samples

We processed and sequenced tissue samples from three Arctic fox individuals resident to Borgafjäll, Sweden, and three from Børgefjell and Lierne, Norway. Tissue samples from Sweden were collected during ear tagging in 2010, as a part of the four-decades-long close monitoring of the Arctic fox population by the Swedish Arctic Fox Project. The Norwegian ear tissue samples were collected in 2004 and 2013, representing some of the founders of the captive breeding programme implemented by the Norwegian Institute for Nature Research (NINA). All tissue samples were preserved in 99% ethanol and stored at -20°C after collection. We extracted total DNA using the DNeasy Tissue Kit (Qiagen). Following quality control, TruSeq PCR-free libraries were constructed for the Swedish samples at the SciLifeLab (Stockholm) and sequenced at the National Genomics Infrastructure (NGI, Stockholm) on the Illumina HiSeq X platform using a 2 × 150 bp set-up. The TruSeq DNA PCR-Free LT Sample Preparation Kit was used for library construction of the Norwegian samples, which were subsequently sequenced on an Illumina HiSeq 4000 platform at the Genomics Core Facility, Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology (NTNU), Norway.

In addition, we included previously published raw sequencing data from 17 modern samples from the southern and northern Scandinavian subpopulations, and six modern Russian samples (Hasselgren *et al.* 2021, Cockerill *et al.* 2022, Hasselgren 2022). All modern samples pre-date known immigration events from 2010 and onwards in Helags and Vindelfjällen, and in Lierne the sample from 2013 pre-dates any known immigrant reproducing events in this region, which have been the result of a recently

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initiated captive breeding programme in Norway (Hasselgren *et al.* 2018, Wallén *et al.* 2023b).

The total of 34 samples were divided into groups corresponding to populations or subpopulations, where five samples belonged to the historical Scandinavian population, while seven, six, and ten samples belonged to the southern, central, and northern contemporary Scandinavian subpopulations, respectively. Six Russian samples were included, five samples belonging to the contemporary Siberian population, and one sample originating from the Kola Peninsula, a region that connects the Scandinavian and the large Siberian populations (Dalén *et al.* 2006).

Data processing

The raw sequencing data was processed in a beta version of GenErode (Kutschera *et al.* 2022). For historical and modern fastq read processing we used SeqPrep v.1.1 and Trimmomatic v.0.36, respectively, following von Seth *et al.* (2021). We mapped the raw data to two reference genome assemblies in parallel, Arctic fox (PRJNA704825; Hasselgren *et al.* 2021) and red fox (GCF_003160815.1; Kukekova *et al.* 2018), for different types of data analyses (see below). We used the bwa aln and mem algorithms to map historical and modern processed read data, respectively, with recommended settings adjustments for ancient/historical data applied to the historical data (Li and Durbin 2010, van der Valk *et al.* 2021, de Filippo *et al.* 2018, Palkopoulou *et al.* 2015, Li 2013). After PCR duplicate removal, realignment around indels, repeat masking, as well as mapping and base quality filtering of ≥ 30, we estimated average depth of genome coverage, excluding sites with zero coverage (Smit and Hubley 2008, Li *et al.* 2009, McKenna *et al.* 2010, Smit *et al.* 2015). The individual average genome coverage range was 9–16X and 8–30X for the historical and modern samples, respectively, both when mapped to the Arctic fox (PRJNA704825; Hasselgren *et al.* 2021) and the red fox (GCF_003160815.1; Kukekova *et al.* 2018) reference genome.

In addition to the subsequent data filtering steps applied in GenErode during variant calling (i.e. removal of CpG sites identified in the reference genomes, indel sites as well as sites within 5 bp of indels, and heterozygous sites with an allelic imbalance greater than 20% vs. 80%), we also removed data mapped to scaffolds identified as potentially X chromosome linked (Briggs *et al.* 2010, Díez-Del-Molino *et al.* 2020, Wagner *et al.* 2020, Danecek *et al.* 2021, Kutschera *et al.* 2022). Such scaffolds were previously identified in the Arctic fox reference genome assembly by Hasselgren *et al.* (2021), and in the red fox reference genome assembly we identified candidate scaffolds using Lastal v.847 (Kiełbasa *et al.* 2011). Scaffolds shorter than 25 kilobase pairs (kbp) were also removed to minimize the risk of including mitochondrial DNA scaffolds. After filtering the corresponding scaffolds in the red fox reference genome assembly, and removing scaffolds with a length less than 25 kbp, 91% of the total scaffold length was retained, distributed across 673 scaffolds. For the Arctic fox reference genome assembly, 94% of the total scaffold length was retained after filtering, distributed across 75 scaffolds. For each sample, we only kept sites with a coverage depth above one-third and below 10× of the average depth of genome coverage, although we also implemented hard depth thresholds of a minimum of 6 and a maximum of 100 called bases per site for a site to be included. We subsequently merged all individual vcf files into one and excluded all sites where any sample had missing data while retaining only biallelic sites. In addition, to exclude potentially species-specific fixed variants from the red fox reference mapped dataset, we used the 'mutational load pipeline' utility within the GenErode workflow (https://github.com/NBISweden/GenErode/tree/d60d260ab63bf6cbbbb022e96e87c7fa3f13e2cc/utilities/mutational_load_snpeff) to remove all sites where all individuals had a derived allele, relative to the reference, in the homozygous state. Thus, for downstream data analyses, the Arctic fox and red fox reference mapped dataset comprised 1 674 379 and 1 600 773 variable sites, respectively.

The data mapped to the Arctic fox reference genome was used for a Principal Component Analysis (PCA) and to estimate genome-wide diversity and inbreeding. However, using a modern Arctic fox from a highly inbred population such as the one in the southern Scandinavian subpopulation, as is the case with the Arctic fox reference genome used in this study, to build an annotation and a snpEff database can introduce a bias in the results since the probability of classifying a mutation as deleterious is lower if the reference genome contains the corresponding mutation compared to if the reference genome contains the ancestral allele (Fu *et al.* 2014, Simons *et al.* 2014). In addition, conducting between-population comparisons (both in relation to other Scandinavian subpopulations and to the historical population) based on data mapped to the focal species can introduce biases as some individuals will be more closely related to the reference genome compared to others, and thus will artificially appear to have fewer functional mutations (von Seth *et al.* 2021, Dussex *et al.* 2021). Therefore, to estimate genetic load within coding regions we used the data mapped to the red fox reference genome (see Data analysis).

Data analysis

Population structure

To visualize population and subpopulation structure, we conducted a PCA with PLINK v.1.9 in a beta version of GenErode, and plotted the data using R (Purcell *et al.* 2007, R Core Team 2020, Kutschera *et al.* 2022). The PCA showed a closer affinity of the sample from the Kola Peninsula to the Scandinavian samples in comparison to the Siberian samples (see Results section), implying that this individual is genetically distinct from both the Scandinavian and Russian populations, which is also in line with previous findings (Tirronen *et al.* 2021), and so this sample was left out during subsequent population comparisons.

Genome-wide heterozygosity, inbreeding, and genetic load

Both individual genome-wide heterozygosity, measured as θ (i.e. the approximated number of heterozygous sites per 1 kbp under the infinite sites model) with the software mlRho (Haubold *et al.* 2010), and inbreeding, estimated as the proportion of the genome comprising Runs Of Homozygosity (F_{ROH}) regions using the sliding-window approach in PLINK v.1.9, were estimated in a beta version of GenErode (Purcell *et al.* 2007, Kutschera *et al.* 2022). For F_{ROH} we used the same settings as in Hasselgren *et al.* (2021), since these best match the near-complete and genetically verified pedigree of the southernmost Scandinavian Arctic fox subpopulation (Norén *et al.* 2016). For each individual, since the length of ROH reflects whether inbreeding can be traced to more ancient

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(i.e. background relatedness) or recent ancestors (i.e. between closely related individuals), we estimated F_{ROH} as the total length of ROH regions ≥ 100 kbp as well as ≥ 2 Mega base pairs (Mbp) divided by the approximate total length of the Arctic fox nuclear, autosomal genome (Pemberton *et al.* 2012).

Estimating genetic load is difficult without data on fitness-related traits, but individual mutational load in coding regions can serve as a proxy for genetic load (Bertorelle *et al.* 2022, Dussex *et al.* 2023). To do this, we followed von Seth *et al.* (2021) by first using the cufflinks -V option to remove in-stop codons and snpEff v.4.3 to build a database based on the protein sequences extracted from the red fox annotation (Cingolani *et al.* 2012, Trapnell *et al.* 2012). We obtained a total of 37 526 genes. SnpEff was subsequently used to predict the effects of identified variants within coding regions, excluding introns and intergenic regions, and categorize them according to their predicted impact on protein function as: 'high' (likely to be disruptive, e.g. causing protein loss-of-function or truncation), 'moderate' (probably non-disruptive, but might change protein effectiveness), or 'low' (non-disruptive and most likely harmless; Cingolani *et al.* 2012). For each individual genome, we also used the 'mutational load pipeline' utility within the GenErode workflow to remove intergenic and intronic variants, and subsequently estimated (i) total genetic load as the number of derived alleles per impact category, (ii) realized load as the number of derived alleles in homozygous state per impact category, and (iii) masked load as the number of derived alleles in heterozygous state per impact category. For all three measures, we divided the individual number of derived alleles per impact category by the individual total number of derived alleles.

For all population comparisons in all analyses, two-sided pairwise Wilcoxon rank sum tests with continuity correction were conducted in R v.4.0.3 (R Core Team 2020) for significance tests.

RESULTS

Population structure

The PCA showed the Scandinavian populations clustering together on PC1 and PC2, which explained 10.8% and 8.0%, respectively, of the variation in the dataset (Fig. 1). The sample from the Kola Peninsula (ruskol) showed a closer affinity to the Scandinavian populations in comparison to the other Russian samples. When excluding non-Scandinavian samples, samples belonging to the southern modern Scandinavian subpopulation clustered together on PC1, which explained 10.5% of the variation (Supporting Information, Fig. S1, Table S1). PC2, which explained 8.7% of the variation, separated the modern and historical populations.

Genome-wide heterozygosity, inbreeding, and genetic load

The historical Scandinavian population had significantly lower heterozygosity compared to the modern Siberian population, and higher heterozygosity in comparison to the modern southern Scandinavian subpopulation ($p_{hist.-Sib.}$ = 0.012, $p_{hist.-south.}$ = 0.023, Fig. 2A; Supporting Information, Fig. S2A, Tables S2–S4), but not compared to the central and northern subpopulations.

The modern Scandinavian subpopulations had significantly higher inbreeding, measured as F_{ROH} ≥ 100 kb and ≥ 2 Mb, respectively, compared to both the historical Scandinavian and the modern Siberian populations (Fig. 2B; Supporting Information, Fig. S2B, Tables S2, S5, S6). The proportion of the genome comprising ROH ≥ 2 Mb increased from 0.058 in the historical population to 0.26 in the southern subpopulation, whereas both the central and northern Scandinavian subpopulations had approximately twice as high a proportion of ROH regions ≥ 2 Mb compared to the historical population (F_{ROH} ≥ 2 Mb: central = 0.11, northern = 0.13; $p_{hist.-south.}$ = 0.0025, $p_{hist.-centr.}$ = 0.0043, $p_{hist.-north.}$ = 0.013). The historical population also had a significantly higher

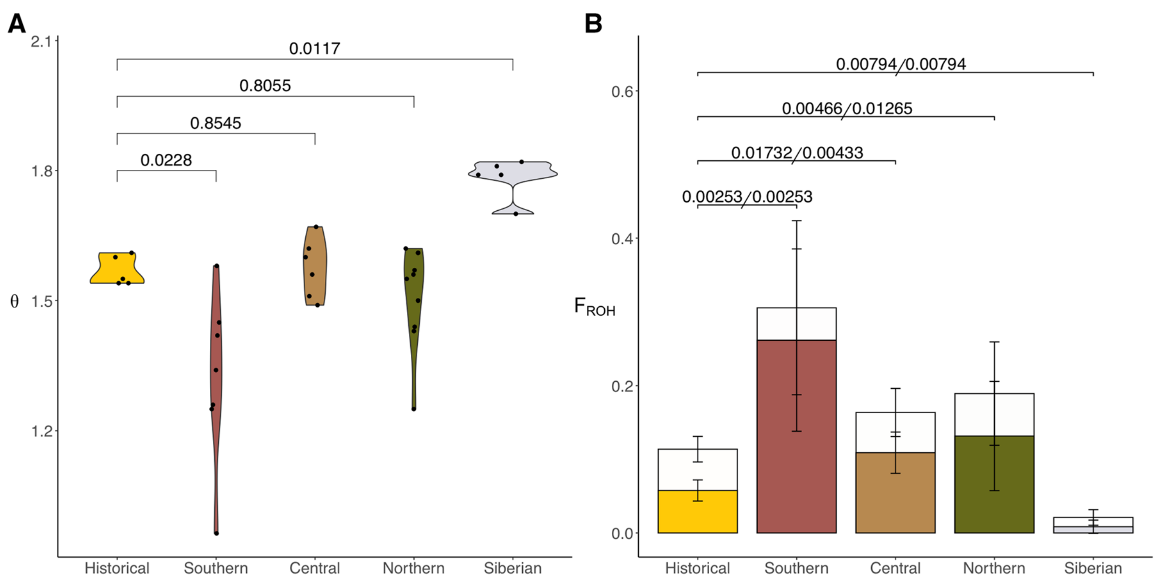

Figure 2. Individual genome-wide heterozygosity and inbreeding in historical and modern Scandinavian, as well as modern Siberian Arctic fox. A, θ, representing the approximated number of heterozygous sites per 1 kbp. B, Proportion of genome contained within Runs-Of-Homozygosity (ROH) regions. Filled portion of bars corresponds to the proportion of genome in ROH regions ≥ 2 Mb, total portion of bars corresponds to the proportion of genome in ROH regions ≥ 100 kb. P-values refer to temporal differences only (see Supporting Information for modern comparisons).

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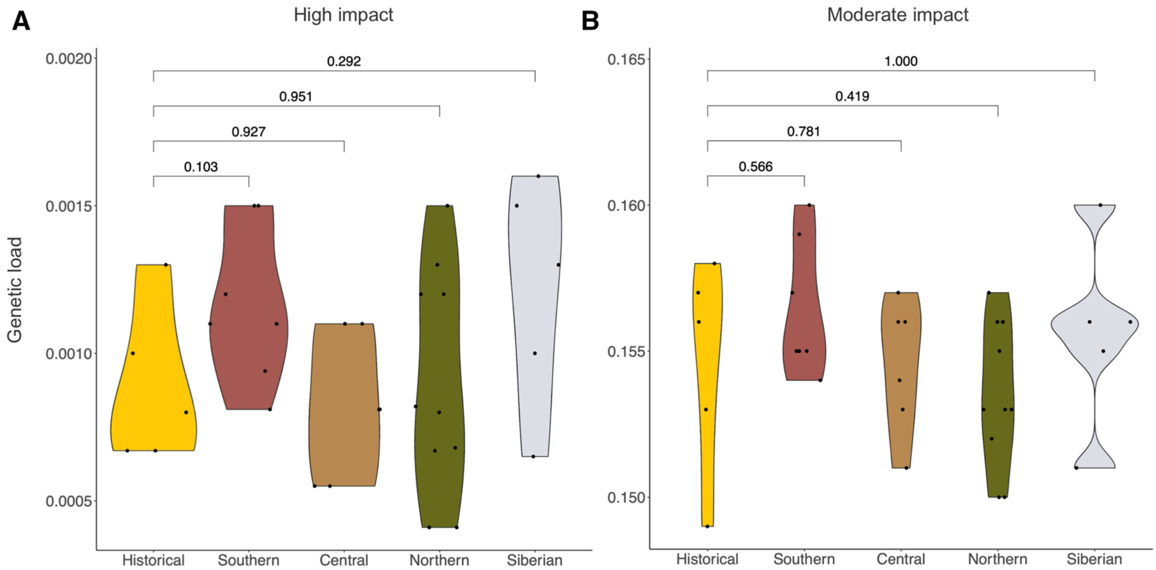

Figure 3. Genetic load in the historical and modern Scandinavian, as well as modern Siberian Arctic fox. Genetic load was estimated by dividing the individual number of derived alleles in coding regions that was classified as having (A) high and (B) moderate disruptive impact, with the individual total number of derived alleles (homozygous alleles were counted twice; see Material and methods). P-values refer to temporal differences only (see Supporting Information for modern comparisons).

proportion of the genome comprising ROH regions compared to the modern Siberian population, for both F_{ROH} categories ($p = 0.0079$ for both F_{ROH} categories).

No significant differences were observed in total genetic load in coding regions for either the high or the modest impact categories (Fig. 3; Supporting Information, Fig. S3, Tables S2, S7, S8). The historical population had a significantly lower relative number of derived alleles in homozygous state (i.e. realized load; Bertorelle *et al.* 2022, Dussex *et al.* 2023), and a significantly higher relative number in heterozygous state (i.e. masked load), for all impact categories compared to the southern subpopulation (Supporting Information, Fig. S4, Tables S9, S10). For the moderate (i.e. non-disruptive, but potentially protein effectiveness altering; Cingolani *et al.* 2012) and low (i.e. non-disruptive and likely to be harmless) impact categories, the historical population had a significantly higher realized load, and a significantly lower masked load, compared to the modern Siberian population.

DISCUSSION

The genetic composition of the modern Arctic fox population in Scandinavia has to a large extent been shaped by demographic processes during three time periods. First, climatic changes at the end of the Pleistocene led to the establishment, but also relative isolation, of the population. Second, intense hunting pressure in the early 20th century led to a severe decline in population size. Third, there was a further demographic decline in the 1980s caused by disruption of rodent cycles combined with increased competition from red foxes (Angerbjörn *et al.* 2001, Henden *et al.* 2009, Elmhagen *et al.* 2011, Ims*et al.* 2011, Angerbjörn *et al.* 2013, Framstad 2015), and exacerbated by the small population size itself (Loison *et al.* 2001, Herfindal *et al.* 2010), although the population has to some extent recovered in size over the past 20 years.

At the end of the last glaciation, the melting of the Weichselian ice sheet allowed Arctic foxes from Siberia to expand into Scandinavia (Dalén *et al.* 2007). Although most of Scandinavia subsequently became forested, Arctic foxes still inhabit the far north and the treeless tundra at higher elevations in the Scandes Mountains. It has been estimated that the Scandinavian population comprised approximately 10 000 individuals throughout most of the Holocene (Tannerfeldt 1997). As the oceans surrounding Scandinavia mostly are ice-free throughout the year, the Arctic fox population in Scandinavia has been comparatively isolated from other Arctic fox populations during the Holocene. Consequently, connectivity between the large Siberian population and the Scandinavian population has mainly been maintained through gene flow across the White Sea to the Kola Peninsula in northwestern Russia, and from there into northernmost Norway and Finland. This stepping stone role of the Kola Peninsula is reflected in the intermediate position of the Kola Peninsula genome in our PCA analysis (Fig. 1B). Moreover, the significantly lower genome-wide heterozygosity and higher inbreeding levels in the historical Scandinavian Arctic fox population compared to those in the present-day Siberian population (Fig. 2; Supporting Information, Fig. S2) are likely a consequence of a founder event during the end-Pleistocene establishment of the Scandinavian population (Dalén *et al.* 2007), one or more bottlenecks during the Holocene (e.g. during the Holocene thermal maximum; Frafjord and Hufthammer 1994), and/or its relative isolation throughout the Holocene. The inclusion of additional historical and ancient Arctic fox genomes would enable further investigation into the processes underlying the genome-wide patterns observed in historical Scandinavia.

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When comparing historical and modern Scandinavian Arctic foxes, our results suggest that the severe demographic decline approximately 100 years ago had a marked impact on the population's genomic composition. Our PCA analysis showed a clear differentiation between the historical and modern genomes (Supporting Information, Fig. S1), which is consistent with a shift in allele frequencies caused by genetic drift during the past 100 years. These findings are in line with earlier observations based on mitochondrial DNA and microsatellites (Nyström *et al.* 2006, Larsson *et al.* 2019). Moreover, we found that inbreeding, measured as the proportion of the genome comprising ROH regions, has significantly increased in all of Scandinavia during the past 100 years, with inbreeding levels being approximately two-fold higher in northern and central Scandinavia, and approximately three-fold higher in southern Scandinavia, compared to the historical population (Fig. 2B). Interestingly, we observed no difference in genome-wide heterozygosity when comparing northern and central Scandinavia with the historical population (Fig. 2A). The observed pattern could potentially be attributed to increased gene flow into the Scandinavian population, for example from Siberia. There have been earlier findings of similar patterns that suggest recent gene flow from Siberia, where, for example, Dalén *et al.* (2006) observed a positive correlation between microsatellite genetic divergence and geographical distance from Russia among Scandinavian populations. Moreover, Cockerill *et al.* (2022) recently proposed a stepping-stone model of decreasing genome-wide heterozygosity and increasing inbreeding levels westwards from Siberia. Collectively, although the 20th century bottleneck reduced Scandinavian–Siberian connectivity (Dalén *et al.* 2006, Nyström *et al.* 2006, Cockerill *et al.* 2022), our findings are consistent with a scenario where intermittent gene flow from the Kola Peninsula into northern and central Scandinavia during the past 100 years may have helped maintain genome-wide heterozygosity despite the increase in inbreeding levels in these two subpopulations.

In contrast to the subpopulations in northern and central Scandinavia, our results show that the subpopulation in southern Scandinavia has significantly lower genome-wide heterozygosity compared to the historical population. This is likely a consequence of both a higher degree of isolation (Dalén *et al.* 2006), and that the southern subpopulation was particularly affected by the disruption of the rodent cycles and increased red fox abundance in the 1980s. The southern subpopulation is thought to have become functionally extinct in the 1980s and was subsequently re-established by only seven individuals in the early 2000s (Norén *et al.* 2016, Hasselgren *et al.* 2021). Previous studies have shown that inbreeding increased substantially in the decade following this re-establishment (Norén *et al.* 2016, Hasselgren *et al.* 2021). With the exclusion of one sample, the samples from the southern subpopulation included in our study are from 2010 (i.e. the year that exhibited the highest level of inbreeding prior to establishment of captive bred foxes; Lotsander *et al.* 2021). Thus, the higher proportion of ROH observed in the genomes we sequenced from the southern subpopulation compared to the other ones is very likely a consequence of this recent increase in inbreeding.

From a conservation perspective, one of the most important genomic parameters that affects population viability is the number of deleterious mutations (i.e. genetic load) in the population, and to what extent this has changed in connection with demographic declines (Díez-del-Molino *et al.* 2018). When comparing the historical Scandinavian and present-day Scandinavian and Siberian populations, we found no significant differences in total genetic load in the moderate impact category (i.e. non-disruptive, but potentially protein effectiveness altering; Cingolani *et al.* 2012, Fig. 3B), which is consistent with an expected lower selection pressure on this category of mutations. Similarly, genetic load in the high impact category (i.e. likely to be disruptive; Fig. 3A) was not statistically different in the modern populations compared to the historical population. Although we note that our small sample size for these populations may have resulted in limited statistical power to detect small differences, the comparable levels of genetic load between historical Scandinavia and present-day Siberia could indicate that the Holocene population size in Scandinavia was too large for efficient purging of genetic load to take place (Kyriazis *et al.* 2021). Alternatively, it is possible that purging reduced genetic load from an even higher level in Scandinavia prior to the 20th century.

The lack of change in genetic load during the past 100 years in Scandinavia is surprising, as it has been estimated that the population declined from *c.* 10 000 to *c.* 100 individuals (Lönnberg 1927, Tannerfeldt 1997). Theory, simulations, and previous empirical studies on similar scenarios for other species indicate that such dramatic demographic declines often lead to changes in the composition, or the amount, of genetic load (e.g. Lynch *et al.* 1995, Kirkpatrick and Jarne 2000, Feng *et al.* 2019, Grossen *et al.* 2020, Hoelzel *et al.* 2024, Hoffman *et al.* 2024). Although speculative, if gene flow from Siberia via the Kola Peninsula during the past 100 years helped maintain genome-wide heterozygosity in the central and northern parts of Scandinavia, a bi-product of gene flow might have been an inflow of deleterious variants (Kyriazis *et al.* 2021). If genetic load was simultaneously purged in the Scandinavian subpopulations via purifying selection, these two processes combined might result in overall genetic load having been balanced through time. Generating additional genomes with a broader temporal and geographic representation from both the historical population and the modern Scandinavian and Siberian populations to study the amount of deleterious variation that is private and shared between the populations could potentially further disentangle the trajectory of genetic load within Scandinavia during the past 100 years.

Even more surprising is the lack of difference in total genetic load in the southern subpopulation compared to the historical population, despite the former displaying the highest inbreeding levels and being isolated from the other Scandinavian subpopulations (Norén *et al.* 2016). High levels of inbreeding, isolation, and small population size comprise three important factors that are expected to lead to either an accumulation or purging of genetic load (Caughley 1994, Lynch *et al.* 1995, Glémin 2003, Dussex *et al.* 2023). If additional genomes validate the estimated level of genetic load, it would suggest that the southern subpopulation, when it was re-established in the 2000s, may have been founded by individuals that on average had a comparatively high amount of genetic load in the high impact category. Additional genomes from the historical population and the modern subpopulations could thus help resolve whether this pattern is due to stochastic

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factors that resulted in the seven founders having a higher-than-expected genetic load, whether they originated from a yet unsampled subpopulation that had not undergone purging, or whether purging was obscured by an influx of deleterious variation. A fourth hypothesis is that the founders originated from different subpopulations, each of which had undergone purging for different high impact variants, leading to an increased level of total genetic load once the southern subpopulation was re-established.

It is notable that when comparing the amount of both high and moderate impact derived alleles in homozygous state (i.e. realized load; Bertorelle *et al.* 2022), all modern subpopulations had significantly higher realized load than the historical population, except for the northern subpopulation in the moderate impact category (Supporting Information, Fig. S4A, B). This likely reflects an ongoing inbreeding depression in the Scandinavian population during the first decade of the 2000s, as has been observed for the southern subpopulation in previous studies (Norén *et al.* 2016, Hasselgren *et al.* 2021).

CONCLUSION

Our results suggest that the present-day genomic architecture of the Scandinavian Arctic fox is the result of a series of complex demographic changes that took place over several thousand years. The increase in inbreeding levels during the past 100 years is consistent with a small and fragmented population that has struggled to recover. However, gene flow into the Scandinavian population appears to have helped maintain standing genetic variation and thus possibly the population's adaptive potential. This highlights the importance of sea ice between the Kola and Kanin Peninsulas in maintaining the connectivity between the Russian and Scandinavian populations. On the other hand, this process might also have counteracted the effect of purging in the Scandinavian population, if more deleterious mutations were also introduced as a consequence of such gene flow from Russia. Finally, we note that the observed level of inbreeding in the historical genomes (*c.* 5–10%) could serve as a useful target for future conservation actions, since this represents the level of inbreeding one should expect in a relatively large and viable Arctic fox population that is partially isolated on the periphery of the Arctic biome.

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AUTHOR CONTRIBUTIONS

Johanna von Seth (Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing—Original Draft, Writing—Review & Editing, Visualization, Project administration), Petter Larsson (Investigation), Malin Hasselgren (Investigation), Nicolas Dussex (Investigation, Validation), Liliana Farelo (Investigation), Johan Wallén (Investigation, Visualization), Verena Kutschera (Software, Validation), Nina E. Eide (Resources), Arild Landa (Resources), Anders Angerbjörn (Resources), Øystein Flagstad (Resources), José Melo-Ferreira (Resources, Investigation), Karin Norén (Resources, Supervision), and Love Dalén (Conceptualization, Methodology, Validation, Resources, Writing—Original Draft, Writing—Review & Editing, Supervision, Project administration, Funding acquisition)

SUPPLEMENTARY DATA

Supplementary data is available at *Zoological Journal of the Linnean Society* online.

CONFLICT OF INTEREST

None declared.

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DATA AVAILABILITY

The *V. lagopus* and the *V. vulpes* assemblies are available at the National Center for Biotechnology Information [NCBI, *V. lagopus*: BioProject: PRJNA704825, assembly: GCA_018835635.1; *V. vulpes*: BioProjectID: PRJNA378561, assembly: (GCF_003160815.1; Kukekova *et al.* 2018)]. Previously published modern fastq files are available at the European Nucleotide Archive (ENA, project PRJEB43377 and PRJEB55788). Modern and historical re-sequencing data (fastq files) generated for this project are also available at ENA (project PRJEB77095).

REFERENCES

Angerbjörn A, Eide NE, Dalén L *et al.* Carnivore conservation in practice: replicated management actions on a large spatial scale. *The Journal of Applied Ecology* 2013;**50**:59–67.

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Angerbjörn A, Tannerfeldt M, Bjärvall A *et al.* Dynamics of the Arctic fox population in Sweden. *Annales Zoologici Fennici* 1995;**32**:55–68.

Angerbjörn A, Tannerfeldt M, Lundberg H. Geographical and temporal patterns of lemming population dynamics in Fennoscandia. *Ecography* 2001;**24**:298–308.

Barber DG, Lukovich JV, Keogak J *et al.* The changing climate of the Arctic. *Arctic* 2009;**61**:7–26.

Bertorelle G, Raffini F, Bosse M *et al.* Genetic load: genomic estimates and applications in non-model animals. *Nature Reviews Genetics* 2022;**23**:492–503. https://doi.org/10.1038/s41576-022-00448-x.

Briggs AW, Stenzel U, Meyer M *et al.* Removal of deaminated cytosines and detection of *in vivo* methylation in ancient DNA. *Nucleic Acids Research* 2010;**38**:e87.

Callaghan TV, Björn LO, Chernov Y *et al.* Biodiversity, distributions and adaptations of Arctic species in the context of environmental change. *Ambio* 2004;**33**:404–17.

Caughley G. Directions in conservation biology. *The Journal of Animal Ecology* 1994;**63**:215.

Cingolani P, Platts A, Wang LL *et al.* A program for annotating and predicting the effects of single nucleotide polymorphisms, SnpEff: SNPs in the genome of *Drosophila melanogaster* strain w^{1118}; Iso-2; Iso-3. *Fly* 2012;**6**:80–92.

Cockerill CA, Hasselgren M, Dussex N *et al.* Genomic consequences of fragmentation in the endangered Fennoscandian Arctic fox (*Vulpes lagopus*). *Genes* 2022;**13**:2124. https://doi.org/10.3390/genes13112124.

Dalén L, Kvaløy K, Linnell JDC *et al.* Population structure in a critically endangered Arctic fox population: does genetics matter?*Molecular Ecology* 2006;**15**:2809–19.

Dalén L, Fuglei E, Hersteinsson P *et al.* Population history and genetic structure of a circumpolar species: the Arctic fox. *Biological Journal of the Linnean Society* 2004;**84**:79–89.

Dalén L, Nyström V, Valdiosera C *et al.* Ancient DNA reveals lack of postglacial habitat tracking in the Arctic fox. *Proceedings of the National Academy of Sciences* 2007;**104**:6726–9. https://doi.org/10.1073/pnas.0701341104.

Danecek P, Bonfield JK, Liddle J *et al.* Twelve years of SAMtools and BCFtools. *GigaScience* 2021;**10**:giab008. https://doi.org/10.1093/gigascience/giab008.

Díez-del-Molino D, Sánchez-Barreiro F, Barnes I *et al.* Quantifying temporal genomic erosion in endangered species. *Trends in Ecology and Evolution* 2018;**33**:176–85. https://doi.org/10.1016/j.tree.2017.12.002.

Díez-Del-Molino D, von Seth J, Gyllenstrand N *et al.* Population genomics reveals lack of greater white-fronted introgression into the Swedish lesser white-fronted goose. *Scientific Reports* 2020;**10**:18347.

Dirzo R, Young HS, Galetti M, Ceballos G, Isaac NJB, Collen B. Defaunation in the Anthropocene. *Science* 2014;**345**:401–6.

Dussex N, Morales HE, Grossen C, Dalén L, van Oosterhout C. Purging and accumulation of genetic load in conservation. *Trends in Ecology & Evolution* 2023;**38**:961–9.

Dussex N, van der Valk T, Morales HE *et al.* Population genomics of the critically endangered kākāpō. *Cell Genomics* 2021;**1**:100002.

Elmhagen B, Hellström P, Angerbjörn A, Kindberg J. Changes in vole and lemming fluctuations in Northern Sweden 1960–2008 revealed by fox dynamics. *Annales Zoologici Fennici* 2011;**48**:167–79.

Elmhagen B, Kindberg J, Hellström P, Angerbjörn A. A boreal invasion in response to climate change? Range shifts and community effects in the borderland between forest and tundra. *Ambio* 2015;**44**:39–50.

Elmhagen B, Tannerfeldt M, Verucci P, Angerbjörn A. The Arctic fox (*Alopex lagopus*): an opportunistic specialist. *Journal of Zoology* 2000;**251**:139–49.

Ersmark E, Orlando L, Sandoval-Castellanos E *et al.* Population demography and genetic diversity in the Pleistocene cave lion. *Open Quaternary* 2015;**1**:4–14.

Feng S, Fang Q, Barnett R *et al.* The genomic footprints of the fall and recovery of the crested ibis. *Current Biology* 2019;**29**:340–9.e7.

de Filippo C, Meyer M, Prüfer K. Quantifying and reducing spurious alignments for the analysis of ultra-short ancient DNA sequences. *BMC Biology* 2018;**16**:121.

Frafjord K, Hufthammer AK. Subfossil records of the Arctic fox (*Alopex lagopus*) compared to its present distribution in Norway. *Arctic* 1994;**47**:65–8.

Framstad E. 2015. Terrestrisk Naturovervåking I 2014: Markvegetasjon, Smågnagere Og Fugl. Sammenfatning Av Resultater. NINA Rapport 1186; Norsk institutt for naturforskning.

Frankham R. Genetics and extinction. *Biological Conservation* 2005;**126**:131–40.

Fuglei E, Tarroux A. Arctic fox dispersal from Svalbard to Canada: one female's long run across sea ice. *Polar Research* 2019;**38**. https://doi.org/10.33265/polar.v38.3512.

Fu W, Gittelman RM, Bamshad MJ *et al.* Characteristics of neutral and deleterious protein-coding variation among individuals and populations. *American Journal of Human Genetics* 2014;**95**:421–36. https://doi.org/10.1016/j.ajhg.2014.09.006.

Gagnon CA, Berteaux D. Integrating traditional ecological knowledge and ecological science: a question of scale. *Ecology and Society* 2009;**14**:19. https://www.jstor.org/stable/26268305.

Geffen E, Waidyaratne S, Dalén L *et al.* Sea ice occurrence predicts genetic isolation in the Arctic fox. *Molecular Ecology* 2007;**16**:4241–55.

Glémin S. How are deleterious mutations purged? Drift versus nonrandom mating. *Evolution* 2003;**57**:2678–87.

Grossen C, Guillaume F, Keller LF, Croll D. Purging of highly deleterious mutations through severe bottlenecks in alpine ibex. *Nature Communications* 2020;**11**:1001.

Hasselgren M. *Dynamics of Inbreeding and Genetic Rescue in a Small Population.* D. Phil. Thesis, Stockholm University, 2022.

Hasselgren M, Angerbjörn A, Eide NE *et al.* Genetic rescue in an inbred Arctic fox (*Vulpes lagopus*) population. *Proceedings of the Royal Society B: Biological Sciences* 2018;**285**:20172814. https://doi.org/10.1098/rspb.2017.2814.

Hasselgren M, Dussex N, von Seth J *et al.* Genomic and fitness consequences of inbreeding in an endangered carnivore. *Molecular Ecology* 2021;**30**:2790–9.

Haubold B, Pfaffelhuber P, Lynch M. mlRho—a program for estimating the population mutation and recombination rates from shotgun-sequenced diploid genomes. *Molecular Ecology* 2010;**19**:277–84.

Hedrick PW, Garcia-Dorado A. Understanding inbreeding depression, purging, and genetic rescue. *Trends in Ecology & Evolution* 2016;**31**:940–52.

Hemphill EJK, Flagstad Ø, Jensen H *et al.* Genetic consequences of conservation action: restoring the Arctic fox (*Vulpes lagopus*) population in Scandinavia. *Biological Conservation* 2020;**248**:108534.

Henden J-A, Yoccoz NG, Ims RA *et al.* Phase-dependent effect of conservation efforts in cyclically fluctuating populations of Arctic fox (*Vulpes lagopus*). *Biological Conservation* 2009;**142**:2586–92.

Herfindal I, Linnell JDC, Elmhagen B *et al.* Population persistence in a landscape context: the case of endangered Arctic fox populations in Fennoscandia. *Ecography* 2010;**33**:932–41.

Hersteinsson P, Angerbjörn A, Frafjord K *et al.* The Arctic fox in Fennoscandia and Iceland: management problems. *Biological Conservation* 1989;**49**:67–81.

Hersteinsson P, MacDonald DW. Interspecific competition and the geographical distribution of red and Arctic foxes *Vulpes vulpes* and *Alopex lagopus*. *Oikos* 1992;**64**:505–15.

Hoelzel AR, Gkafas GA, Kang H *et al.* Genomics of post-bottleneck recovery in the northern elephant seal. *Nature Ecology & Evolution* 2024;**8**:686–94.

Hoffman JI, Vendrami DLJ, Hench K *et al.* Genomic and fitness consequences of a near-extinction event in the northern elephant seal. *Nature Ecology & Evolution* 2024;**8**:2309–24.

Ims RA, Yoccoz NG, Killengreen ST. Determinants of lemming outbreaks. *Proceedings of the National Academy of Sciences of the United States of America* 2011;**108**:1970–4.

Kiełbasa SM, Wan R, Sato K *et al.* Adaptive seeds tame genomic sequence comparison. *Genome Research* 2011;**21**:487–93.

Kircher M, Sawyer S, Meyer M. Double indexing overcomes inaccuracies in multiplex sequencing on the illumina platform. *Nucleic Acids Research* 2012;**40**:e3.

Kirkpatrick M, Jarne P. The effects of a bottleneck on inbreeding depression and the genetic load. *The American Naturalist* 2000;**155**:154–67.

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Kukekova AV, Johnson JL, Xiang X *et al.* Red fox genome assembly identifies genomic regions associated with tame and aggressive behaviours. *Nature Ecology & Evolution* 2018;**2**:1479–91.

Kutschera VE, Kierczak M, van der Valk T *et al.* GenErode: a bioinformatics pipeline to investigate genome erosion in endangered and extinct species. *BMC Bioinformatics* 2022;**23**:228.

Kyriazis CC, Wayne RK, Lohmueller KE. Strongly deleterious mutations are a primary determinant of extinction risk due to inbreeding depression. *Evolution Letters* 2021;**5**:33–47.

Lai S, Bêty J, Berteaux D. Spatio-temporal hotspots of satellite-tracked Arctic foxes reveal a large detection range in a mammalian predator. *Movement Ecology* 2015;**3**:37.

Larsson P, von Seth J, Hagen IJ *et al.* Consequences of past climate change and recent human persecution on mitogenomic diversity in the Arctic fox. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 2019;**374**:20190212. https://doi.org/10.1098/rstb.2019.0212.

Li H. Aligning Sequence Reads, Clone Sequences and Assembly Contigs with BWA-MEM. arXiv:1303.3997v2 [q-bio.GN]. 2013. http://arxiv.org/abs/1303.3997, preprint: not peer reviewed.

Li H, Durbin R. Fast and accurate long-read alignment with Burrows–Wheeler transform. *Bioinformatics* 2010;**26**:589–95.

Li H, Handsaker B, Wysoker A *et al.*; 1000 Genome Project Data Processing Subgroup. The Sequence Alignment/Map Format and SAMtools. *Bioinformatics* 2009;**25**:2078–9. https://doi.org/10.1093/bioinformatics/btp352.

Loison A, Strand O, Linnell JDC. Effect of temporal variation in reproduction on models of population viability: a case study for remnant Arctic fox (*Alopex lagopus*) populations in Scandinavia. *Biological Conservation* 2001;**97**:347–59.

Lönnberg E. *Fjällrävstammen I Sverige 1926*. Uppsala, Sweden: Kungliga Svenska Vetenskapsakademiens Skrifter i Naturskyddsärenden 7, 1927.

Lotsander A, Hasselgren M, Larm M *et al.* Low persistence of genetic rescue across generations in the Arctic fox (*Vulpes lagopus*). *The Journal of Heredity* 2021;**112**:276–85.

Lynch M, Conery J, Burger R. Mutation accumulation and the extinction of small populations. *The American Naturalist* 1995;**146**:489–518.

McKenna A, Hanna M, Banks E *et al.* The genome analysis toolkit: a mapreduce framework for analyzing next-generation DNA sequencing data. *Genome Research* 2010;**20**:1297–303.

Meyer M, Kircher M. Illumina sequencing library preparation for highly multiplexed target capture and sequencing. *Cold Spring Harbor Protocols* 2010;**2010**:pdb.prot5448.

Murphy GEP, Romanuk TN. A meta-analysis of declines in local species richness from human disturbances. *Ecology and Evolution* 2014;**4**:91–103.

Norén K, Carmichael L, Dalén L *et al.* Arctic fox *Vulpes lagopus* population structure: circumpolar patterns and processes. *Oikos* 2011;**120**:873–85.

Norén K, Dalén L, Flagstad Ø *et al.* Evolution, ecology and conservation—revisiting three decades of Arctic fox population genetic research. *Polar Research* 2017;**36**:4.

Norén K, Godoy E, Dalén L *et al.* Inbreeding depression in a critically endangered carnivore. *Molecular Ecology* 2016;**25**:3309–18.

Nyström V, Angerbjörn A, Dalén L. Genetic consequences of a demographic bottleneck in the Scandinavian Arctic fox. *Oikos* 2006;**114**:84–94.

Palkopoulou E, Mallick S, Skoglund P *et al.* Complete genomes reveal signatures of demographic and genetic declines in the woolly mammoth. *Current Biology* 2015;**25**:1395–400. https://doi.org/10.1016/j.cub.2015.04.007.

Pamperin NJ, Follmann EH, Person BT. Sea-ice use by Arctic foxes in Northern Alaska. *Polar Biology* 2008;**31**:1421–6. https://doi.org/10.1007/s00300-008-0481-5.

Pemberton TJ, Absher D, Feldman MW *et al.* Genomic patterns of homozygosity in worldwide human populations. *American Journal of Human Genetics* 2012;**91**:275–92.

Post E, Bhatt US, Bitz CM *et al.* Ecological consequences of sea-ice decline. *Science* 2013;**341**:519–24.

Purcell S, Neale B, Todd-Brown K *et al.* PLINK: a tool set for whole--genome association and population-based linkage analyses. *American Journal of Human Genetics* 2007;**81**:559–75.

R Core Team. *R: a Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing, 2020. http://www. R-project. org.

Robinson JA, Räikkönen J, Vucetich LM *et al.* Genomic signatures of extensive inbreeding in Isle Royale wolves, a population on the threshold of extinction. *Science Advances* 2019;**5**:eaau0757. https://doi.org/10.1126/sciadv.aau0757.

Sánchez-Barreiro F, Gopalakrishnan S, Ramos-Madrigal J *et al.* Historical population declines prompted significant genomic erosion in the northern and southern white rhinoceros (*Ceratotherium simum*). *Molecular Ecology* 2021;**30**:6355–69.

von Seth J, Dussex N, Díez-del-Molino D *et al.* Genomic insights into the conservation status of the world's last remaining Sumatran rhinoceros populations. *Nature Communications* 2021;**12**:2393.

Simons YB, Turchin MC, Pritchard JK *et al.* The deleterious mutation load is insensitive to recent population history. *Nature Genetics* 2014; **46**:220–4.

Smit AFA, Hubley R, Green P. *RepeatMasker Open-4.0.*2015; *2013–2015*. http://www.repeatmasker.org (3 July 2025, date last accessed).

Smit AFA, Hubley R. *RepeatModeler Open-1.0*. 2008. http://www.repeatmasker.org (3 July 2025, date last accessed).

Stirling I, Parkinson CL. Possible effects of climate warming on selected populations of polar bears (*Ursus maritimus*) in the Canadian Arctic. *Arctic* 2006;**59**:261–75.

Tannerfeldt M. *Population Fluctuations and Life History Consequences in the Arctic Fox*. D. Phil. Thesis, Stockholm University, 1997.

Tannerfeldt M, Elmhagen B, Angerbjörn A. Exclusion by interference competition? The relationship between red and Arctic foxes. *Oecologia* 2002;**132**:213–20.

Tarroux A, Berteaux D, Bêty J. Northern nomads: ability for extensive movements in adult Arctic foxes. *Polar Biology* 2010;**33**:1021–6.

Tirronen K, Ehrich D, Panchenko D, Dalén L, Angerbjörn A. The Arctic fox (*Vulpes lagopus* L.) on the Kola Peninsula (Russia): silently disappearing in the mist of data deficiency?*Polar Biology* 2021;**44**:913–25. https://doi.org/10.1007/s00300-021-02847-y.

Trapnell C, Roberts A, Goff L *et al.* Differential gene and transcript expression analysis of RNA-Seq experiments with TopHat and Cufflinks. *Nature Protocols* 2012;**7**:562–78.

van der Valk T, Díez-Del-Molino D, Marques-Bonet T, Guschanski K, Dalén L. Historical genomes reveal the genomic consequences of recent population decline in eastern gorillas. *Current Biology* 2019;**29**:165–70.e6.

van der Valk T, Pečnerová P, Díez-del-Molino D *et al.* Million-year-old DNA sheds light on the genomic history of mammoths. *Nature* 2021; **591**:265–9.

Wagner S, Plomion C, Orlando L. Uncovering signatures of DNA methylation in ancient plant remains from patterns of post-mortem DNA damage. *Frontiers in Ecology and Evolution* 2020;**8**:11. https://doi.org/10.3389/fevo.2020.00011.

Wallén J, Norén K, Angerbjörn A *et al.* Context-dependent demographic and genetic effects of translocation from a captive breeding project. *Animal Conservation* 2023a;**26**:412–23.

Wallén J, Ulvund K, Rød-Eriksen L *et al.* Inventering Av Fjällräv I Norge, Sverige Och Finland 2023/Overvåking Av Fjellrev I Norge, Sverige Og Finland 2023/Naaliseuranta Norjassa, Ruotsissa Ja Suomessa 2023. Beståndsstatus För Fjällräv I Fennoskandia/Bestandsstatus for Fjellrev I Fennoskandia/Naalikannan Tila Fennoskandia. 1-2023. Naturhistoriska riksmuseet (NRM), Stockholm, Sweden; Norsk institutt for naturforskning (NINA), Trondheim, Norway; Metsähallitus (MH), Helsinki, Finland. 2023b.

Xue Y, Prado-Martinez J, Sudmant PH *et al.* Mountain gorilla genomes reveal the impact of long-term population decline and inbreeding. *Science* 2015;**348**:242–5.

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