Master's thesis

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Department of Biology

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The Landscape Genomics of the Scandinavian Red Fox

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Supervisor: Henrik Jensen
Co-supervisor: Ingerid J. Hagen, Nina E. Eide, Andrea Miller, Knut Madslien, Øystein Flagstad and Stefan Blumentranth

May 2022

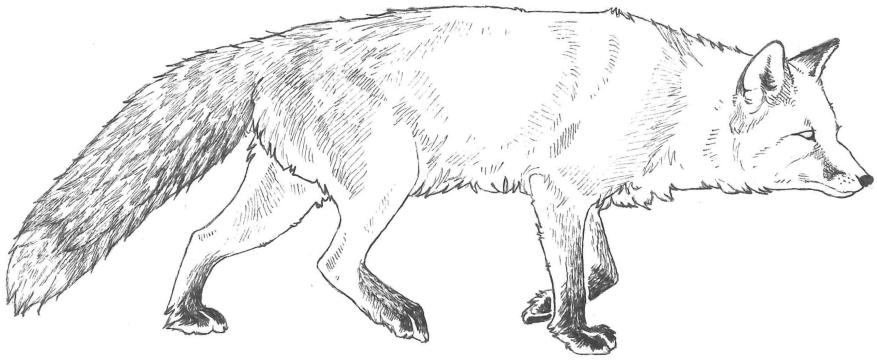

Illustration by Lina Gansmoe Arntsen

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Abstract

Global environmental and land use change have brought about changes in ecosystems and induced range expansion in several boreal species. Landscape genomics is a growing field of study in the intersection between ecology and genetics. In the context of global change, this field provides powerful tools to investigate the genetic structure and gene flow shaped by the landscape and environment. In this thesis I applied a landscape genomics approach to study the Scandinavian red fox (*Vulpes vulpes*), an important generalist species which has undergone range expansion. The species is highly relevant for wildlife conservation and public health, for instance through its competition with the endangered arctic fox (*Vulpes lagopus),* and its role as a host species for infectious diseases. By using genome-wide SNP data, I explored the genetic structure of the Scandinavian red fox. In the context of red fox range expansion, I also investigated whether any genomic regions were associated with high elevational or northern areas.

I showed that the red fox is characterised by weak genetic structure and limited genetic differentiation in Scandinavia. This indicated high levels of gene flow and movement of individuals across the landscape. Denmark, however, was more genetically differentiated from the rest of Scandinavia, which might be explained by the landscape barrier represented by the straits that separate Denmark from the Scandinavian peninsula. I also observed lower genome-wide heterozygosity in Denmark relative to Norway and Sweden. Signals of phylogeographical structuring were detected, and north-to-south and east-to-west gradients determined some of the genetic structure on the Scandinavian peninsula. Despite this, Norwegian and Swedish red foxes were genetically highly similar. This study therefore shows that the red fox represents a channel for pathogen spread across Scandinavia. There was no significant association between genomic regions and high elevational or northern areas. It therefore appear unlikely that a few large-effect genes mediate a phenotype that makes red foxes relatively better adapted for dispersal to- and colonisation of such habitats. Although one cannot rule out the possibility for a genetic aspect involved in dispersal and range expansion, previous literature points towards environmental change and human impacts as the most important factors driving red fox range expansion. The red fox, with no apparent strong landscape barriers that prevents it from crossing the Scandinavian peninsula, seen in connection with its role as a pathogen vector, is a species highly relevant in the context of public health and for the management and conservation of Scandinavian fauna.

Sammendrag

Som følge av globale endringer i miljø og arealbruk har man sett endringer i økosystemer og ekspansjon i boreale arter. Landskapsgenomikk er et spirende fagfelt som kombinerer økologi og genetikk. I sammenheng med globale endringer, er landskapsgenomikk et kraftig verktøy for å undersøke genetisk struktur og genflyt som formes av landskap og miljø. I denne avhandlingen studerte jeg den Skandinaviske rødreven (*Vulpes vulpes*), gjennom en tilnærming basert på landskapsgenomikk. Rødreven er en viktig generalist-art som har ekspandert lenger nord og høyere opp i fjellet. Den er også høyst relevant for viltforvaltning og folkehelse, for eksempel gjennom konkurranse med den truede fjellreven (*Vulpes lagopus*), og gjennom sin rolle som bærer av smittsomme sykdommer. Jeg brukte SNP-data fra hele genomet for å undersøke den genetiske strukturen hos Skandinavisk rødrev. I sammenheng med ekspansjon av rødrevens utbredelse, undersøkte jeg også om deler av genomet var assosiert med høyfjells- og nordlige områder.

Jeg har vist at rødreven er preget av svak genetisk struktur og begrenset genetisk differensiering i Skandinavia. Dette tydet på en høy grad av genflyt og forflytning av individer på tvers av landskap. Danmark var derimot mer genetisk forskjellig fra resten av Skandinavia, som antakelig kan forklares med at stredene som skiller Danmark fra den Skandinaviske halvøy utgjør en landskapsbarriere for rødreven. I tillegg ble lavere heterozygositet observert i Danmark sammenlignet med Norge og Sverige. Jeg fant signaler fra mulig fylogeografisk struktur, og at nord-til-sør og øst-til-vest gradienter bestemte deler av den genetiske strukturen på den Skandinaviske halvøy. På tross av dette, var Norske og Svenske rødrever svært like genetisk sett. Denne studien viser derfor at rødreven representerer en spredningsvei for sykdommer i Skandinavia. Det var ingen assosiasjon mellom deler av genomet og områder lengre nord og høyere opp i fjellet. Det virker derfor usannsynlig at noen få gener frembringer en fenotype gunstig for slike habitater. Selv om man ikke kan utelukke at det er et genetisk aspekt involvert i vandring og ekspansjon, har tidligere studier pekt på miljøforandringer og menneskelig påvirkning som de viktigste årsakene for ekspansjon av rødrevens utbredelse. Uten åpenbare sterke landskapsbarrierer som hindrer rødreven i å krysse den Skandinaviske halvøy, og sett i sammenheng med sin rolle som sykdomsbærer, er rødreven en art som er høyst relevant i forbindelse med folkehelse og for forvaltningen og bevaringen av Skandinavisk fauna.

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Lina Gansmoe Arntsen,

Trondheim, May 2022

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Abbreviations

SNP	Single nucleotide polymorphism
LD	Linkage-disequilibrium
EAA	Ecological association analysis
F_{ST}	Fixation index
LGM	Last glacial maximum

1 Introduction

Climate warming and land use change have been shown to affect community compositions, negatively impacting specialist species by favouring generalists (Davey et al., 2012) and inducing range expansions to higher altitudes and latitudes in boreal species (Elmhagen et al., 2015). In this context, landscape genomics provides a powerful tool to discover environmental factors or landscape features that impact adaptive genetic diversity (Manel and Holderegger, 2013). Landscape genomics also provides insight into the structure of populations, the connectivity and gene flow between them, and to what extent the landscape and environment shape connectivity, and has been used as a tool to provide insights for wildlife conservation and management (Jaffe et al., 2019; Ruegg et al., 2018). As a relatively young and growing field in the intersection between ecology and genomics, landscape genomics will likely be an important asset in predicting the effects of global change on genetic diversity (Manel and Holderegger, 2013). Moreover, genetic structure and composition play part in determining how populations respond to climate change (Aguirre-Liguori et al., 2021).

The degree of connectivity and gene flow, local selection pressures, and random processes such as mutation and genetic drift, shape the distribution of genetic variation between and within populations. For instance, environmental variables, and selection towards these, is important in explaining the genetic structure seen in highly mobile North American grey wolves (*Canis lupus*) (Schweizer et al., 2016). Gene flow can increase genetic diversity within populations, and limit genetic differentiation and structuring between populations (Bubac and Spellman, 2016). Landscape features which function as barriers to gene flow, for instance highways, can reduce the genetic diversity within populations, increase the genetic differentiation between populations, and shape genetic structure, as was seen in desert big horn sheep (*Ovis canadensis nelsoni*) (Epps et al., 2005). Landscapes can thereby impose control on pathogen populations, because they affect the distribution, abundance, and connectivity of host populations on which the pathogens rely (Biek and Real, 2010). Through the understanding of genetic structure and gene flow of host species, landscape genomics can therefore provide clues to the likelihood and pathways by which pathogens may spread. For instance, Fountain-Jones et al. (2021) found that gene flow in pumas (*Puma concolor*) was tightly linked to spread of feline immunodeficiency virus (FIV) in a region affected by anthropogenic development.

Being both an ecologically significant species that can impose control on prey communities (Smedshaug et al., 1999; Henden et al., 2021) and an important pathogen vector (Woodroffe et al., 2004; Holmala and Kauhala, 2006; Hodzic et al., 2015), the red fox (*Vulpes vulpes*) is an interesting study species in a changing environment. The red fox is an adaptable and opportunistic generalist, widespread throughout the northern hemisphere, and even successful in urban landscapes (Hoffmann and Sillero-Zubiri, 2016). The impact of humans, such as roadkill and increased littering can facilitate the presence of the species in alpine tundra areas (Rød-Eriksen et al., 2020). The Fennoscandian red fox population appears to exhibit a source-sink dynamic in which immigrants disperse from several southern source populations to northern areas (Norén et al., 2015). In Sweden, boreal zones have indeed been found to contribute immigrants to tundra zones to a larger degree than boreal zones receive immigrants (Norén et al., 2017). Previous studies based

on 15 to 30 genetic markers indicate that Scandinavian red foxes show indications of weak genetic structuring and high gene flow (Norén et al., 2015; Norén et al., 2017; Hagenlund et al., 2019), similar to other populations in Europe (Teacher et al., 2011; Galov et al., 2014; Basto et al., 2016; Zecchin et al., 2019).

One aspect of the red fox which is of great ecological importance, is the observed range expansion during the last century (Elmhagen et al., 2015; Elmhagen et al., 2017). Dispersal in animals is often both condition-dependent, i.e. dependent on external factors; and phenotype-dependent, i.e. there is a correlation between dispersal and phenotypic traits, where dispersers are morphologically, physiologically, or behaviourally distinct from non-dispersers (Clobert et al., 2009). Phenotype-dependent dispersal is therefore expected to result in populations at the edge of the range composed of individuals with certain phenotypic traits (Michelangeli et al., 2017). Previous studies have found traits associated with dispersal in various species, e.g. fat and luteinising hormone levels, and a preference for mating with non-colony members in naked mole-rats (*Heterocephalus glaber*) (O´Riain et al., 1996), aggressiveness in delicate skinks (*Lampropholis delicata*) (Michelangeli et al., 2017), asociality in mosquitofish (*Gambusia affinis*) (Cote et al., 2010), aggressiveness in western bluebirds (*Sialia mexicana*) (Duckworth and Kruuk, 2009), and serotonin activity in rhesus macaques (*Macaca mulatta*) (Trefilov et al., 2000), where the latter two traits have been found to have a genetic basis. Individual red foxes which choose to disperse and do so successfully, could be expected to possess traits that make them more adapted to high latitude and altitude areas at the edge of their range, or traits that otherwise facilitate dispersal and/or successful establishment in new areas. If such traits have a genetic basis this may also represent an adaptive potential (Saastamoinen et al., 2018). The genetic architecture of such traits may be identified through analysis of whole genome data of red foxes in different habitats (Schwartz et al., 2010). For instance, several loci were found to be associated with range expansion in the coyote (*Canis latrans*) in North America (Heppenheimer et al., 2018). Should the success of dispersal be determined by genetics, any positive selection acting on dispersal at margins of the red fox range distribution, could result in adaptive expansion into areas beyond their current range. This could however have detrimental impacts on species resident in alpine areas, such as the arctic fox (*Vulpes lagopus*).

The arctic fox is an alpine and arctic specialist, classified as endangered on the Swedish (SLU Artdatabanken, 2020) and Norwegian red list of species (Eldegard et al., 2021), and critically endangered on the Finnish red list of species (Liukko et al., 2019). Although the species on the European and global level is listed as least concern by the IUCN (International Union for Conservation of Nature), the IUCN recognises the Fennoscandian population as critically endangered (Hersteinsson et al., 2007; Angerbjörn and Tannerfeldt, 2014). The species has been legally protected since 1928, 1930 and 1940 in Sweden, Norway, and Finland respectively. The decline of the Arctic fox in Fennoscandia was initiated by extensive trapping and hunting (Linnell et al., 1999b), and the populations readily fluctuate with the rodent cycle (Kaikusalo and Angerbjorn, 1995; Ims et al., 2017). Additionally, Hersteinsson and Macdonald (1992) hypothesised that the southern limit of the arctic fox is determined by interspecific competition with the red fox, while the red fox northern limit is determined by food availability and climate. Later literature has supported this hypothesis (Elmhagen et al., 2017) and red fox population levels have indeed been found to be limited by deep snow and supported by carcass availability (Selås and Vik, 2006). Norwegian red foxes have colonised denning areas previously occupied by arctic foxes (Linnell et al., 1999a). In Northern Sweden, there have been observations of range expansion and increase in the red fox population, while the arctic fox population, despite

protection, has failed to recover (Elmhagen et al., 2015). At the individual level, red foxes may exclude arctic foxes from breeding sites, as arctic foxes breeding in the vicinity of red foxes experience a higher pup mortality risk and therefore generally avoid breeding in dens close to red foxes (Tannerfeldt et al., 2002). Red foxes may also exclude arctic foxes from important food resources (Ims et al., 2017). Selås and Vik (2007) argue that interspecific competition with the red fox may be the leading cause for the lack of recovery of the Fennoscandian arctic fox population. Along with arctic fox legal protection and reintroductions (Ulvund et al., 2020), red fox management is an essential part of the conservation and management of the arctic fox (Linnell et al., 2004; Eide et al., 2017).

Canines are generally highly mobile with the potential for long distance dispersal, and thereby represent a channel for pathogen spread (Macdonald and Sillero-Zubiri, 2004). A manifestation of their dispersal potential comes from a satellite tracked female arctic fox, who dispersed on sea ice from Spitsbergen (Svalbard Archipelago) to Ellesmere Island (Canada) in the course of 76 days, covering a cumulative distance of over 3500 km (Fuglei and Tarroux, 2019). Similarly, a female red fox was recorded covering a cumulative distance of over 1000 km over a period of 100 days (Walton et al., 2018). Emerging infectious diseases, which are important to account for in wildlife conservation, can be carried and transmitted by the red fox, including canine distemper virus, rabies virus, and sarcoptic mange (*Sarcoptes scabiei*) (Woodroffe et al., 2004; Pisano et al., 2019; Zecchin et al., 2019). Additionally, the red fox and the arctic fox are the main definitive hosts for the dwarf fox tapeworm, *Echinococcus multilocularis* (Eckert and Deplazes, 2004). Infected individuals excrete eggs in their faeces, which can be transmitted to intermediate hosts, predominantly small rodents (Eckert and Deplazes, 2004). Although human infection does not allow for further transmission of the parasite, humans can develop alveolar echinococcosis, a serious disease which can cause formation of tumour-like parasitic lesions in the liver (Kern et al., 2003; National Veterinary Institute (SVA), 2021). *Echinococcus multilocularis* has not yet been detected in Finland (EFSA and Zancanaro, 2021) or mainland Norway (Hamnes et al., 2021), but was in 1999 detected on the Svalbard archipelago (Henttonen et al., 2001). It was detected in Denmark in 2000, first on the Zealand island (Kapel and Saeed, 2000), and on the Jutland peninsula in 2012 (Enemark and Nielsen, 2012). In 2011 it was detected in Sweden (Osterman Lind et al., 2011). In a surveillance study from 2012 to 2015 of red foxes and raccoon dogs (*Nyctereutes procyonoides*) in Denmark, red foxes positive for *E. multilocularis* were found across all years of the study (Petersen et al., 2018). The positive carnivores were all located in South Jutland, in which two areas had a high local prevalence of *E. multilocularis*, while no positive carnivores were detected in the rest of Jutland or Zealand (Petersen et al., 2018). The parasite has a low prevalence in Sweden, and have so far been detected in five counties, all located in Southern Sweden; Västra Götaland, Södermanland, Kronoberg, Östergötland, and Dalarna (National Veterinary Institute (SVA), 2021). Due to public health concern, monitoring of this parasite in Fennoscandian countries is essential to further understand this parasite's geographical distribution and to determine whether prevalence is increasing (Wahlström et al., 2015). Landscape genomics and genetics have previously been applied to investigate the potential for pathogen spread by different host species, e.g. rabies in racoons (*Procyon lotor*) (Cote et al., 2012) and striped skunks (*Mephitis mephitis*) (Rioux Paquette et al., 2014), bovine tuberculosis in white-tailed deer (*Odocoileus virginianus*) (Vander Wal et al., 2013), ectoparasites in black-tailed prairie dogs (*Cynomys ludovicianus*) (Jones and Britten, 2010) and big brown bats (*Eptesicus fuscus*) (Talbot et al., 2017), and rabies and canine distemper virus in red foxes (Zecchin et al., 2019). The Norwegian-Swedish action plan for the arctic fox lists disease, along with

the red fox as a pathogen vector, among the potential threats to the survival of the Scandinavian arctic fox population (Eide et al., 2017). When examining the connectivity across the Scandinavian landscape, considering the potential for spread of pathogens by the red fox will be of key importance. In addition to posing a severe threat to human health, understanding the risk for spread of wildlife disease is essential in planning conservation and management actions for vulnerable populations, for instance the arctic fox in Fennoscandia (Woodroffe et al., 2004; Eide et al., 2017). An example of the potential severity of wildlife disease comes from a population of arctic foxes on Mednyi Island in the Bering Sea, that crashed in the 1970s, following an outbreak of otodectic mange caused by ear canker mites (*Otodectes cynotis*) that lead to high pup mortality (Goltsman et al., 2005; Sillero-Zubiri, 2009). By investigating the genetic structure of the Scandinavian red foxes across the landscape, with the assumption that genetic structure and gene flow will be related to parasite spread potential, one can use landscape genomics to shed light on the likely infection pathways for *E. multilocularis* and other pathogens (Biek and Real, 2010).

This thesis had two main aims. The first aim was to investigate large scale genetic structure on the whole-genome level in the Scandinavian red fox population, including how genome-wide levels of heterozygosity vary across Scandinavia. High-density SNP data from red foxes collected in Norway, Sweden, and Denmark was used to infer the number of genetic clusters and the connectivity between them. Part of the motivation for investigating genetic structure was to be able to evaluate infection pathways for pathogen spread. The second aim was to investigate whether specific genomic regions are associated with dispersal to- and colonisation of areas of higher altitude and latitude.

2 Methods

Tissue samples from hunted red foxes were collected in Norway, Sweden, and Denmark. The Norwegian samples were obtained through the Norwegian Institute for Nature Research (NINA) and the Norwegian Veterinary Institute (NVI). The Swedish samples were obtained through the Swedish National Veterinary Institute (SVA), and the Danish samples from the Danish National Veterinary Institute. DNA extracted from muscle tissue of red foxes was genotyped on a custom Applied Biosystems SNP-array for arctic fox and red fox (Hagen et al. In prep.). The individuals originated from 17 watersheds, 10 in Norway, 5 in Sweden, and 2 in Denmark. The definition of the watersheds was based on the River Basin Districts (RBDs) (European Environment Agency, 2011).

The unfiltered data consisted of 181 individuals, and 148 401 biallelic SNPs, along with information on approximate location, sex, and colour variant for each individual. A variable called *3D distance* was also included in the dataset, to describe range expansion to areas of higher altitude and latitude. Based on their location, each individual was assigned to one of three levels of 3D distance, a combined measurement of altitude and distance from the position of each individual to a defined point located just south of Falsterbo at the south-western tip of Southern Sweden (longitude ≈ 12.81, latitude ≈ 55.35). The dataset contained red foxes of three different colour variants, the common red colour morph, the black colour morph, and the silver colour morph. The dataset contained six silver morphs and nine black morphs. The remaining individuals were of the red colour morph. 14 red morphs and two black morphs were genotyped twice, leaving 165 unique individuals. The silver morphs were farmed foxes of North American origin and were assumed to have a heritage different from that of the other two morphs present in the dataset (Eide, 2015). The silver morphs were therefore excluded from the dataset, leaving 159 individuals to be included in subsequent analyses. Because the dataset lacked phenotypic sex for many individuals, and recorded phenotypic sex was deemed untrustworthy, the X-linked SNPs (SNPs located on the X chromosome) were extracted from the unfiltered SNP data to genetically infer the sex by calculating the F-values for each individual. This was done in the computer software PLINK 1.9 (Chang et al., 2015; Purcell and Chang, 2020). Based on the distribution of the F-values, a threshold F of 0.7 was set as a boundary between male and female (Supplementary Figure 19). This yielded 73 females and 86 males. There was an 88% match between phenotypic and genotypic sex for those individuals for which phenotypic sex had been recorded.

In PLINK, the X-linked SNPs were removed from the SNP data, and the individuals divided into appropriate subsets for analysis on different geographical and hierarchical levels. The genotype data underwent linkage disequilibrium-based pruning. Linkage disequilibrium (LD) was calculated for all SNP pairs in a 50 SNP-wide sliding window, which was shifted 5 SNPs with each calculation. For each pair in the window, one of the SNPs was removed if that pair had a LD higher than the threshold (0.5). The genotype data was also filtered on minor allele frequencies (threshold = 0.01), and individuals were filtered on missing call rates (threshold = 0.1). Average heterozygosity was calculated for all individuals. Subsets and sample sizes after filtering are listed below (Table 1).

Table 1: Subsets.
Overview table of the subsets used in the analyses, with number of individuals, and number of SNPs. The versions of the subsets used in PCA did not contain SNPs with missing values. The versions of the subset used in STRUCTURE analysis were filtered on a strict LD threshold (0.04) to reduce the subset size.

Subset	n individuals	n SNPs
All	159	117 423
All (PCA)		79 672
All (STRUCTURE)		12 926
Norway/Sweden	146	115 694
Norway/Sweden (PCA)		81 103
Norway/Sweden (STRUCTURE)		11 593
Denmark (PCA)	13	56 114

The majority of the analyses were conducted in the software R 4.0.3 (R Core Team, 2020) and Rstudio (Rstudio Team, 2016). Using the R package *Stats* and function prcomp (R Core Team, 2020), principal components analyses (PCAs) were run on different hierarchical levels; all individuals, individuals in Norway and Sweden, and individuals in Denmark. For the PCAs, SNPs with any missing genotypes were excluded. Sample sizes for PCA are listed above (Table 1). The results were plotted using the R package *ggplot2* (Wickham et al., 2016), and longitude, latitude, 3D distance, country origin, watershed ID, average heterozygosity, and colour morph was included as colour or shape. The individuals were plotted on the map, also using *ggplot2,* to show the approximate locations from where the individuals originated. Latitude and longitude was missing for three individuals originating from watershed *NO 23* and these individuals were therefore not included in any of the maps. Because some of the individuals had overlapping positions, all maps included here were plotted with a jitter-function, which slightly shifts the positions of overlapping individuals so that one can get an accurate impression of the number of individuals. This means that the map positions are not exact, and individuals may have slightly different positions on the different maps. There is large variability in red fox home range sizes (Walton et al., 2017; Main et al., 2020), and the conditions of sampling locations were assumed to be representative for the general area in which each individual resided (as a resident or immigrant).

Genetic structure was examined using the R package *LEA* and function *snmf* (as described in Frichot and François, 2015b; François, 2016), which applies an admixture analysis, and provides least-squares estimates of ancestry proportions (Frichot and François, 2015a). The analysis was run on the hierarchical level that includes Norway, Sweden, and Denmark (higher level), and on the level that includes only Norway and Sweden (lower level). The analyses were run on K from 1 to 8, and on K from 1 to 5, for the higher and lower hierarchical level, respectively. Ten replicate runs were carried out for each number of K. The most likely number of ancestral populations on each hierarchical level was calculated. Ancestry matrices were created based on the number of ancestral populations and the ancestry coefficients of each individual. Individuals were assigned to clusters based on

their dominant ancestry. Different colours were used to indicate individual cluster membership in the PCA plots.

Genetic structure was also examined in STRUCTURE 2.3.4 (Pritchard et al., 2000; Falush et al., 2003), which applies a Bayesian clustering approach. For the same amount of data, the run time is considerably longer for STRUCTURE than for the LEA method described above. For this reason, the number of SNPs used in the STRUCTURE analyses were reduced to a manageable number. This was done by LD-based pruning in the same fashion as described earlier, but with a lower threshold (0.04). Because LD filtering was done separately for each of the two hierarchical levels, this yielded approximately 13 000 and 11 500 SNPs for the subset on the higher (all individuals) and lower (individuals in Norway and Sweden) hierarchical level, respectively. The analyses were run on K from 1 to 8, and on K from 1 to 5, for the higher and lower hierarchical level, respectively. The model was run with 10 000 iterations, and a burn-in of 5 000. Simulations were repeated 10 times for each value of K. The output from Structure was interpreted using STRUCTURE HARVESTER 0.6.94 (Earl and Vonholdt, 2012), following the Evanno method (Evanno et al., 2005). Cluster membership from the Structure simulations were also included as colour in the PCA plots.

To examine the relative genetic distance between geographical areas in Scandinavia, pairwise fixation indices (F_{ST}-values) were estimated among five areas. The areas were defined as follows: Denmark, Southern Sweden (< 65°N), Northern Sweden (≥ 65°N), Southern Norway (< 65°N), and Northern Norway (≥ 65°N). Pairwise F_{ST} was estimated according to Weir and Cockerham (1984), using the R package *hierfstat* (Goudet and Jombart, 2020). Pairwise F_{ST} was also estimated for the Jutland peninsula and Zealand island, from which the Danish red foxes originated. The 95% confidence interval was estimated for all pairwise F_{ST}-values.

To investigate whether dispersal to- and colonisation of high elevational and northern areas have a genetic basis, an ecological association analysis (EAA) was conducted, using the R package LEA and the function *lfmm*. This implements a genome-wide association analysis, based on latent factor mixed models, in which the response variable is a genotypic matrix, in this case a SNP matrix, and the exploratory variables are environmental (or phenotypic) variables (Frichot and François, 2015a; Frichot and François, 2015b), in this case three levels of 3D distance. The analysis was run on the subset that contained all individuals, but the three individuals in watershed *NO 23*, which lacked recorded latitude and longitude and therefore also lacked level of 3D distance, were excluded. Approximately 117 500 SNPs were included in the analysis. Unlike the LEA admixture analysis, the EAA fares poorly when missing values are present. Missing genotype values were therefore imputed as described in Frichot and François (2015b). The analysis was run with 10 000 iterations, a burn-in of 5 000, and was repeated 10 times. Obtained p-values for SNPs were adjusted by the Benjamini-Hochberg algorithm (q=0.05).

3 Results

3.1 Genetic structure

The admixture analysis ran by applying the LEA package in R, indicated that the most likely number of clusters was three on the higher hierarchical level (including Norway, Sweden and Denmark). The three clusters corresponded to three geographical areas: (A) Northern Norway and Northern Sweden, (B) Southern Norway and Southern Sweden, and (C) Denmark. Figure 1 shows the ancestry proportions for each individual. Figure 2 shows the genetic structure as inferred by PCA, with the dominant cluster membership indicated with colours. The approximate locations of individuals in the different clusters can be found in Figure 3.

The admixture analysis in STRUCTURE found the most likely number of clusters to be two, where one cluster (C) was composed of all the Danish individuals, and the other cluster (D) was composed of the Norwegian and Swedish individuals that constituted the A and B clusters in the LEA analysis. The ancestry proportions can be found in Supplementary Figure 1, along with a PCA plot and map similar to those mentioned above (Supplementary Figure 2 and Supplementary Figure 3).

Visual inspection of PCA plots where individuals were coloured according to geographical location indicated that genome-wide genetic differences between red fox individuals increased when going from the south to the north (Supplementary Figure 7) and from the east to the west (Supplementary Figure 8) in Scandinavia. In contrast, PCA plots where individuals were coloured according to 3D distance level suggested this distance was not related to genetic differentiation between individuals (Supplementary Figure 9). A figure showing the 3D distance level at the individual positions on the map can be found in the supplement (Supplementary Figure 10). When individuals were coloured according to their watershed ID, the PCA plot showed that there was overlap in the genetic identity of several watersheds (Supplementary Figure 13 and Supplementary Figure 15).

Individuals within Denmark appeared to generally have a lower average genome-wide level of heterozygosity relative to individuals in Norway and Sweden (Map, Figure 4; PCA plot, Supplementary Figure 16). Additionally, individuals which showed a relatively low level of heterozygosity on the Scandinavian peninsula, appeared to be located in peripheral areas, such as along the Norwegian southwestern coast, the Lofoten Islands, and on the coast of northernmost Norway.

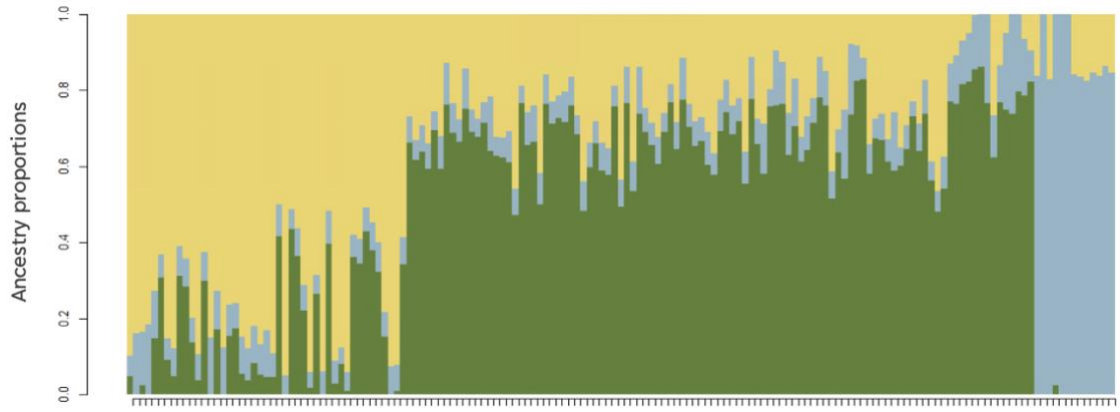

Figure 1: Ancestry proportions for all individuals according to LEA

Each vertical line represents one individual. Ancestry proportions are given on the y-axis. Colours correspond to ancestry populations: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green, (C) Denmark = blue.

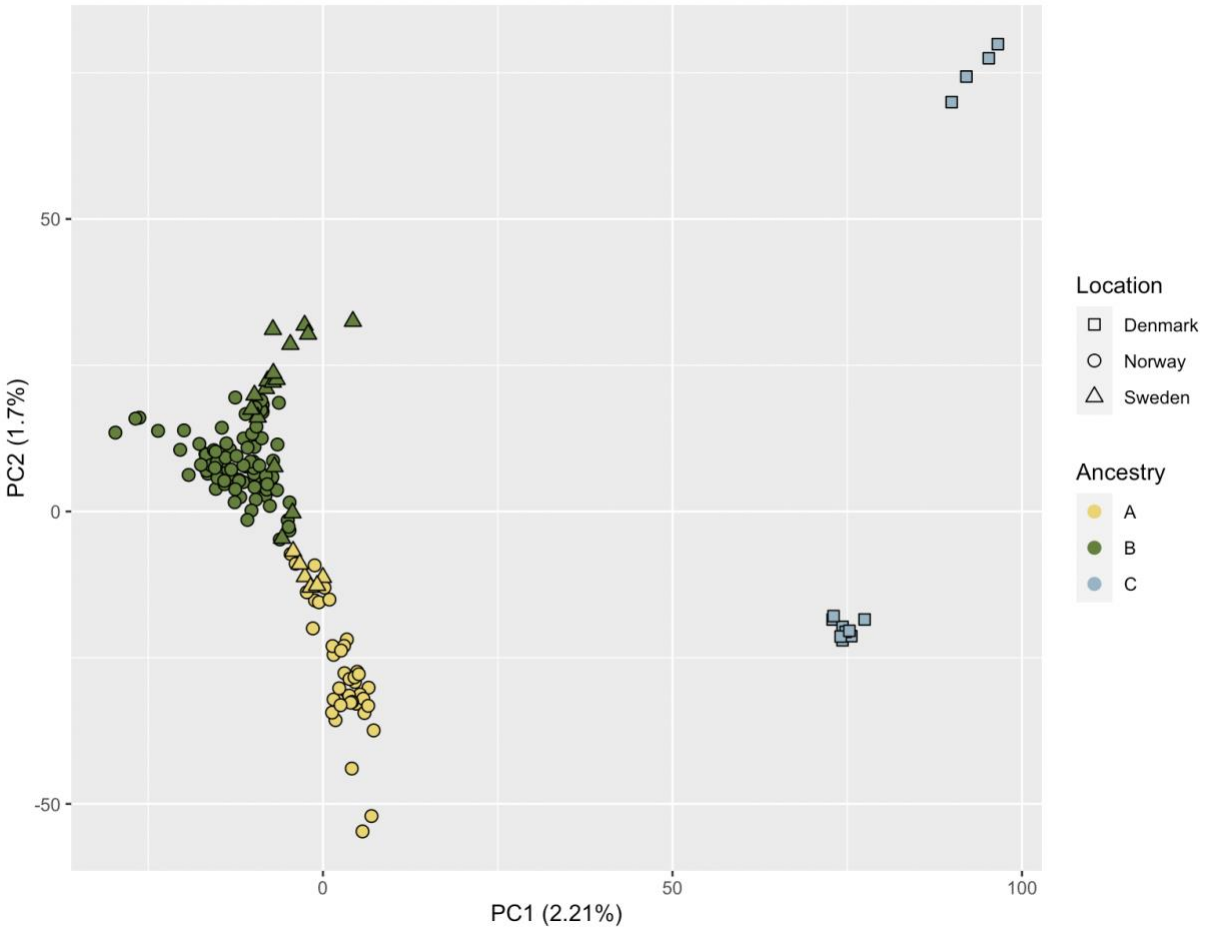

Figure 2: PCA plot with cluster membership for all individuals

PCA plot of individuals in Norway, Sweden, and Denmark. The x- and y-axis show the first and second principal components respectively. Colours correspond to the dominant ancestry in each individual according to the LEA analysis: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green, (C) Denmark = blue. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.

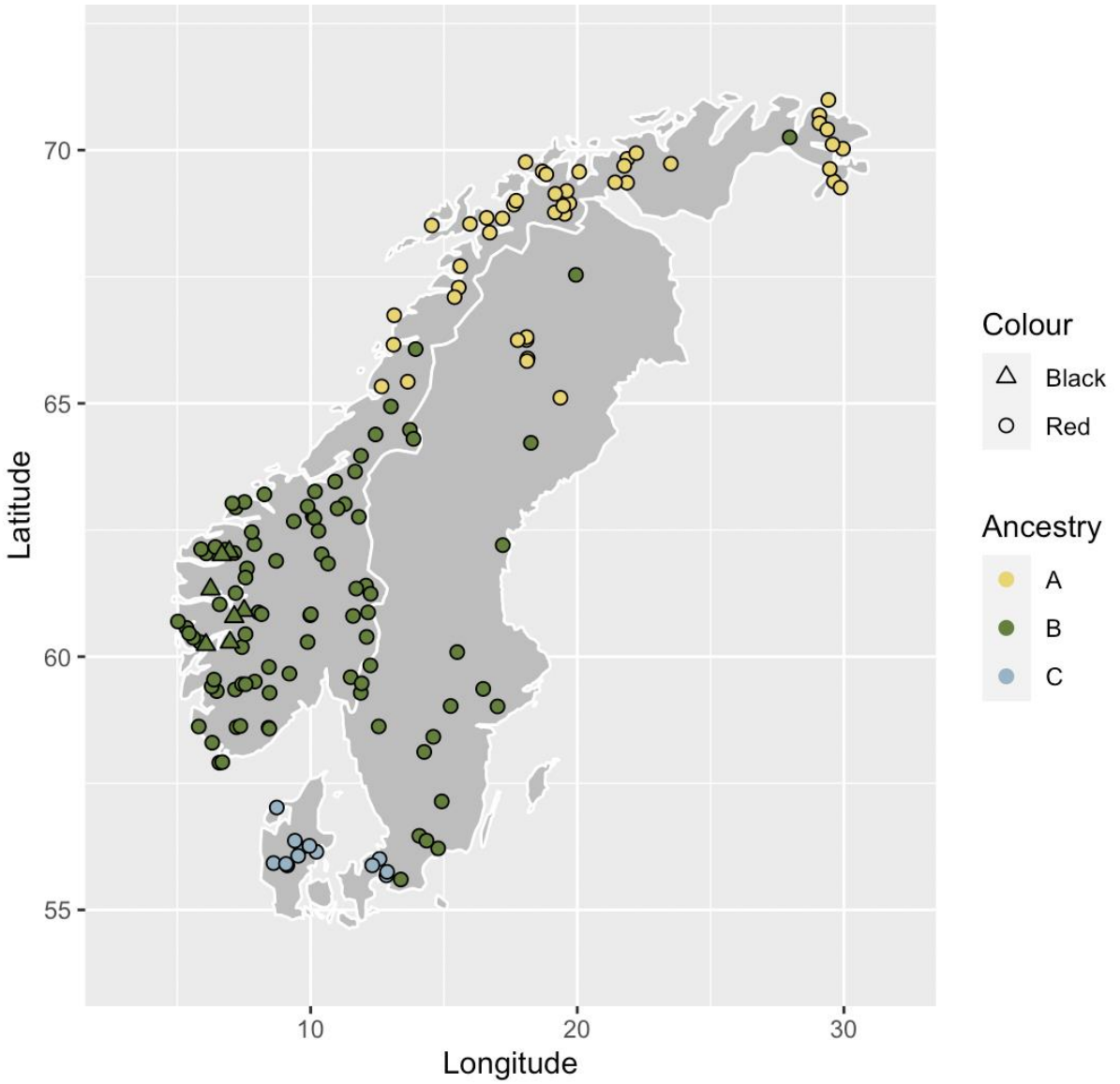

Figure 3: Map with cluster membership for all individuals

Map of Scandinavia with the approximate positions of individuals. Colours correspond to the dominant ancestry in each individual according to the LEA analysis: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green, (C) Denmark = blue. Colour morph is indicated by shape: red morphs are indicated by circles and black morphs are indicated by triangles. The individual positions have been plotted with a jitter-function, and positions of individuals may have shifted somewhat from their sample-location.

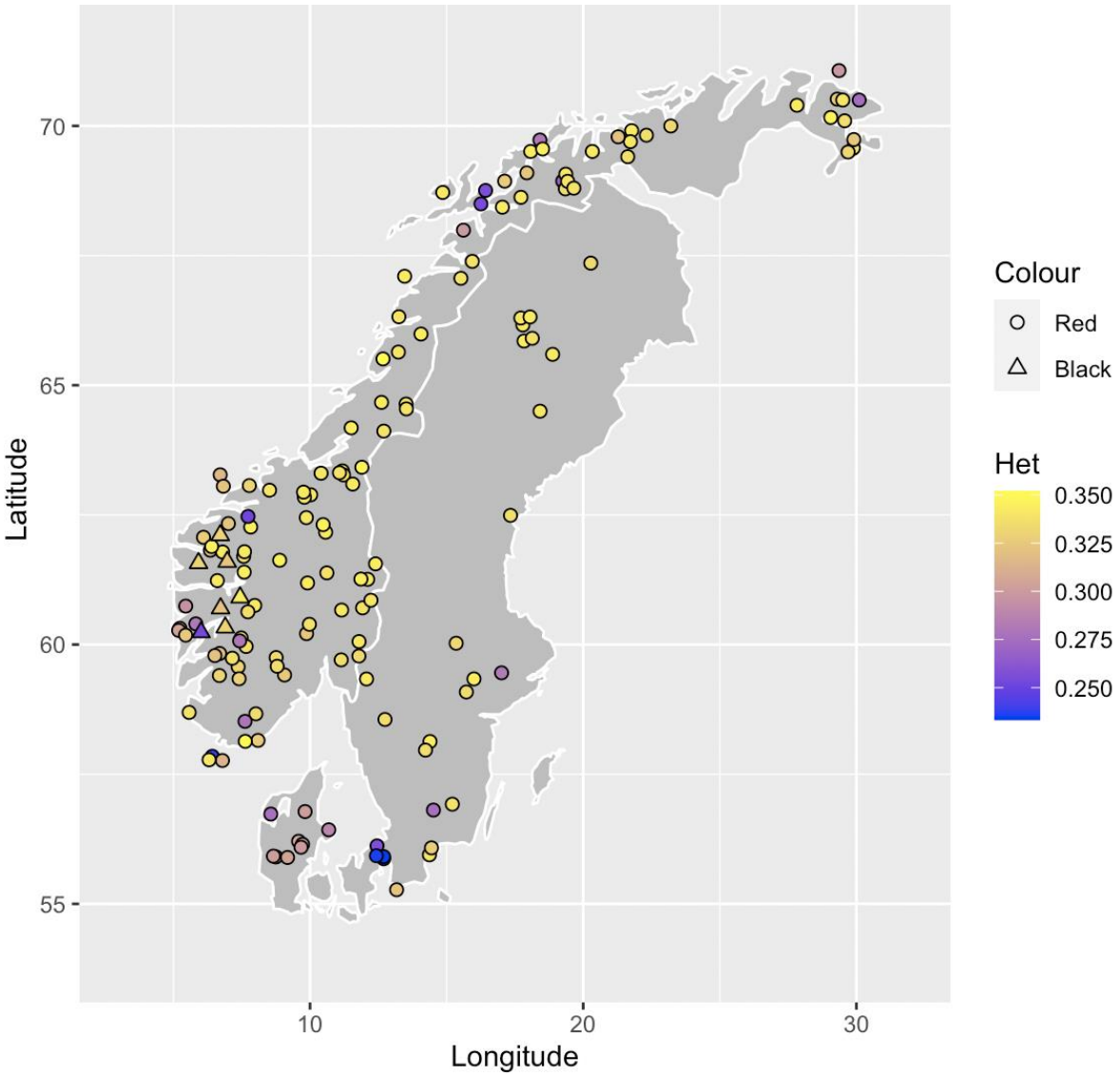

Figure 4: Map with average heterozygosity for all individuals

Colour corresponds to average heterozygosity across non-missing loci. Higher heterozygosity is shown in yellow, and lower heterozygosity is shown in blue. Colour morph is indicated by shape: red morphs are indicated by circles and black morphs are indicated by triangles. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.

When the LEA admixture analysis was applied on the lower hierarchical level, with data from Norway and Sweden only, no clear clustering was detected, and the most likely number of clusters was one. In contrast, the admixture analysis in STRUCTURE found the most likely number of clusters on this level to be two. These two clusters were essentially the same that were found when applying the LEA admixture analysis on the higher hierarchical level; one cluster (A) composed of individuals in Northern Norway and Northern Sweden, and another (B) composed of individuals in Southern Norway and Southern Sweden. The ancestry proportions of the individuals can be found in the Supplement (Supplementary Figure 4), along with the corresponding PCA plot (Supplementary Figure 5) and map (Supplementary Figure 6). When comparing the results from STRUCTURE on the lower hierarchical level and LEA on the higher hierarchical level, there was only one individual in Norway and Sweden that was not assigned to the same cluster by the two methods. This individual was sampled at a latitude ≈ 65.40, around the

same area where the A and B cluster meet on the map. Both methods place the black morphs within the B cluster.

When the PCA was carried out on the lower hierarchical level, the structure present within Norway and Sweden became clearer (Figure 5). There were still Norwegian and Swedish individuals that grouped together, but the distinction between Southern Norway and Southern Sweden was clearer; the bottom left was dominated by Southern Norway, the top left was dominated by Southern Sweden, and Northern Norway and Northern Sweden could be seen dominating the right side of the plot. As above, latitudinal and longitudinal gradients both appeared to partially explain the genetic structure seen in the PCA plot (Figure 5 and Supplementary Figure 11). PCA plots where individuals were coloured according to 3D distance suggested this distance was not related to genetic differentiation between individuals (Supplementary Figure 12).

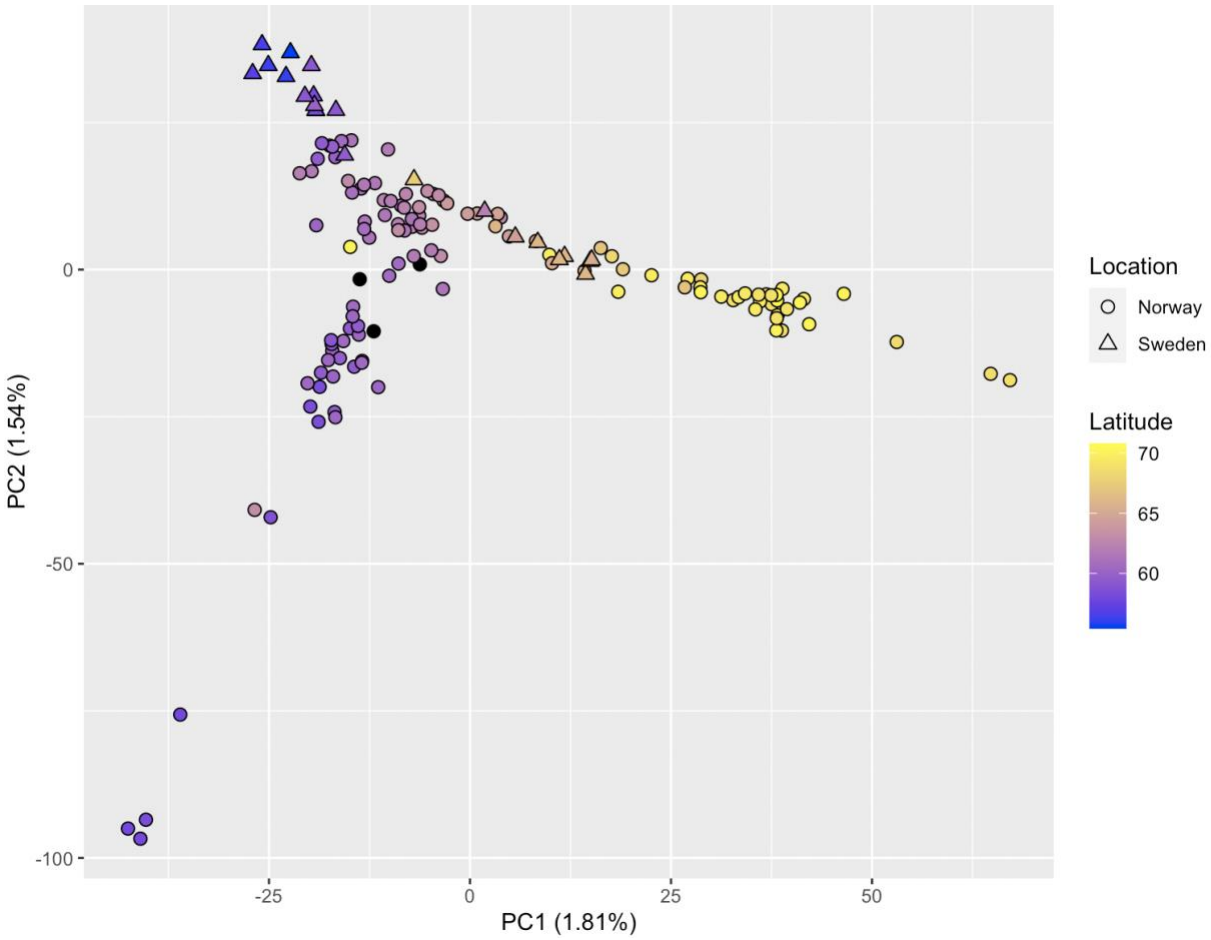

Figure 5: PCA with individuals in Sweden and Norway including latitude
The x- and y-axis show the first and second principal components respectively. Individuals are coloured according to the latitude at their location, where yellow = north and blue = south. Individuals with missing latitude value are coloured black. Location is indicated by shape: Norwegian individuals are indicated by circles and Swedish individuals are indicated by triangles.

All the Danish individuals were dominated by the same ancestry. This is a pattern that was found in both the LEA and Structure admixture analyses, and that can also be recognised in the PCA plot (Figure 2). In regard to the pairwise F_{ST} values (Table 2), Denmark stood out, by being the most genetically different from all the other regions. The two Danish subgroups that are seen in the PCA corresponds to Jutland (top) and Zealand (bottom), which is separated by ocean and smaller islands. When Denmark is considered apart from

the rest of Scandinavia, the two groups are still apparent (see PCA: Supplementary Figure 17, and map: Supplementary Figure 18).

Table 2 contains the pairwise F_{ST}-values among five geographical areas within Scandinavia: Denmark, Southern Norway, Northern Norway, Southern Sweden, and Northern Sweden. Pairs which included Denmark yielded the highest pairwise F_{ST}-values. The highest value (0.0150) was the pairwise F_{ST} between Denmark and Southern Sweden. The smallest value (0.0012) was the pairwise F_{ST} between Northern Norway and Northern Sweden. The Pairwise F_{ST} for Zealand and Jutland was 0.0329 (95% CI [0.0325, 0.0333]).

Table 2: Pairwise F_{st}-values for geographical areas in Scandinavia

Areas include Southern Norway (< 65°N), Northern Norway (≥ 65°N), Southern Sweden (< 65°N), Northern Sweden (≥ 65°N), and Denmark. The 95% confidence intervals for pairwise F_{ST} are included in brackets. The colour gradient corresponds to cell values: blue for lower values, green for middle values, and yellow for higher values.

	S Norway	N Norway	S Sweden	N Sweden	Denmark
S Norway		0.0026 [0.0026-0.0027]	0.0025 [0.0024-0.0026]	0.0013 [0.0012-0.0015]	0.0133 [0.0131-0.0134]
N Norway	0.0026 [0.0026-0.0027]		0.0051 [0.0051-0.0052]	0.0012 [0.0011-0.0014]	0.0126 [0.0125-0.0128]
S Sweden	0.0025 [0.0024-0.0026]	0.0051 [0.0051-0.0052]		0.0037 [0.0035-0.0039]	0.0150 [0.0148-0.0151]
N Sweden	0.0013 [0.0012-0.0015]	0.0012 [0.0011-0.0014]	0.0037 [0.0035-0.0039]		0.0143 [0.0141-0.0146]
Denmark	0.0133 [0.0131-0.0134]	0.0126 [0.0125-0.0128]	0.0150 [0.0148-0.0151]	0.0143 [0.0141-0.0146]	

3.2 Ecological association analysis

After correction for false discovery rate, no SNPs were significantly associated with 3D distance (Figure 6). Therefore, it appears to be no genomic regions that differ consistently between red foxes at different levels of 3D distance from the reference point.

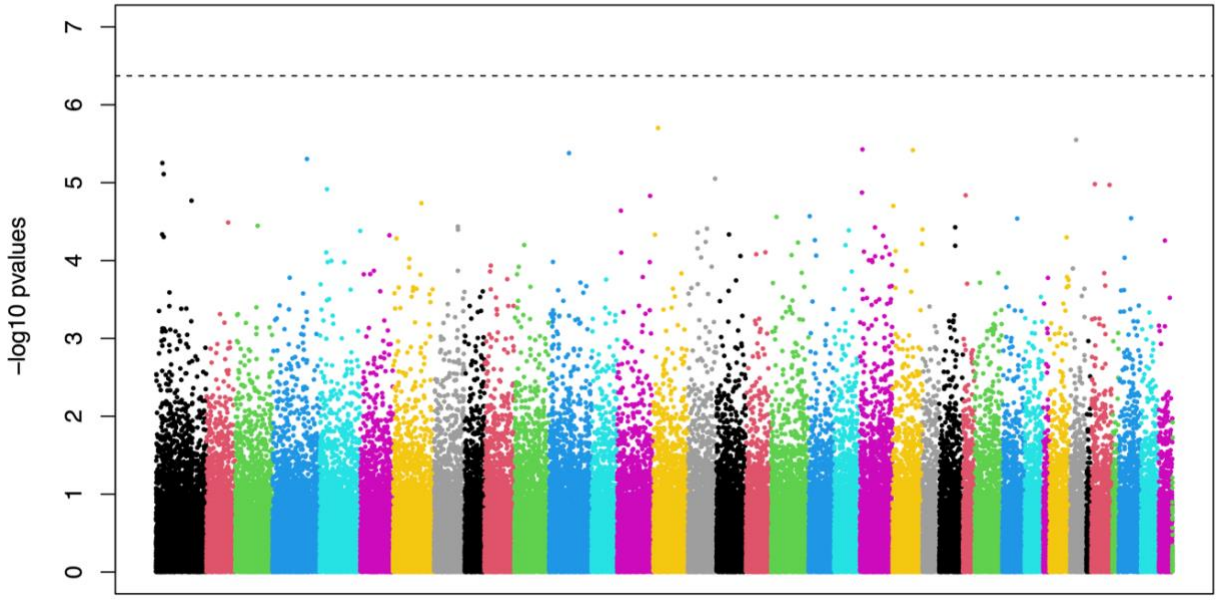

Figure 6: Manhattan plot for EAA

The plot includes SNPs and respective p-values for the EAA with 3D distance. The x-axis shows SNPs in order of chromosome, indicated by colour, and position within chromosome. Each dot represents one SNP, and their position on the y-axis shows the respective p-value for each SNP. The dashed line marks the significance threshold value (q-value) for the genome-wide level of significance.

4 Discussion

Overall, there was little genetic differentiation between red foxes across Scandinavia, aside from red foxes in Denmark which showed indications of being relatively more differentiated from red foxes in Norway and Sweden. However, north-to-south and west-to-east gradients showed that there was some genetic differentiation also within Norway and Sweden. Denmark, along with some peripheral areas in Norway, showed lower average genome-wide heterozygosity relative to the rest of the individuals in the dataset. No genomic regions were significantly associated with 3D distance. The low F_{ST}-values along with indications of weak structure seen in the PCA plots suggested high gene flow. The division into northern and southern regions when calculating the pairwise F_{ST}-values, was informed by the LEA and STRUCTURE analyses. The division into Norwegian and Swedish regions was arbitrary, because the border does not represent a physical barrier. The values were estimated this way, however, because it is relevant in a management perspective. The results demonstrate that although the management may be separated by country borders, the red foxes traverse these freely.

4.1 Denmark and the Scandinavian peninsula

The Danish islands are separated from Norway and Sweden by the Skagerrak, Kattegat, and Øresund straits. The narrowest point measures four km wide and spans across the Øresund strait. The only current point of direct connection is the 16 km long Øresund bridge, which connects Copenhagen on Zealand to Malmö in Sweden. However, Denmark and continental Europe have been connected to the Scandinavian peninsula at several points in time after the last glacial maximum (LGM), by temporary land bridges that formed between glacial retreats and advances of the southernmost areas of Scandinavia (Jaarola et al., 1999). For instance, the first land bridge after the LGM was formed 14 000 years ago, and the final land bridge was closed 8 200 years ago by the formation of the Øresund strait (Jaarola et al., 1999). A possible explanation for the observations regarding genetic differentiation between Danish islands, and distance between Denmark and the Scandinavian peninsula, could therefore be that bodies of water, straits, and fjords represent a barrier not easily traversed by the red fox. For instance, rivers have been suggested as a barrier to gene flow between red fox populations located between the Eastern and Dinaric Alps (Zecchin et al., 2019; but see Galov et al., 2014). Similar examples have been found in other taxa. For instance, sea lochs limit gene flow in red deer (Cervus elaphus) in the Scottish highlands (Perez-Espona et al., 2008), and mainland and island grey wolves (Canis lupus) in British Colombia show genetic differentiation even though they are capable swimmers (Stronen et al., 2014). Palo et al. (2004) even discovered a similar pattern in common frogs (Rana temporaria) to that of the red foxes on Jutland and Zealand; a relatively large genetic differentiation when compared to geographic distance, along with lower genetic diversity within Zealand relative to Jutland. Palo et al. (2004) explain these patterns by ocean barriers, phylogeographical structuring, and gene flow between individuals on Jutland and mainland Europe. In the case of the red foxes, the patterns seen on Jutland and Zealand should however be interpreted with care as a small number of individuals was involved in this observation. Although the genetic

differentiation between Southern Sweden and Denmark is relatively larger than the genetic distance between e.g. Southern Sweden and Southern Norway, it is important to note that the pairwise F_{ST}-values obtained are in general small. It therefore seems unlikely that the straits represent a perfect barrier. The relatively larger F_{ST}-values for Denmark could indicate that marine barriers, such as straits, provide higher landscape resistance than what is generally experienced by red foxes on the Scandinavian peninsula. This could play a part in why watersheds within Norway and Sweden cluster close together, while they cluster relatively far from watersheds in Denmark in the PCA plot (Supplementary Figure 13). However, it is important to note that the array used in the SNP genotyping was developed using Norwegian samples. The observed genetic differentiation, at least what is attributable to differences in heterozygosity, could therefore be due to ascertainment bias.

4.2 Phylogeographical history

The dominance of either a northern (A) or southern (B) ancestry in the Norwegian and Swedish individuals (Figure 1 and Supplementary Figure 4), and the division of these at about 65°N (Figure 3 and Supplementary Figure 6), may reflect phylogeographical history. This is in accordance with Wallén et al. (2018), whose findings suggest that the Fennoscandian red fox population consists of at least two lineages, divided between southern and northern areas, which were recolonised following retreat of the LGM from southern and eastern refugia respectively. Migration from southern refugia would be possible through the land bridges previously mentioned. However, other phylogeographical studies have indicated that red foxes may have been present across Europe throughout the last glaciation (Edwards et al., 2012), while others did not find evidence of phylogeographical structuring of populations at all (Teacher et al., 2011). Bidirectional recolonisation routes and contact zones on the Scandinavian peninsula have been suggested for several species; for instance the European pine marten (Martes martes) (Ruiz-Gonzalez et al., 2013), the common shrew (Sorex araneus) (Lundqvist et al., 2011), the field vole (Microtus agrestis) (Jaarola and Searle, 2002; Herman et al., 2014), the common European adder (Vipera berus) (Carlsson et al., 2004), the common frog (Rana temporaria) (Palo et al., 2004), and the moor frog (Rana arvalis) (Knopp and Merila, 2009). Hence, the division of Scandinavian red foxes into a southern and northern group is in line with phylogeographical studies on several other species in Scandinavia.

4.3 Dispersal and range expansion

I did not detect any SNPs significantly associated with level of 3D distance. It therefore appears unlikely that a single or a few large-effect genes mediate a phenotype that makes red foxes relatively better adapted for dispersal to and colonisation of high elevational and northern areas. In another canine, the coyote, Heppenheimer et al. (2018) found candidate genes under selection in two expansion fronts in Eastern North America, among which were three genes considered to be related to dispersal. There are examples also from other taxa, in which loci have been detected to be under selection following range expansion, including mammals (White et al., 2013), tunicates (Chen et al., 2018), and insects (Buckley et al., 2012; Swaegers et al., 2015). Dispersal is in itself a complex trait, and although there are examples of dispersal being determined by large-effect genes, multiple small-effect genes are probably responsible most of the time when dispersal has a genetic basis (Saastamoinen et al., 2018). Additionally, dispersal at the local scale may be influenced by social interactions, although this has little effect on dispersal on regional scales (Walton et al., 2021). Phenotypes which are advantageous for expansion in the red fox may to some degree be determined genetically, however, there may be other sources of variance

not explained by genotypes that account for most of the variation observed in phenotypes, such as environmental variation or phenotypic plasticity (Gienapp et al., 2008). Previous studies have suggested further range expansion in the red fox due to future climate warming (Elmhagen et al., 2015; Elmhagen et al., 2017), especially due to change in snow conditions (Gomo et al., 2020). Gallant et al. (2020) found previous range expansion by the red fox in the Canadian arctic to be driven by northwards expansion of human settlements, and less so by climate change. Food waste associated with human settlements was highlighted as the most important factor (Gallant et al., 2020). Similarly, highways and littering have been linked to expansion in the red fox in Fennoscandia (Rød-Eriksen et al., 2020). Range expansion in the red fox might therefore occur due to ecological release as a consequence of the complicated interplay of human impacts, climate warming, and increased productivity in alpine areas, and may not be attributable to changes in allele frequencies.

4.4 Risk of emerging infectious diseases

There appeared to be good connectivity between watersheds within Norway and Sweden. The F_{ST}-values previously discussed also imply that there is gene flow across the Scandinavian peninsula. These findings suggest no strong landscape barriers between Norway and Sweden, except for the branching of the Scandinavian peninsula into southernmost Norway and Sweden. However, these areas are still very genetically similar judging by the F_{ST}-values. Hagenlund et al. (2019) argue that there is indeed high levels of gene flow, and being barely genetically distinguishable, Norwegian and Swedish red foxes can be considered part of the same population. Due to the often complicated relationship between the landscape, gene flow, and pathogen spread, the genetic structure of the host species is often best fit to provide a qualitative measure of spread risk, rather than a quantitative, through providing hints towards the pathogen's likely routes across the landscape (Biek and Real, 2010).

Owing to the straits that separate Denmark from the Scandinavian peninsula, spread of parasites and pathogens to Norway appear more likely westwards from Sweden than northwards from Denmark. Although present in Sweden, *E. multilocularis* is far from widespread, having only been detected in a handful of southern counties (National Veterinary Institute (SVA), 2021). Given that geographic distance seems to determine some of the genetic structure, it is likely that the Swedish and Norwegian counties in closest proximity to areas of *E. multilocularis* occurrence face the largest invasion risk. Wahlström et al. (2015) argue that it is likely that *E. multilocularis* will spread to Norway, as well as to Finland. This may seem likely given the low genetic differentiation seen here, and signals of low genetic differentiation on Fennoscandian scale (Norén et al., 2015), but with no red fox samples from Finland included here, any speculation about invasion risk for Finland is beyond the scope of this thesis. I also recognise that this study would benefit from better coverage in Sweden with a higher number of individuals, especially in central Sweden.

The potential for spread of *E. multilocularis* will not only be dependent on red foxes or other definitive hosts, but also on the presence, density, and identity of intermediate hosts, as there is evidence for variation in parasite susceptibility in different intermediate hosts (Miller et al., 2017). Individual contact rates in red foxes vary with season, sex, and social status of the individual, and a better understanding of social groups will be important in management of other pathogens that spread through contact between individuals (Dorning and Harris, 2019). Spread of wildlife disease can have detrimental impacts on public health, domestic animals, and can even lead to endangerment of wildlife populations (Macphee

and Greenwood, 2013). Potential future outbreaks of sarcoptic mange is for instance a concern for the conservation of the Scandinavian arctic fox (Eide et al., 2017). Examples from other wild canine populations have shown that wildlife disease can have severe impacts. For instance, an outbreak of sarcoptic mange in Scandinavia lead to high mortality and rapid decrease in the red fox population, as was seen in Sweden (Willebrand et al., 2022). Similarly, outbreaks of rabies virus have been known to cause increased mortality in endangered Ethiopian wolf (*Canis simensis*) populations at several times in the past (Randall et al., 2004; Marino et al., 2017), and an outbreak of canine distemper virus caused high mortality in a pack of endangered African wild dogs (*Lyacon pictus*) in the Serengeti ecosystem (Goller et al., 2010). Owing to the weak genetic structure observed in Scandinavian red foxes, the red fox represent a vessel for pathogen spread, and a species highly relevant for public health and wildlife conservation.

5 Conclusions and future prospects

In this study I have demonstrated that there is weak genetic structure in the Scandinavian red fox, in line with previous literature on the species in Europe. The genetic structure implied high gene flow and good connectivity across Scandinavia. This leads to the conclusion that the red fox represents an important invasion pathway for pathogens across Scandinavia. However, there were indications that waterbodies, to some degree, function as barriers to gene flow. An interesting subject for future studies would therefore be the genetic structure of the red fox and its relation to landscape resistance on a more detailed level. From the ecological association analysis, it seemed unlikely that a potentially beneficial phenotype in high elevational and northern areas is mediated by a few large-effect genes, and it might be that range expansion in the red fox is mainly or fully driven by environmental change and human impacts, as earlier studies have suggested. Through its role as a host species for emerging infectious diseases, and the weak genetic structure seen across Scandinavia, the red fox remains a species highly relevant in the context of public health and for the management and conservation of Scandinavian fauna.

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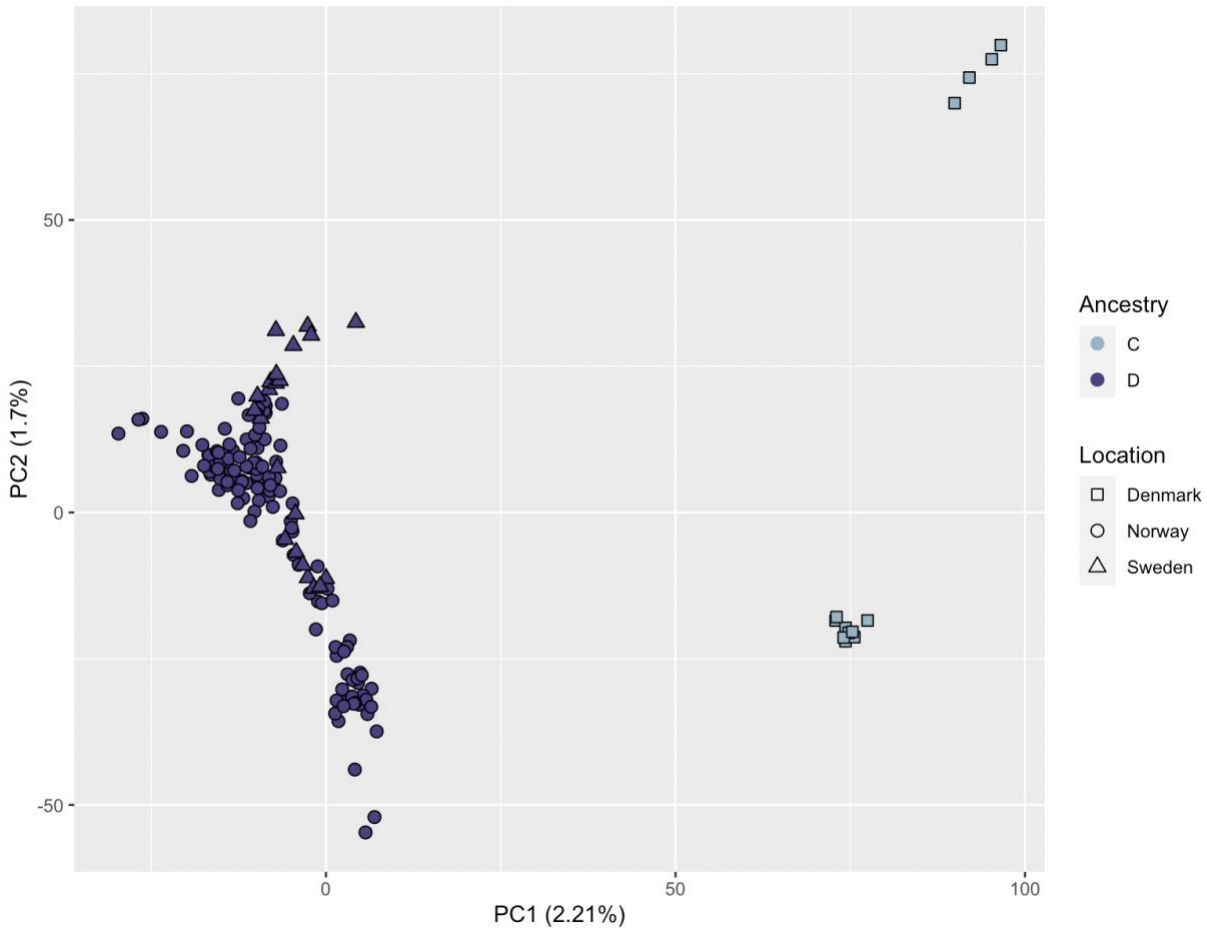
Supplement

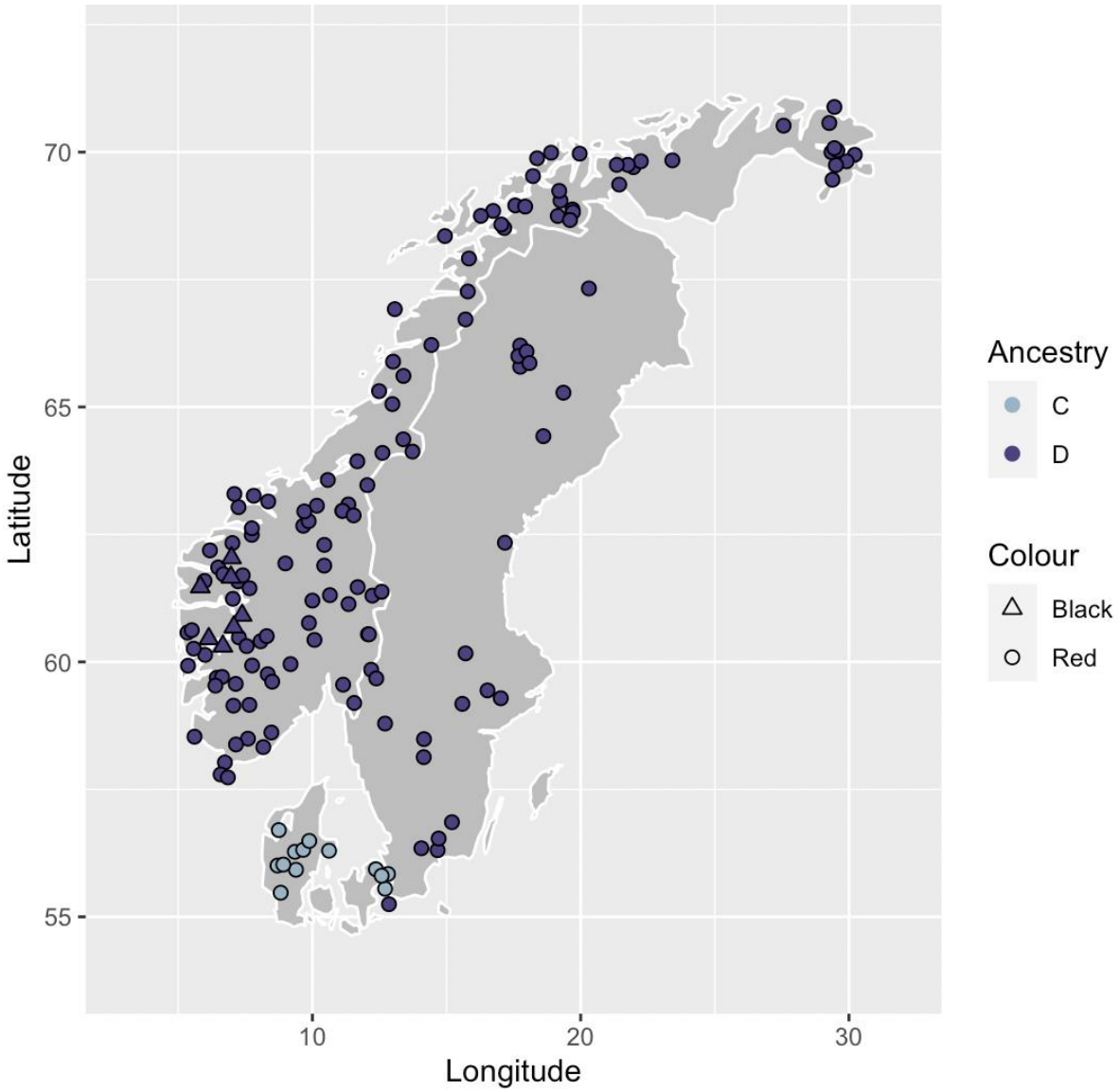
Supplementary Figure 1: STRUCTURE plot for all individuals

The plot shows ancestry proportions. Each vertical line represents one individual. Ancestry proportions are given on the y-axis. Colours correspond to ancestry populations: (C) Denmark = blue, (D) Norway and Sweden = purple.



Supplementary Figure 2: PCA with cluster membership for all individuals

The x- and the y-axis show the first and second principal components respectively. Colours correspond to dominant ancestry according to the STRUCTURE analysis: (C) Denmark = blue, (D) Norway and Sweden = purple. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.

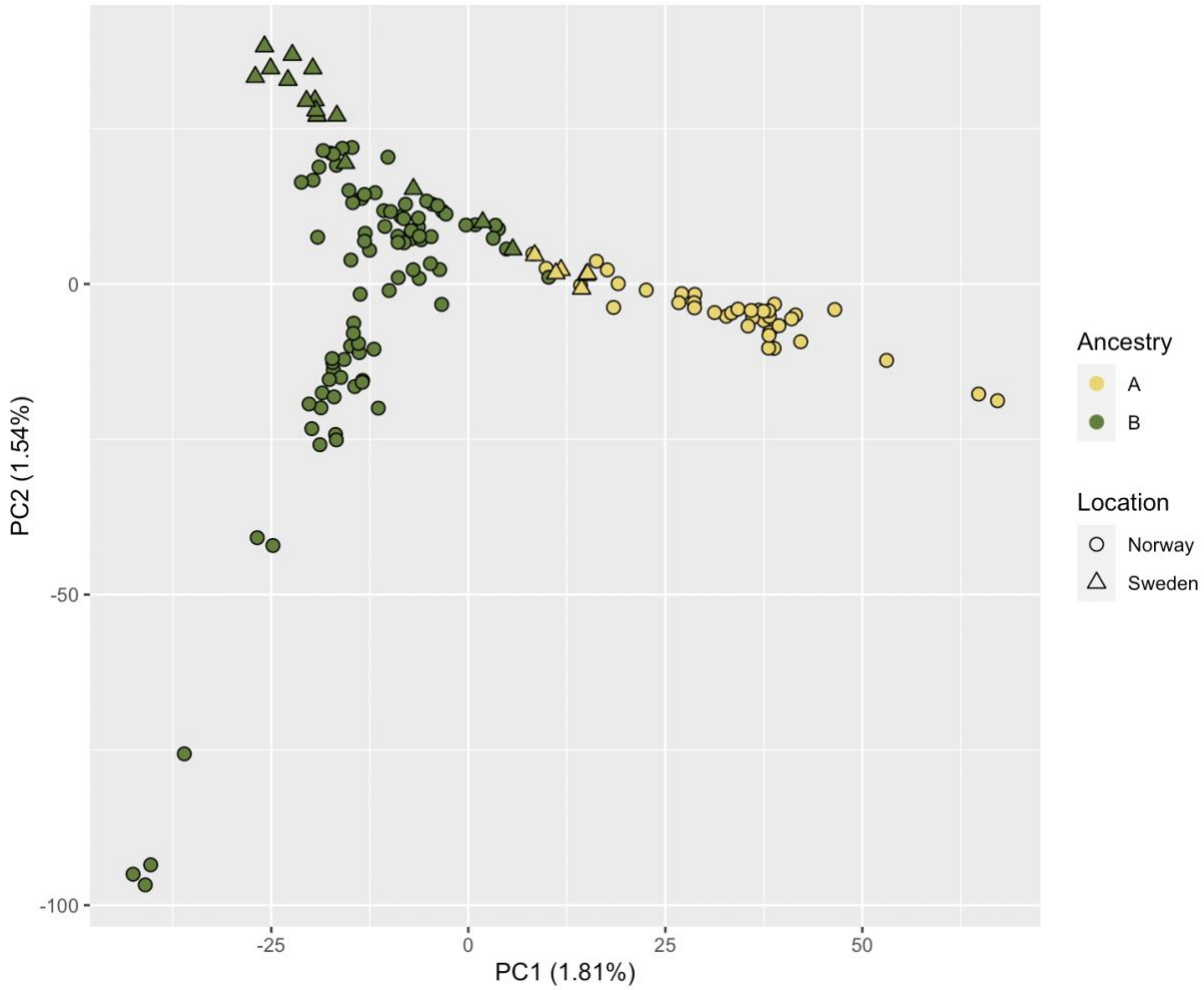


Supplementary Figure 3: Map with cluster membership for all individuals

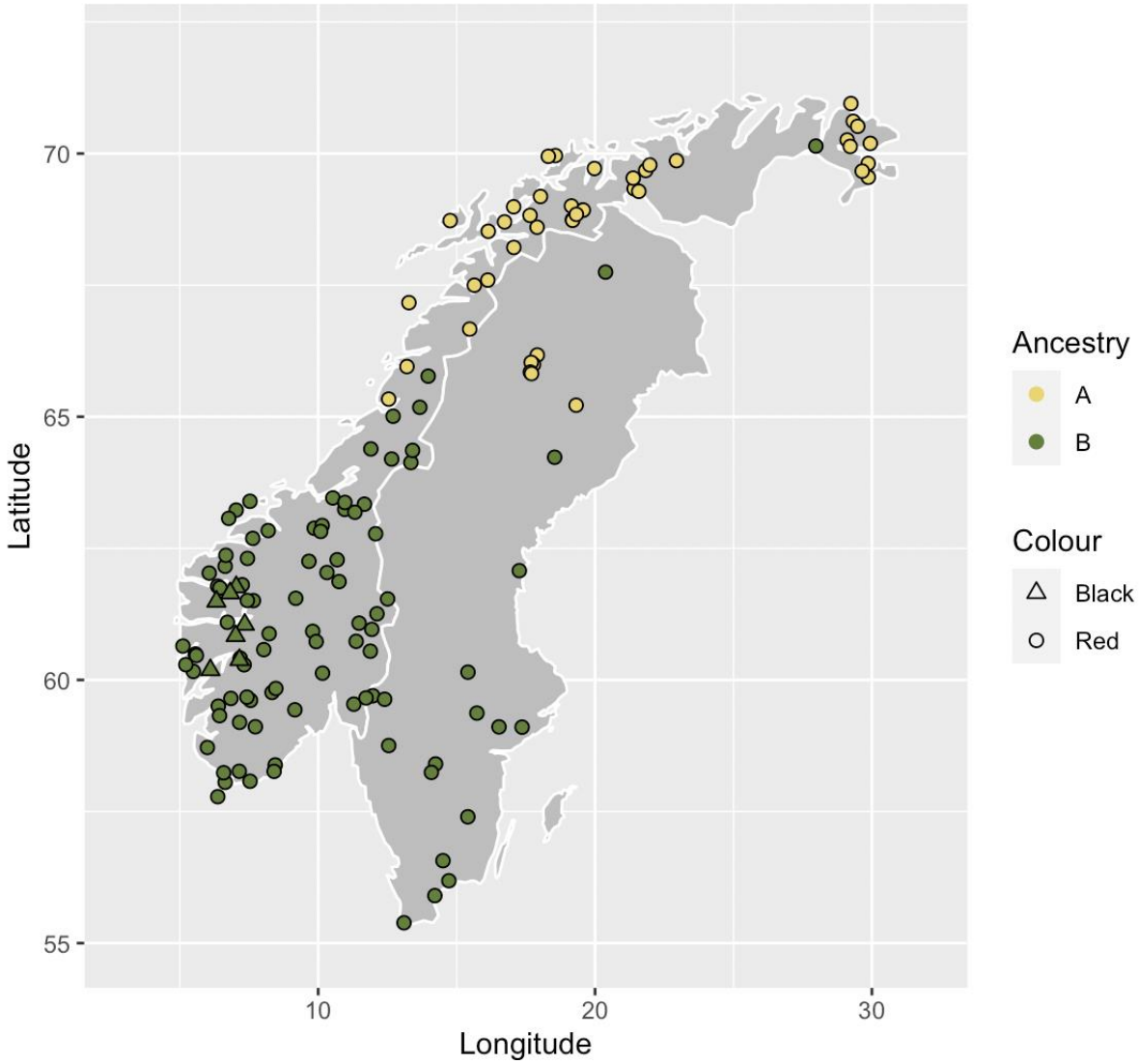
Map of Scandinavia with the approximate positions of individuals. Colours correspond to dominant ancestry according to the STRUCTURE analysis: (C) Denmark = blue, (D) Norway and Sweden = purple. Colour morph is indicated by shape: red morphs are indicated by circles and black morphs are indicated by triangles. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.

Supplementary Figure 4: STRUCTURE plot for Norwegian and Swedish individuals

The plot shows ancestry proportions. Each vertical line represents one individual. Ancestry proportions are given on the y-axis. Colours correspond to ancestry populations: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green.

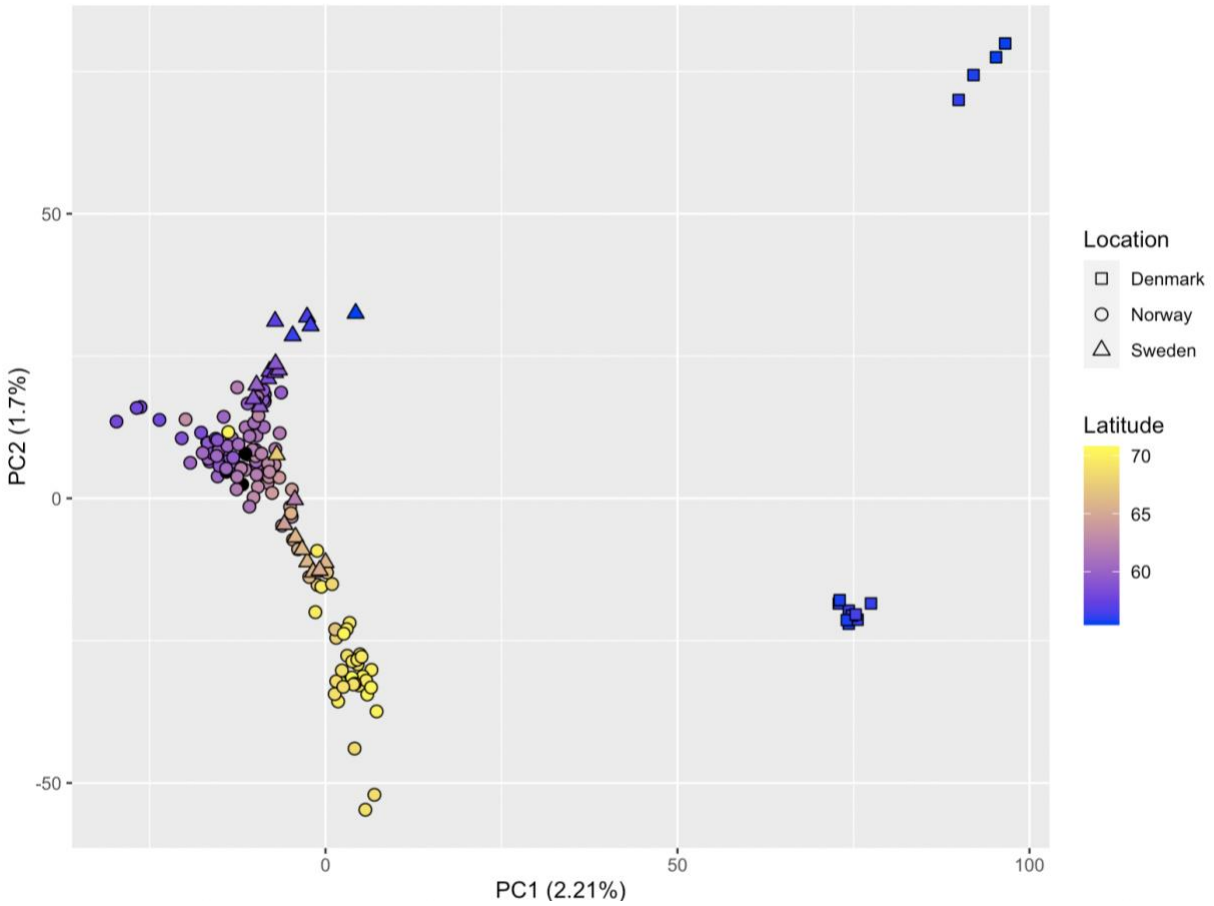


Supplementary Figure 5: PCA with cluster membership for Norway and Sweden.
The x- and the y-axis show the first and second principal components respectively. Colours correspond to dominant ancestry according to the STRUCTURE analysis: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green. Location is indicated by shape: Norwegian individuals are indicated by circles and Swedish individuals are indicated by triangles.

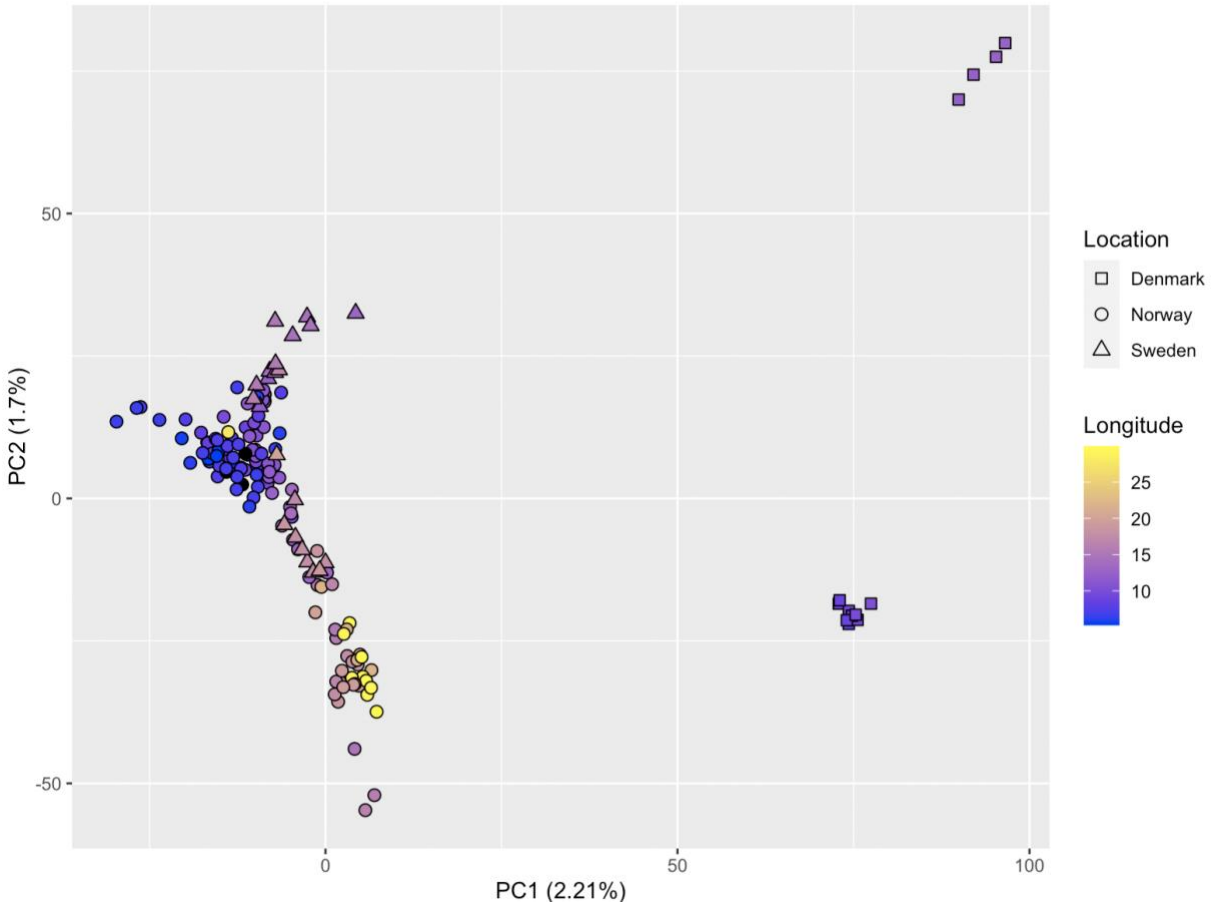


Supplementary Figure 6: Map with cluster membership for individuals in Norway and Sweden.

Map of the Scandinavian peninsula with the approximate positions of individuals. Colours correspond to dominant ancestry according to the STRUCTURE analysis: (A) Northern Norway and Northern Sweden = yellow, (B) Southern Norway and Southern Sweden = green. Colour morph is indicated by shape: red morphs are indicated by circles and black morphs are indicated by triangles. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.

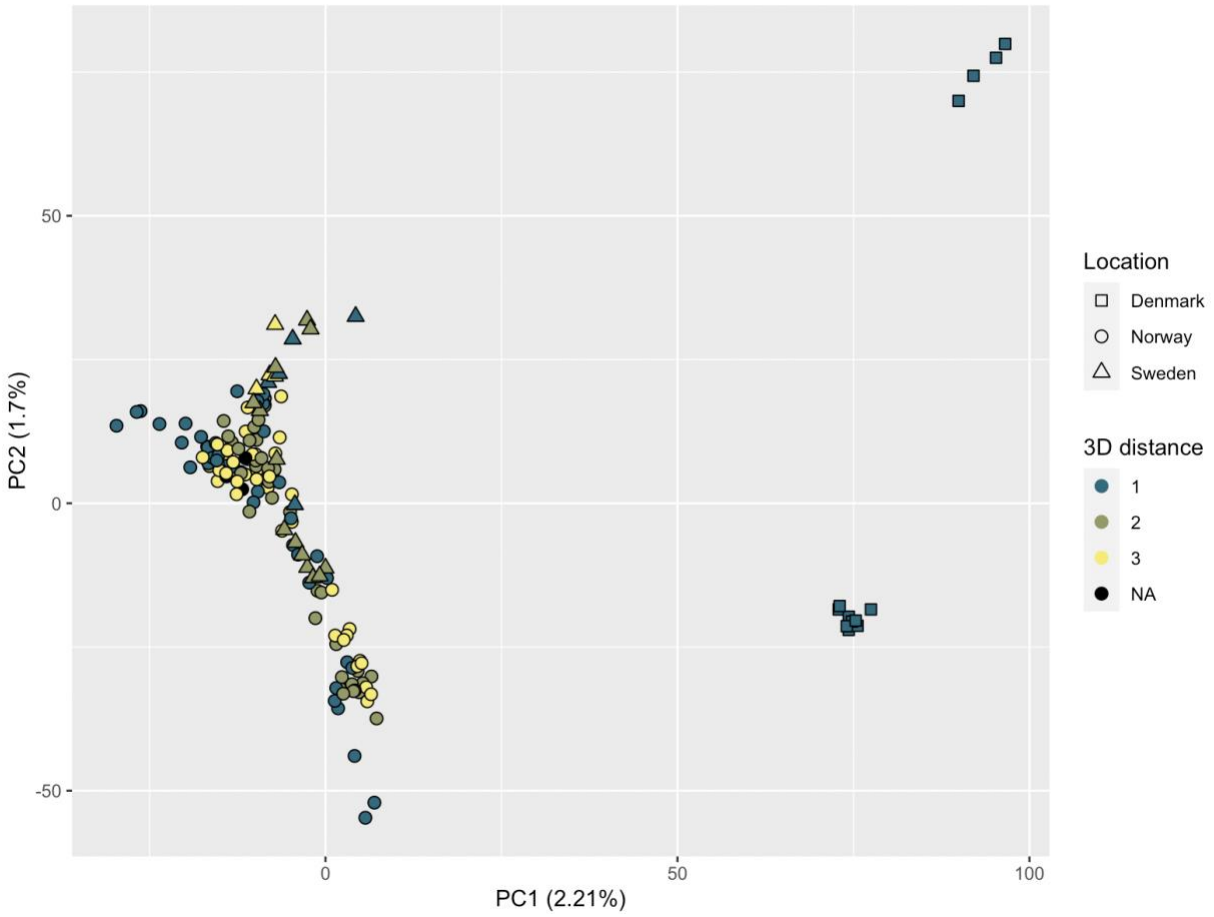


Supplementary Figure 7: PCA plot of all individuals including latitude.
The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to the latitude at their location, where yellow = north and blue = south. Individuals with missing latitude value are coloured black. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.



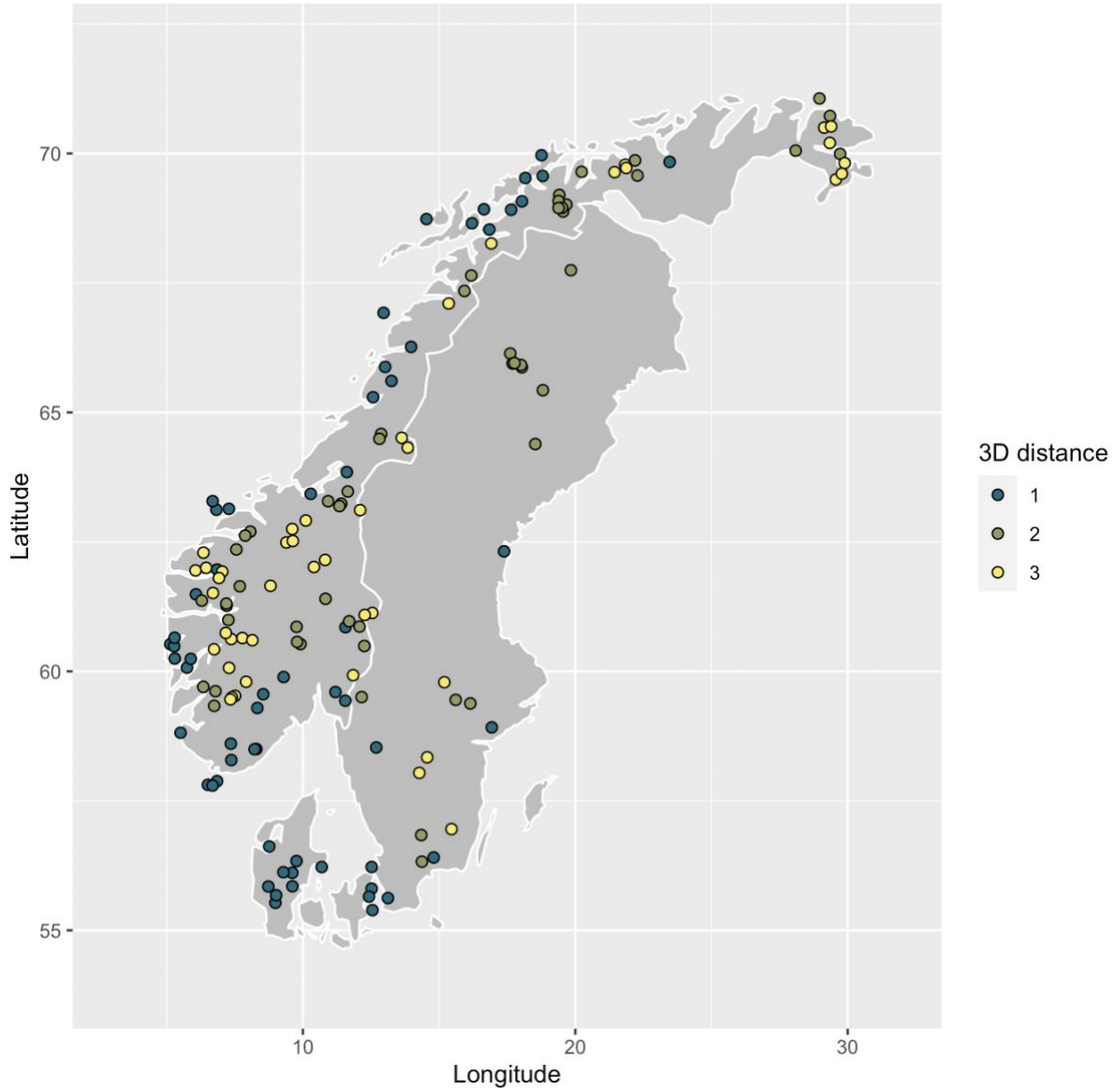
Supplementary Figure 8: PCA plot of all individuals including longitude.

The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to the longitude at their location, where yellow = east and blue = west. Individuals with missing longitude value are coloured black. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.



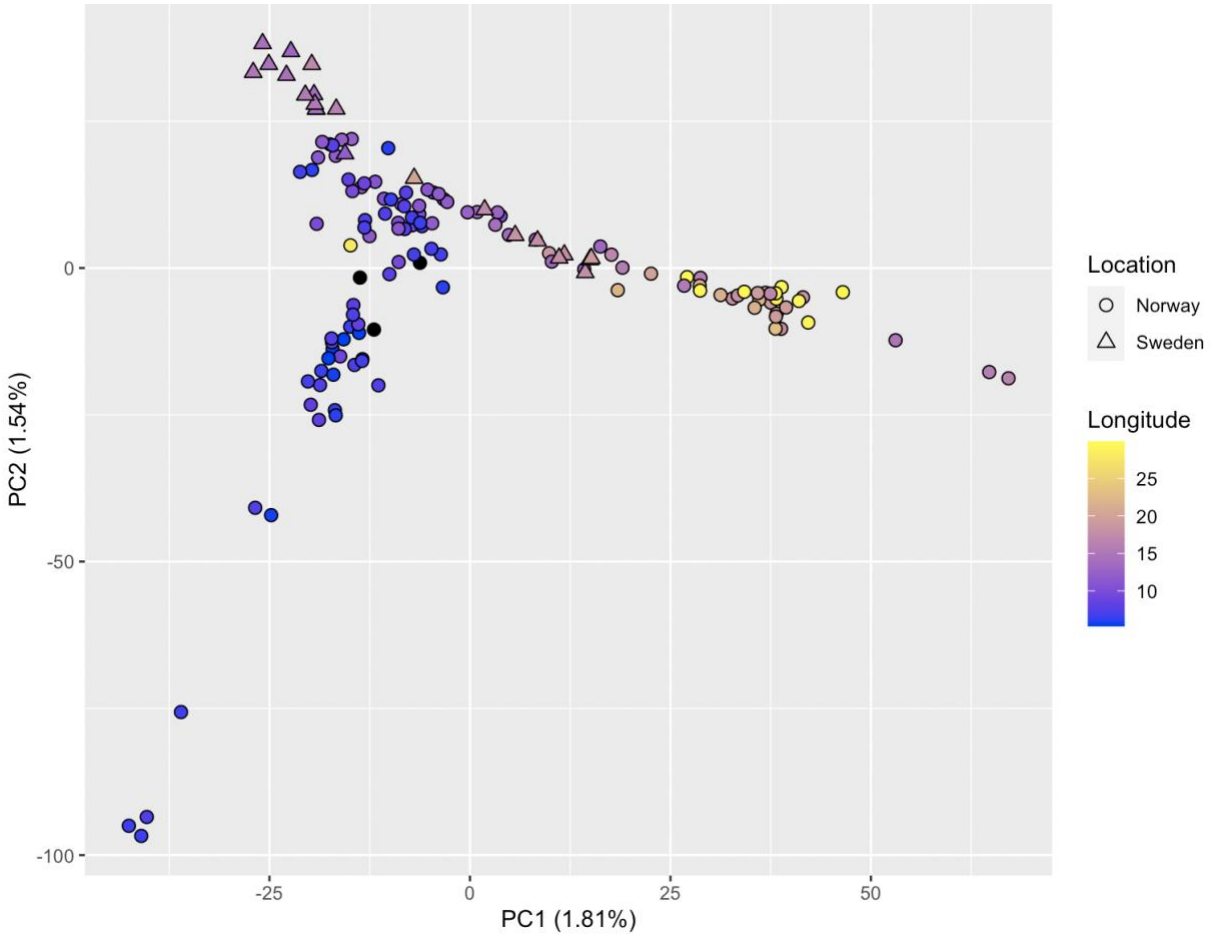
Supplementary Figure 9: PCA plot of all individuals including 3D distance

The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to the 3D distance at their location from the reference point, where longer 3D distance = yellow, and shorter 3D distance = teal. Individual with missing 3D distance value are coloured black. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.



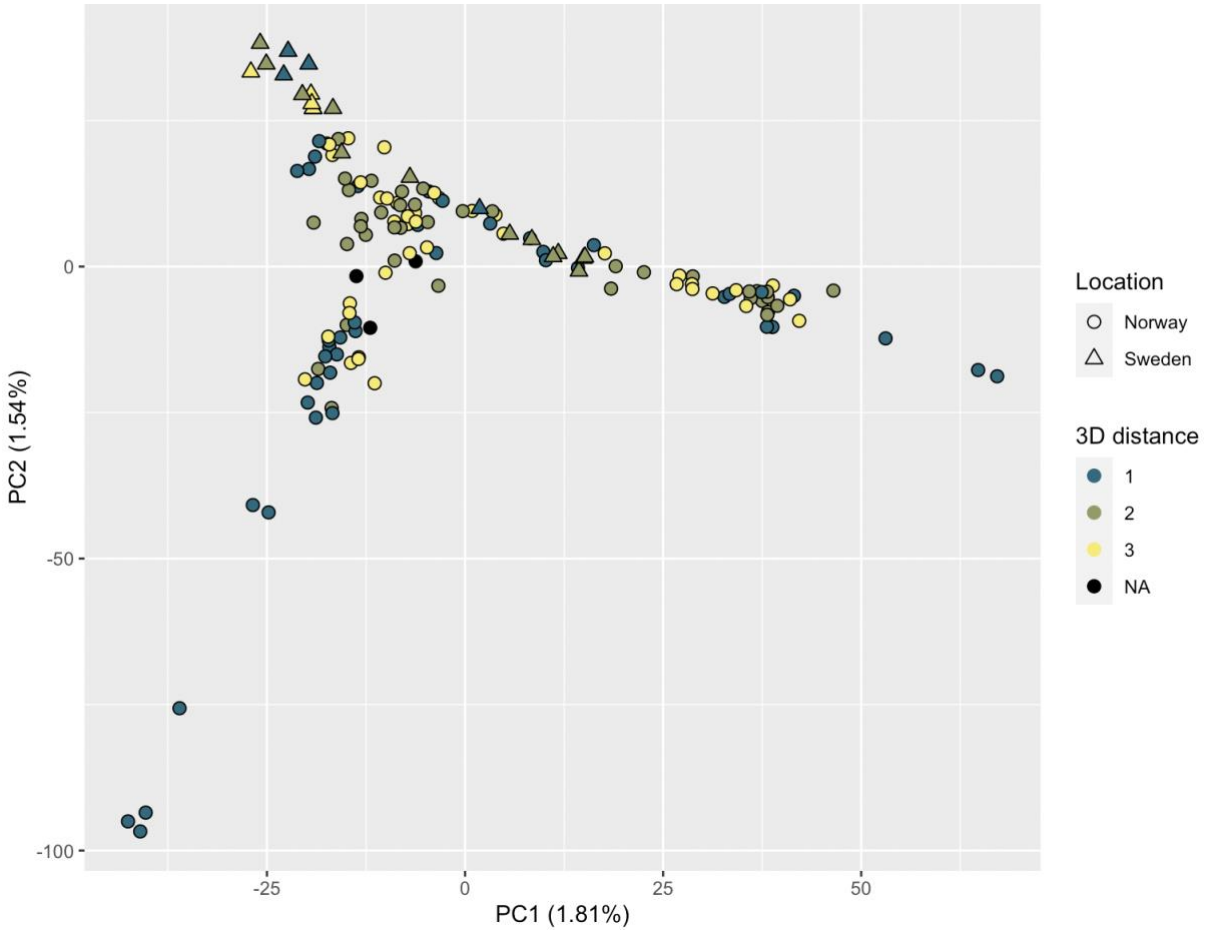
Supplementary Figure 10: Map including 3D distance for all individuals

Map of Scandinavia with the approximate positions of individuals. Individuals are coloured according to the 3D distance at their location from the reference point, where longer 3D distance = yellow, and shorter 3D distance = teal. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.



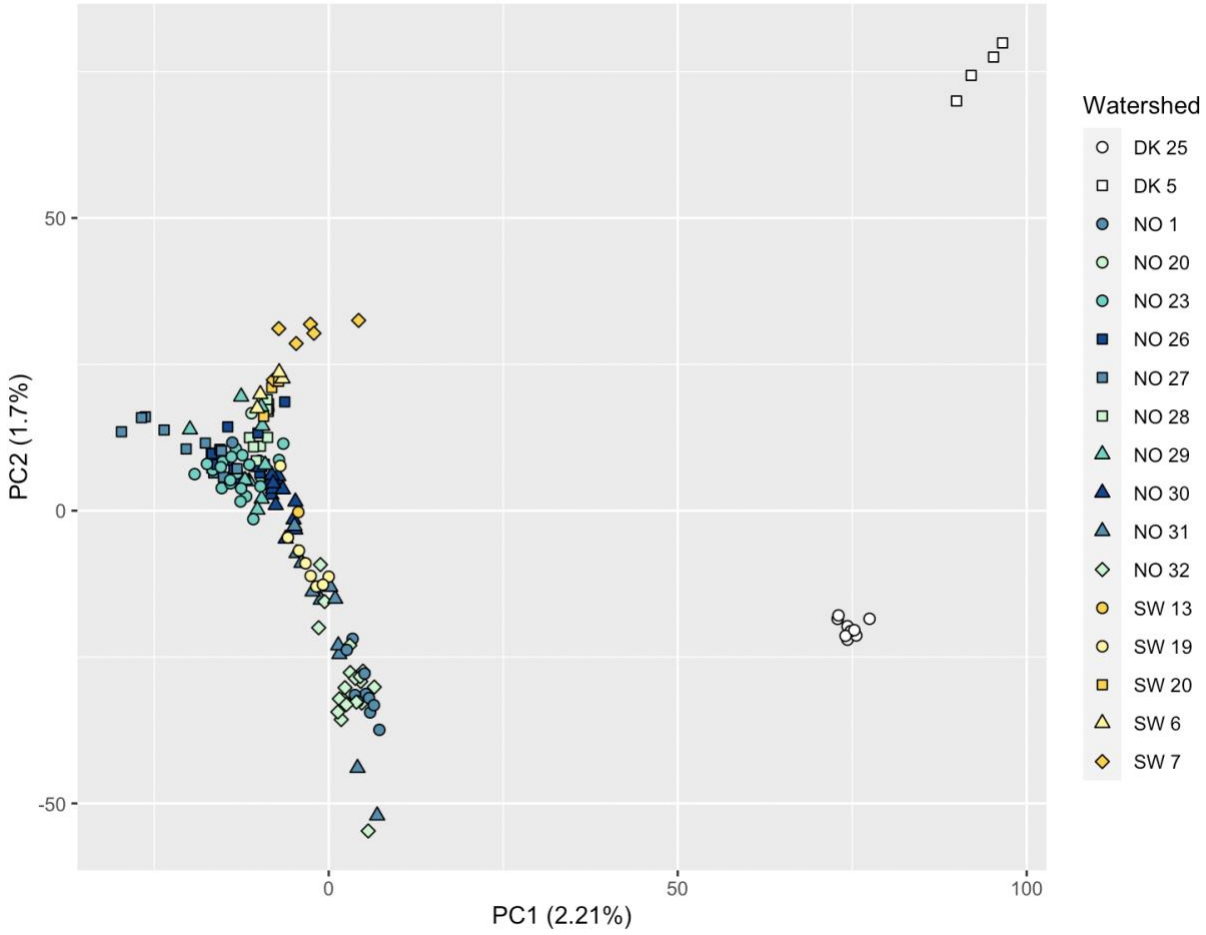
Supplementary Figure 11: PCA plot of individuals in Norway and Sweden including longitude

The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to the longitude at their location, where yellow = east and blue = west. Individuals with missing longitude value are coloured black. Location is indicated by shape: Norwegian individuals are indicated by circles and Swedish individuals are indicated by triangles.



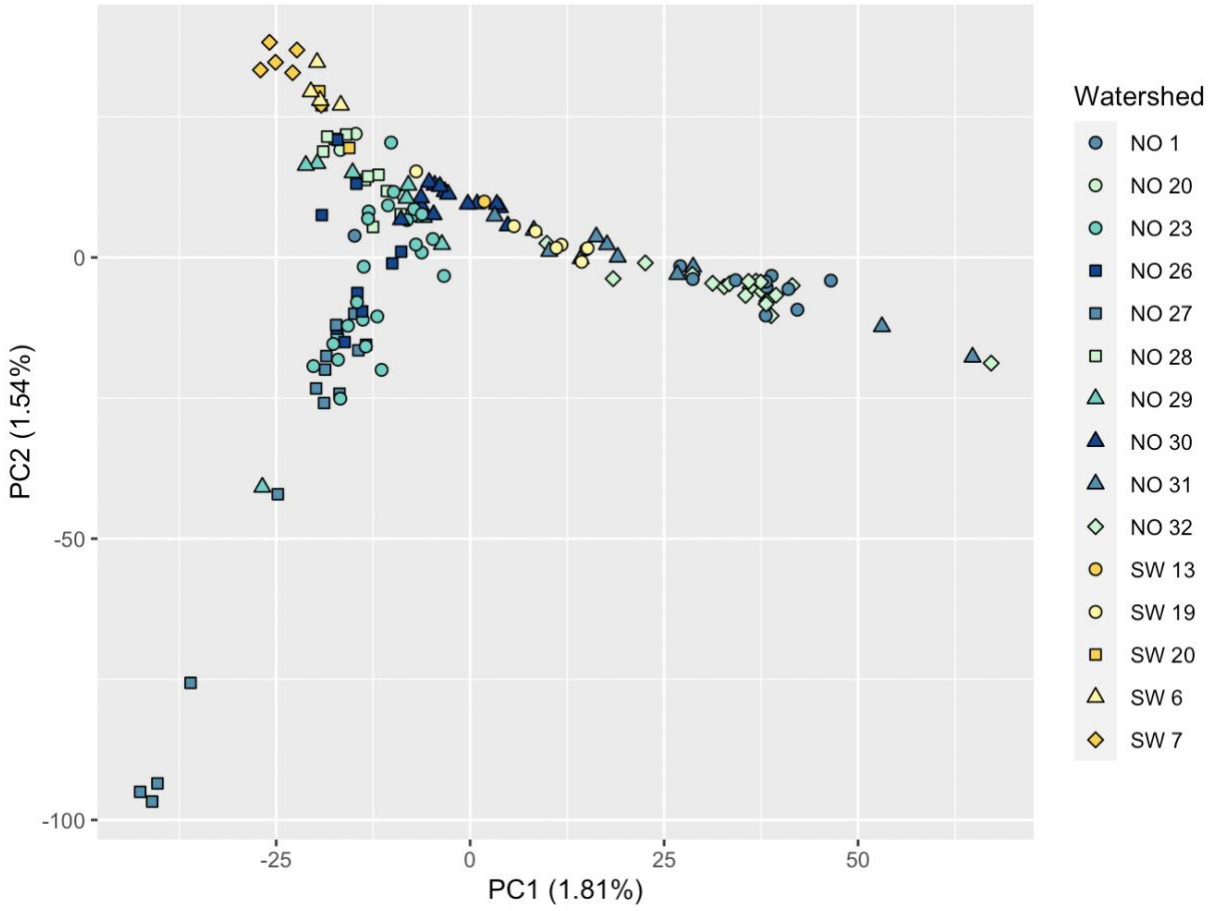
Supplementary Figure 12: PCA plot of individuals in Norway and Sweden including 3D distance

The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to the 3D distance at their location from the reference point, where longer 3D distance = yellow, and shorter 3D distance = teal. Individuals with missing 3D distance value are coloured black. Location is indicated by shape: Norwegian individuals are indicated by circles and Swedish individuals are indicated by triangles.



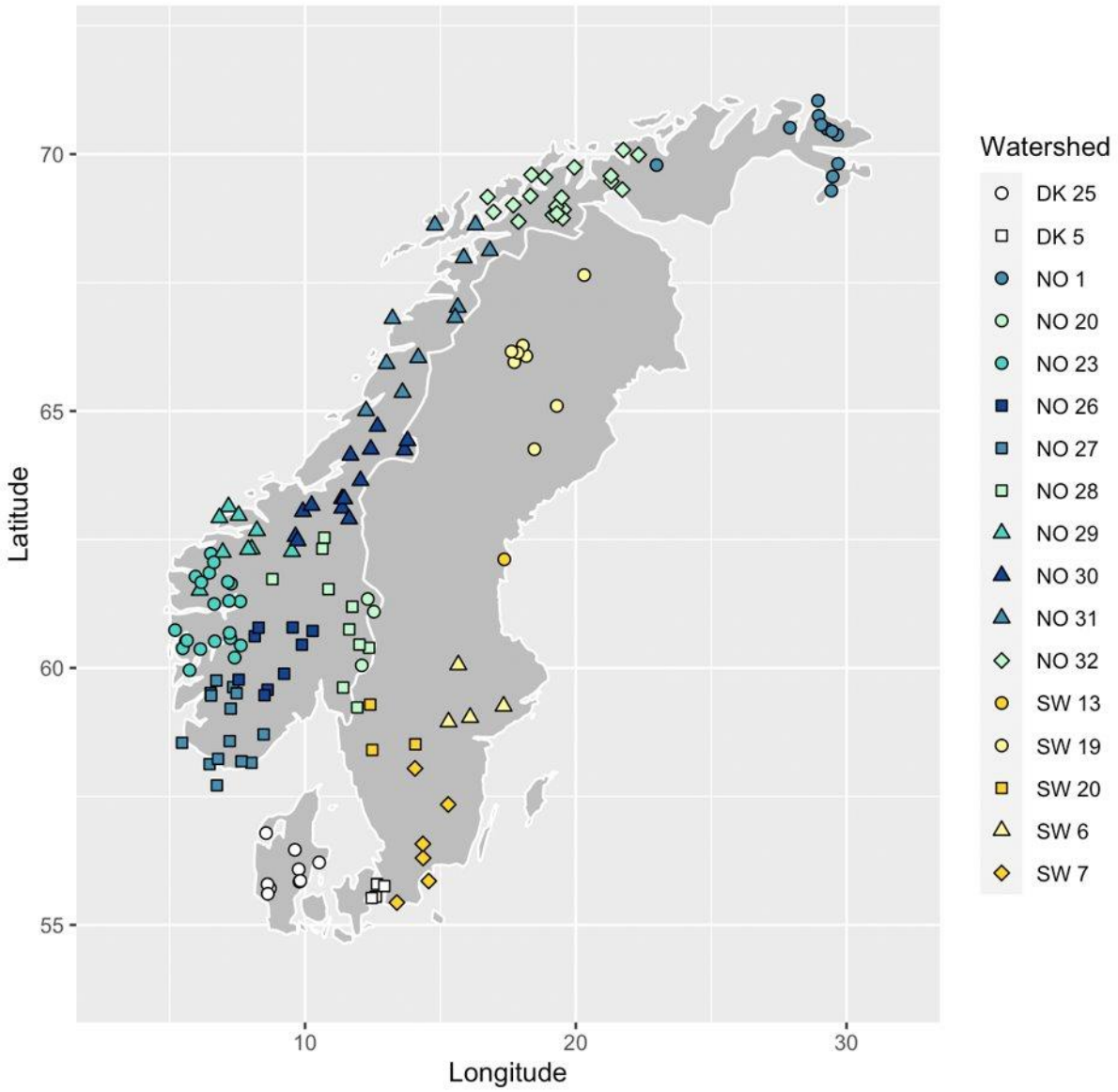
Supplementary Figure 13: PCA plot of all individuals including Watershed ID

The x- and the y-axis show the first and second principal components respectively. Watershed ID is shown as different combinations of colour and shape. Watersheds in Norway are shown in blue and green, watersheds in Sweden are shown in yellow and orange, and watersheds in Denmark are shown in white. Colouration or shapes within these groups does not imply any further meaning and are only for distinction between watersheds.



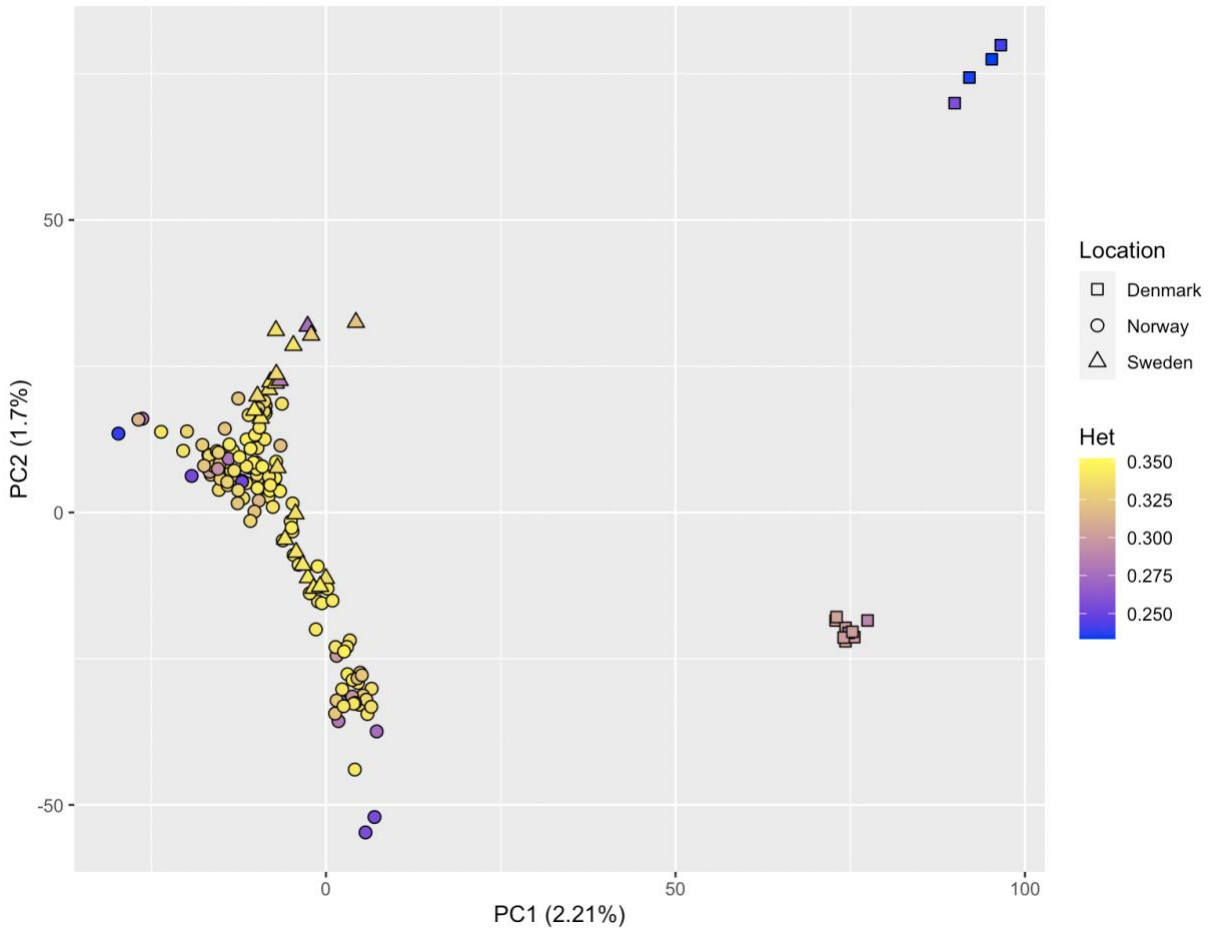
Supplementary Figure 14: PCA plot of individuals in Norway and Sweden including watershed ID

The x- and the y-axis show the first and second principal components respectively. Watershed ID is shown as different combinations of colour and shape. Watersheds in Norway are shown in blue and green, and watersheds in Sweden are shown in yellow and orange. Colouration or shapes within these groups does not imply any further meaning and are only for distinction between watersheds.



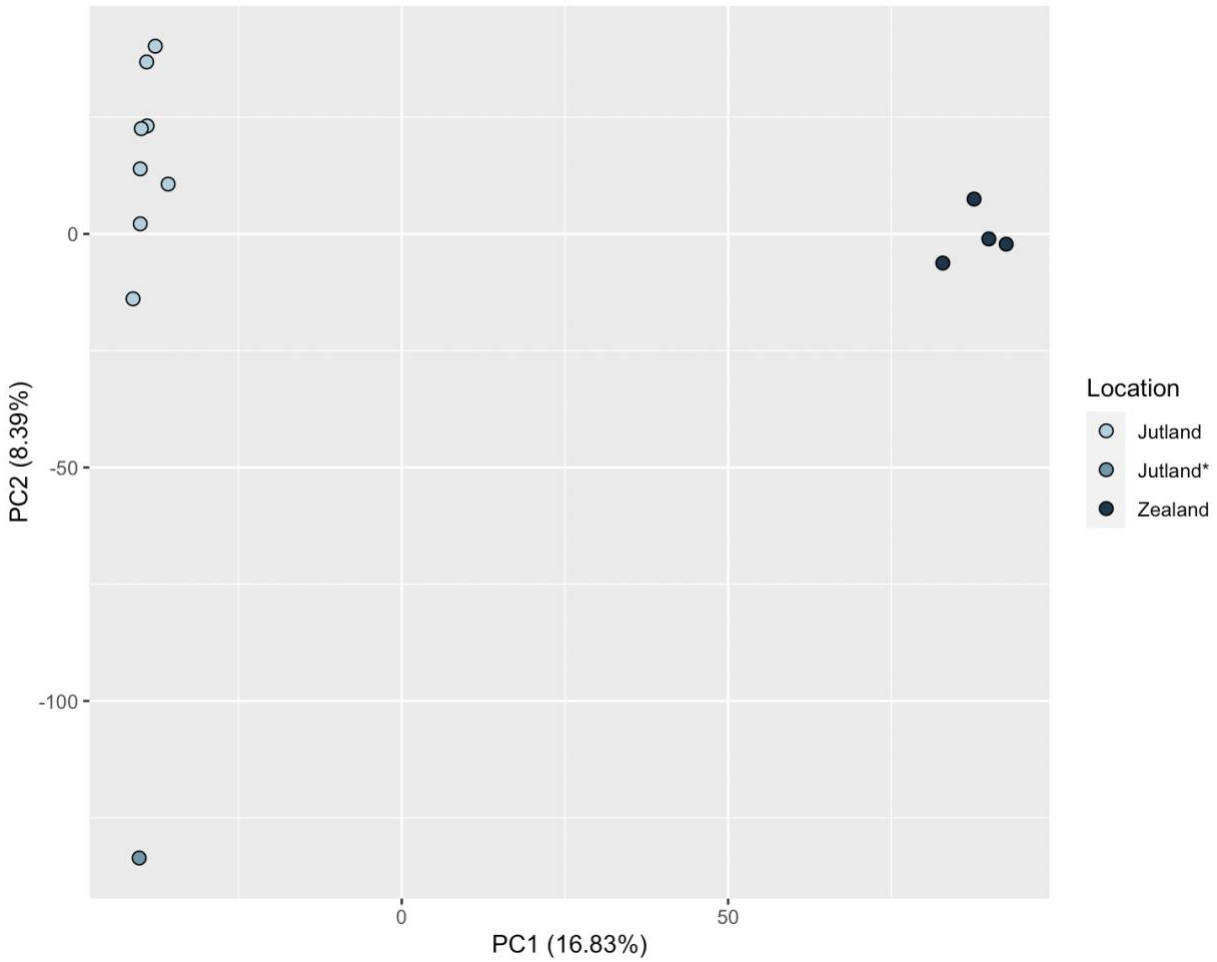
Supplementary Figure 15: Map including Watershed ID for all individuals

Watershed ID is shown as different combinations of colour and shape. Watersheds in Norway are shown in blue and green, watersheds in Sweden are shown in yellow and orange, and watersheds in Denmark are shown in white. Colouration or shapes within these groups does not imply any further meaning and are only for distinction between watersheds. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.



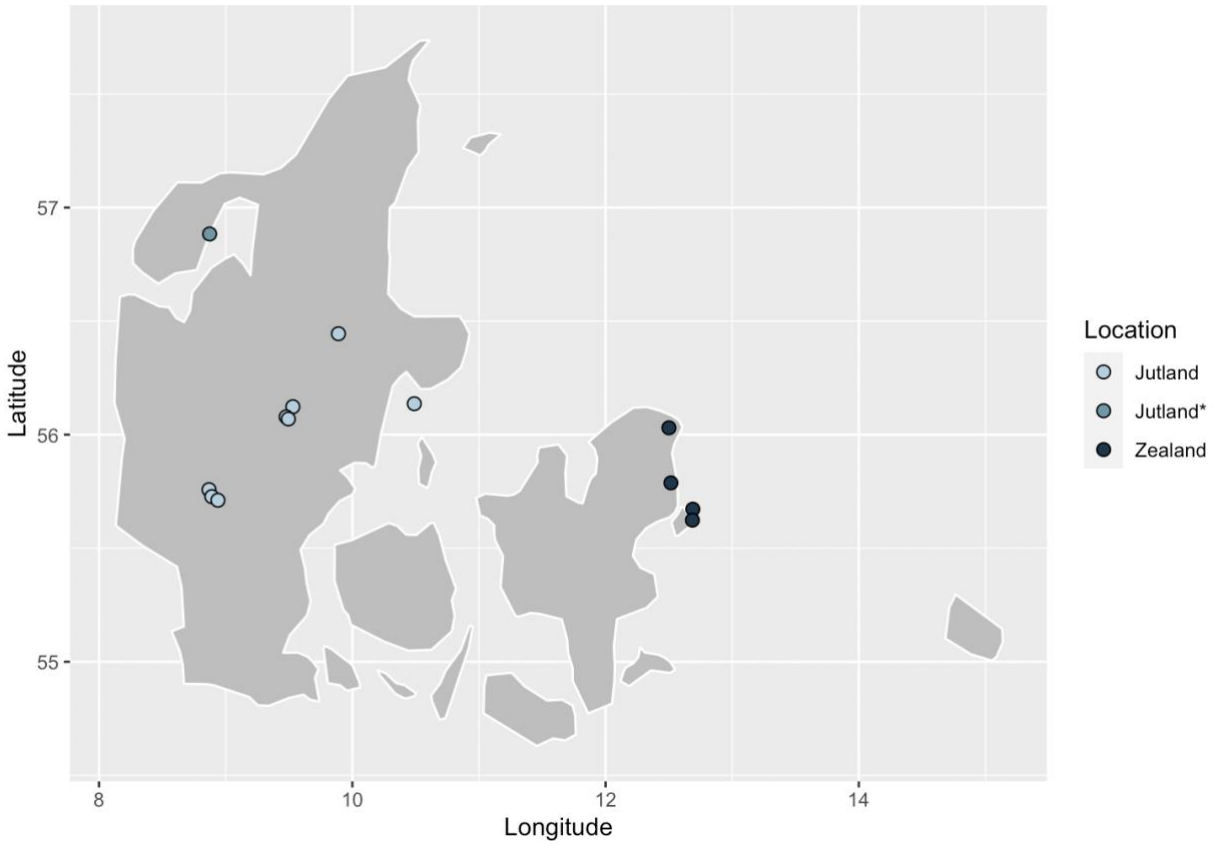
Supplementary Figure 16: PCA plot of all individuals including heterozygosity

The x- and the y-axis show the first and second principal components respectively. Colour corresponds to average heterozygosity across non-missing loci. Higher heterozygosity is shown in yellow, and lower heterozygosity is shown in blue. Location is indicated by shape: Danish individuals are indicated by squares, Norwegian individuals by circles, and Swedish individuals by triangles.



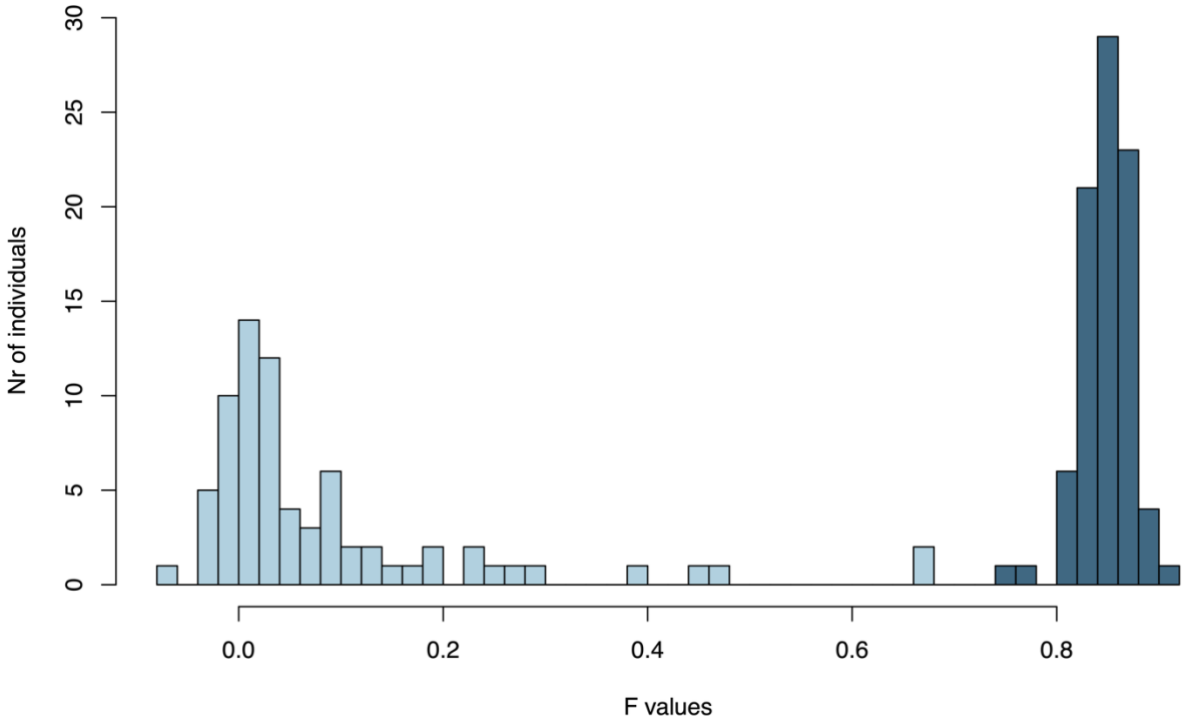
Supplementary Figure 17: PCA plot of individuals in Denmark

The x- and the y-axis show the first and second principal components respectively. Individuals are coloured according to whether they are located on Jutland or Zealand. Jutland* marks the individual in the bottom left corner of the plot.

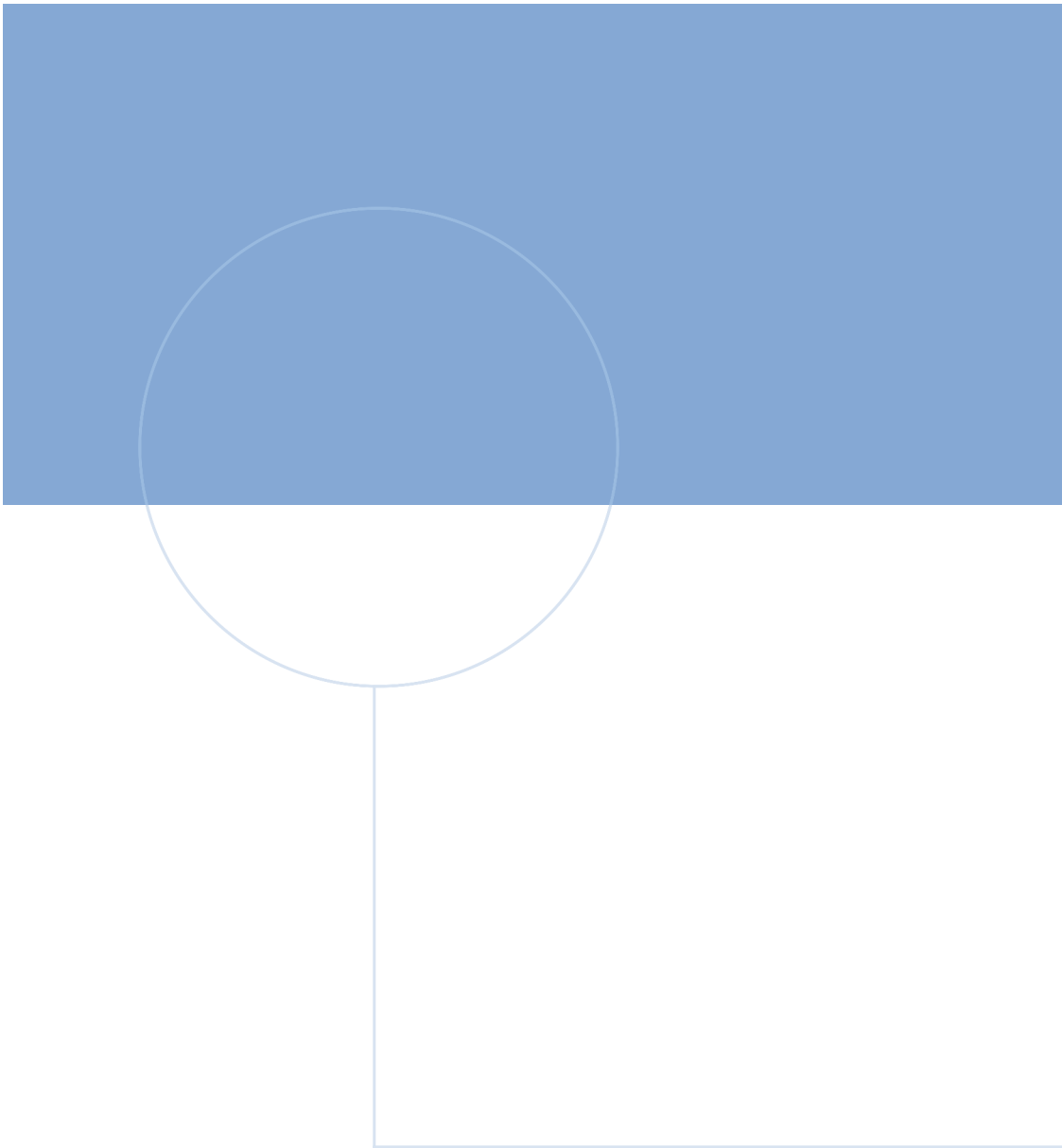


Supplementary Figure 18: Map of Denmark

Colours correspond to Jutland and Zealand. Jutland* marks an individual which, according to the PCA (Supplementary Figure 17), showed larger genetic differentiation from the rest of the individuals on Jutland. The individual positions have been plotted with a jitter-function, and positions of individuals may therefore be shifted somewhat from their sample-location.



Supplementary Figure 19: Distribution of F-values.
The histograms show the distribution of F-values calculated for X-linked SNPs. Genotypic females are shown in light blue and genotypic males in dark blue.



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