Received: 3 March 2017 | Revised: 1 June 2017 | Accepted: 8 June 2017

DOI: 10.1111/mec.14207

ORIGINAL ARTICLE

WILEY MOLECULAR ECOLOGY

Genome architecture enables local adaptation of Atlantic cod despite high connectivity

Julia M. I. Barth[1] | Paul R. Berg[1,2] | Per R. Jonsson[3] | Sara Bonanomi[4,5] | Hanna Corell[3] | Jakob Hemmer-Hansen[4] | Kjetill S. Jakobsen[1] | Kerstin Johannesson[3] | Per Erik Jorde[1] | Halvor Knutsen[1,6,7] | Per-Olav Moksnes[8] | Bastiaan Star[1] | Nils Chr. Stenseth[1,7] | Henrik Svedäng[9] | Sissel Jentoft[1,7] | Carl André[3]

[1]Department of Biosciences, Centre for Ecological and Evolutionary Synthesis (CEES), University of Oslo, Oslo, Norway

[2]Faculty of Medicine, Centre for Molecular Medicine Norway (NCMM), University of Oslo, Oslo, Norway

[3]Department of Marine Sciences – Tjärnö, University of Gothenburg, Strömstad, Sweden

[4]Section for Marine Living Resources, National Institute of Aquatic Resources, Technical University of Denmark, Silkeborg, Denmark

[5]National Research Council (CNR), Fisheries Section, Institute of Marine Sciences (ISMAR), Ancona, Italy

[6]Institute of Marine Research, Flødevigen, His, Norway

[7]Department of Natural Sciences, Centre for Coastal Research, University of Agder, Kristiansand, Norway

[8]Department of Marine Sciences, University of Gothenburg, Gothenburg, Sweden

[9]Swedish Institute for the Marine Environment (SIME), Gothenburg, Sweden

Correspondence
Julia M. I. Barth and Sissel Jentoft, CEES, Department of Biosciences, University of Oslo, Oslo, Norway.
Emails: jmi.barth@gmail.com; sissel.jentoft@ibv.uio.no

Funding information
Centre for Ecological and Evolutionary Synthesis (CEES) at the University of Oslo, Norway; CodS, Interreg, EU, Grant/Award Number: 168975; MarGen Interreg, EU, Grant/Award Number: 175806; Centre for Marine Evolutionary Biology at the University of Gothenburg, Sweden

Abstract

Adaptation to local conditions is a fundamental process in evolution; however, mechanisms maintaining local adaptation despite high gene flow are still poorly understood. Marine ecosystems provide a wide array of diverse habitats that frequently promote ecological adaptation even in species characterized by strong levels of gene flow. As one example, populations of the marine fish Atlantic cod (*Gadus morhua*) are highly connected due to immense dispersal capabilities but nevertheless show local adaptation in several key traits. By combining population genomic analyses based on 12K single nucleotide polymorphisms with larval dispersal patterns inferred using a biophysical ocean model, we show that Atlantic cod individuals residing in sheltered estuarine habitats of Scandinavian fjords mainly belong to offshore oceanic populations with considerable connectivity between these diverse ecosystems. Nevertheless, we also find evidence for discrete fjord populations that are genetically differentiated from offshore populations, indicative of local adaptation, the degree of which appears to be influenced by connectivity. Analyses of the genomic architecture reveal a significant overrepresentation of a large ~5 Mb chromosomal rearrangement in fjord cod, previously proposed to comprise genes critical for the survival at low salinities. This suggests that despite considerable connectivity with offshore populations, local adaptation to fjord environments may be enabled by suppression of recombination in the rearranged region. Our study provides new insights into the potential of local adaptation in high gene flow species within fine geographical scales and highlights the importance of genome architecture in analyses of ecological adaptation.

KEYWORDS
chromosomal inversion, ecological adaptation, *Gadus morhua*, gene flow, population divergence

1 | INTRODUCTION

Local adaptation characterizes populations that experience higher inherited fitness in their native habitat compared to members of other populations transferred to the same environment (Kawecki & Ebert, 2004). The degree of such ecological adaptation depends on the directional selection of advantageous traits and is counteracted by high connectivity and resulting homogenizing gene flow, implicating a limited potential for local adaptation in populations experiencing high gene flow (Dobzhansky, 1937; Mayr, 1942; Wright, 1931). Although environmental adaptation can also involve gene expression-induced plastic responses such as morphological, physiological or behavioural changes, these occur without genotypic changes (Reusch, 2014; Via et al., 1995).

Most marine fish populations have traditionally been regarded as large panmictic entities with high connectivity due to the apparent lack of geographical barriers, high dispersal capabilities and slow genetic drift as a result of large effective population sizes (Allendorf, Hohenlohe, & Luikart, 2010; DeWoody & Avise, 2000; Waples & Gaggiotti, 2006). However, this assumption is challenged by an increasing number of genetic studies reporting high levels of local adaptation in marine fish populations despite substantial gene flow (Clarke, Munch, Thorrold, & Conover, 2010; Limborg et al., 2012; Milano et al., 2014; Nielsen et al., 2009; Therkildsen et al., 2013). Simulation studies have demonstrated that local adaptation can arise in these situations through selection on tightly linked divergent alleles rather than on many single loci (Yeaman & Whitlock, 2011). In line with these expectations, the occurrence of linked alleles (e.g., in the form of chromosomal rearrangements) in locally adapted populations has been reported in studies addressing the genome architecture of fish species such as stickleback (Jones et al., 2012; Roesti, Kueng, Moser, & Berner, 2015), Atlantic herring (Lamichhaney et al., 2017; Martinez-Barrio et al., 2016) and Atlantic cod (Barney, Munkholm, Walt, & Palumbi, 2017; Berg et al., 2015, 2016; Bradbury et al., 2013, 2014; Hemmer-Hansen et al., 2013; Kirubakaran et al., 2016; Sodeland et al., 2016). Chromosomal rearrangements that physically combine genes residing within "supergene clusters" and promote adaptation in connected populations are well known in plants (Lowry & Willis, 2010), and insects (Cheng et al., 2012; Joron et al., 2011) and are widely discussed to play a role in speciation and evolution (Hoffmann & Rieseberg, 2008; Schwander, Libbrecht, & Keller, 2014). However, the relative importance of this mechanism in highly connected marine populations on small geographical scales remains poorly understood.

Atlantic cod (*Gadus morhua* Linnaeus, 1758) is a benthopelagic, high-fecundity, predatory fish of great commercial and ecological value occurring in a variety of habitats in the North Atlantic and hence constitutes an ideal model for the investigation of local adaptation. Molecular studies inferring the potential for local adaptation in Atlantic cod have a long history, which began with the discovery of adaptive allelic variation in the oxygen-binding protein haemoglobin (Sick, 1961) and the observation of a latitudinal gradient in the distribution of its isoforms (Sick, 1965; for recent reviews see Andersen (2012) and Ross, Behrens, Brander, Methling, and Mork (2013)). Since then, extensive research has contributed to the description of several genetically, phenotypically and behaviourally distinct populations occurring in a wide range of different ecosystems (Lilly et al., 2008). One of the best-investigated examples for apparent local adaptation despite high connectivity is the co-occurrence of two ecotypes of Atlantic cod, the migratory Northeast Arctic cod (NEAC) and the stationary Norwegian coastal cod (NCC), at the same spawning areas along the northern Norwegian coast (Neuenfeldt et al., 2013). While genetic differences between NEAC and NCC were already described in the 1960s (Moller, 1966), the mechanism maintaining differentiation despite ongoing gene flow is still a controversial subject (Hemmer-Hansen et al., 2013; Karlsen et al., 2013). The releases of two successive Atlantic cod genome assemblies (Star et al., 2011; Tørresen et al., 2017) facilitated the investigation of such mechanisms, revealing the presence of large chromosomal rearrangements likely permitting differentiation of these ecotypes despite ongoing gene flow (Berg et al., 2016; Kirubakaran et al., 2016).

On a much smaller spatial scale within the Skagerrak and Kattegat, two confined seas connecting the brackish Baltic Sea with the saline North Sea (Figure 1), evidence has recently accumulated for

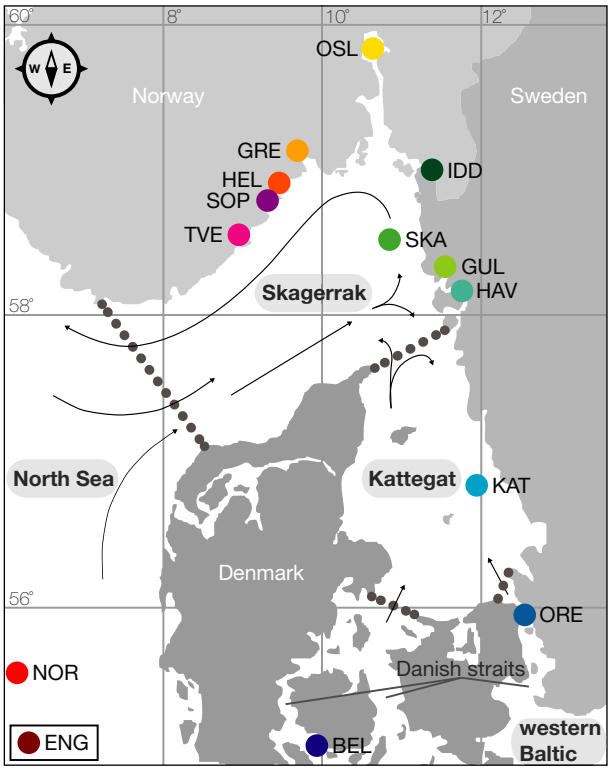

FIGURE 1 Sampling sites of Atlantic cod (coloured points). Dotted lines indicate boundaries between seas (North Sea, Skagerrak, Kattegat and western Baltic Sea) and arrows delineate main water currents. ENG, English Channel; NOR, North Sea; TVE, Tvedestrand; SOP, Soppekilen; HEL, Hellefjord; GRE, Grenland; OSL, Oslofjord; IDD, Iddefjord; SKA, Skagerrak; GUL, Gullmarsfjord; HAV, Havstensfjord; KAT, Kattegat; ORE, Öresund; BEL, Belt Sea

the presence of yet another pair of coexisting Atlantic cod ecotypes (André et al., 2016; Rogers, Olsen, Knutsen, & Stenseth, 2014; Sodeland et al., 2016). These coexisting fish are characterized by distinct lifestyles, with mobile oceanic (offshore) individuals foraging along the coast but possibly returning to North Sea or offshore Skagerrak spawning sites, and sedentary coastal individuals that remain close to the coast and local spawning sites at all times (Espeland et al., 2008; Knutsen et al., 2007; Neuenfeldt et al., 2013; Rogers et al., 2014). In line with this observation, differentiated Atlantic cod has been described between estuarine western Skagerrak fjords and offshore areas, as well as between individual fjords (Jorde, Knutsen, Espeland, & Stenseth, 2007; Knutsen, Jorde, André, & Stenseth, 2003; Knutsen et al., 2011; Olsen et al., 2004). In these cases, the maintenance of differentiation has been associated with seascapes, coastal topography and hydrographic features such as salinity gradients (Ciannelli et al., 2010; Howe et al., 2010; Knutsen et al., 2011; Rogers et al., 2014). Limited migration of coastal cod (Espeland et al., 2007, 2008), spawning site fidelity (Espeland et al., 2007; Skjæraasen, Meager, Karlsen, Hutchings, & Fernö, 2011) and pronounced natal homing behaviour (André et al., 2016; Bonanomi et al., 2016; Svedäng, Righton, & Jonsson, 2007) could further aid differentiation of coastal and oceanic ecotypes by reducing the potential for gene flow. Interestingly, allelic frequency shifts of large chromosomal rearrangements have recently been described between western Skagerrak cod residing in coastal vs. oceanic environments (Sodeland et al., 2016). In contrast, studies have so far failed to delineate genetic structuring of coastal and locally adapted populations within the fine geographical scale along the eastern Skagerrak-Kattegat coast and fjords (André et al., 2016; Svedäng, André, Jonsson, Elfman, & Limburg, 2010), although spawning site fidelity was supported by otolith chemistry (Svedäng et al., 2010).

Whether the hitherto observed sedentary coastal Atlantic cod correspond to locally adapted fjord populations and whether similarly differentiated ecotypes are also present at the eastern Skagerrak coast remain to be investigated. It is also unclear whether the oceanic genotype constitutes of North Sea cod, and whether connectivity and gene flow between these groups exist — and if, whether the exceptional genomic architecture of Atlantic cod contributes to the potential of local adaptation on such fine geographical scales. Answering these questions to improve our knowledge about the mechanism by which local adaptation can be maintained despite high connectivity and gene flow is becoming increasingly relevant in a globally changing world (Bernatchez, 2016; Pinsky & Palumbi, 2014; Savolainen, Lascoux, & Merilä, 2013).

Using a genomewide 12K single nucleotide polymorphism (SNP) array in combination with a comprehensive sampling scheme including several fjords as well as adjacent populations, complemented with biophysical modelling to predict the potential for gene flow among areas, we here address the following research questions: 1.) Can we detect the presence of differentiated cod ecotypes on small spatial scales using genomewide data, and 2.) does the genomic architecture of Atlantic cod contribute to the potential for local adaptation?

2 | MATERIALS AND METHODS

2.1 | Sample collection

Samples of 350 Atlantic cod were obtained from 10 different locations in the Skagerrak-Kattegat area. For comparison, 177 specimens were further sampled from adjacent, but well-differentiated reference locations: English Channel, North Sea and Danish straits (western Baltic) (Figure 1, for details see Table S1). Adult fish were all collected during the spawning period from January to April (except ~60% of Grenland fjord individuals collected in November) by trawling or gill net, and care was taken to choose mature fish that were at or close to spawning. Juvenile 0-group cod were collected either in June or September by beach seine. Muscle tissue or fin clips were stored in ethanol. All cod samples used were collected in compliance with EU Directive 2010/63/EU and the national legislations in Sweden, Denmark, and Norway.

2.2 | Genotyping and filtering

DNA was extracted from muscle tissue using standard DNA extraction kits and normalized to 100 ng/μl as described elsewhere (Berg et al., 2015, 2016). All samples were individually genotyped for 10,913 SNPs using a custom Illumina Infinium II 12K SNP array following the manufacturer's instructions (Illumina, San Diego, CA, USA). The custom chip was designed based on eight individuals representing the global variety of the species, and the Atlantic cod genome (Star et al., 2011). Quality control was performed using the genotyping module in GENOMESTUDIO v2011.1 (Illumina Inc.) and the software PLINK v1.07 (Purcell et al., 2007) leading to a high-quality SNP set of 7,783 SNPs (for details see Appendix S1 and Table S2). Variants were further filtered based on linkage to conform with the expectations of models employed in our genetic analyses: the correlation of allele frequencies (r^2) was calculated based on genotypic allele counts and 1,125 SNPs with an $r^2 > 0.1$ were excluded, resulting in a final data set of 6,658 unlinked SNPs.

A second data set including SNPs with detected linkage was generated to investigate the importance of large chromosomal rearrangements containing tightly linked SNPs that may play important roles in the divergence and adaptation of Atlantic cod (Bradbury et al., 2013; Hemmer-Hansen et al., 2013; Bradbury et al., 2014; Berg et al., 2015, 2016; Sodeland et al., 2016; Kirubakaran et al., 2016; Barney et al., 2017; see section 2.5 below). All format conversions were either accomplished with in-house scripts, or using the software PGDSPIDER v2.0.8.0 (Lischer & Excoffier, 2012).

2.3 | Genetic differentiation

The population structure was investigated to delineate genetic differentiation and admixture of fjord samples and diverged populations, as well as to test for an isolation-by-distance (IBD) pattern as described earlier in the western North Atlantic cod (Beacham, Brattey, Miller, Le, & Withler, 2002; Pogson, Taggart, Mesa, & Boutilier,

2001). Individual ancestry and the number of genetic clusters (*K*) were assessed using a hierarchical framework in STRUCTURE v2.3.2 (Pritchard, Stephens, & Donnelly, 2000) under the admixture model with correlated allele frequencies for closely related populations or highly migratory species (Falush, Stephens, & Pritchard, 2003). Five replicates of 100,000 (Monte Carlo Markov chain (MCMC) iterations (discarding the first 10,000 iterations as burn-in) were performed per model, each testing for $K = 1$ to $K = 5$. Convergence was confirmed by consistent results in all five replicates (see Table S3). In addition, principal component analyses were performed to display the largest variances in the genotype data (PCA, Appendix S2, Table S4).

In an assignment approach to distinguish between mechanical mixture and admixture of individuals (Porras-Hurtado et al., 2013), STRUCTURE analyses were conducted with the USEPOPINFO model, using the North Sea and Kattegat samples as representatives of two potential source populations. Enabling of PFROMPOPFLAGONLY ensured that allele frequency estimates depend only on the reference samples, while MIGRPRIOR was set to 0.05 to allow some misclassification of individuals. Per location *q*-values (estimated ancestry) were log normalized (log(data/(1-data)) and analysed for modality using Hartigans' dip statistic (Hartigan & Hartigan, 1985) implemented in the package DIPTEST v0.75-6 (Mächler, 2014) for R v3.1.0 (R Core Team, R Foundation for Statistical Computing 2016). Test results were corrected for multiple testing by applying a false discovery rate (FDR) of <0.05 using the R package QVALUE v1.43.0 (Storey, Taylor, & Siegmund, 2004). The ancestry of fjord samples was quantified by their hybrid indices (*H*) employing Bayesian genomic cline analysis as implemented in BGC v1.03 (Gompert & Buerkle, 2012). Based on the probability that an individual has inherited a genetic marker from one of the two source populations North Sea and Kattegat, *H* was estimated using two cline parameters that describe the bias (α) and rate (β) of locus-specific introgression into an admixed genomic background (Gompert & Buerkle, 2012). As the full set of 6,658 SNPs was too large to allow convergence, the 50 SNPs with the highest fixation index (F_{ST}) values between the source populations were selected as ancestry informative markers using BAYESCAN v2.1 (Foll & Gaggiotti, 2008) (Appendix S2, Table S5). Ten replicates, each using 100,000 MCMC iterations (discarding the first 20,000 iterations as burn-in), were performed. Convergence of the MCMC chain was assessed using TRACER v1.6 (Rambaut, Suchard, Xie, & Drummond, 2014) and by comparison of the replicates, which produced qualitatively similar results. The replicate with the best fit (highest mean log-likelihood) was selected to present the results.

Pairwise F_{ST} values (Weir & Cockerham, 1984) were calculated using ARLEQUIN v3.5 and ARLECOREMAC_64BIT v3.5.2.2 (Excoffier & Lischer, 2010), and their significance was assessed using 10,000 permutation steps. *p*-values were adjusted for multiple testing by applying the FDR approach for nonindependent tests by Benjamini and Yekutieli (2001). Pairwise F_{ST} values were plotted by means of classic multidimensional scaling (MDS) using the "cmdscale" method implemented in the R package STATS (R Core Team, R Foundation for Statistical Computing 2016) after negative F_{ST} values were set to 0, and a minimal constant (10^{-5}) was added to prevent negative eigenvalues. F_{ST} 95% confidence intervals (200 bootstrap replicates) as well as pairwise genetic and geographical distance matrices for tests of IBD were calculated using the R packages DIVERSITY v1.9.73 (Keenan, McGinnity, Cross, Crozier, & Prodöhl, 2013) and FOSSIL v0.3.7 (Vavrek, 2011). Least-cost path distances were obtained using the R package MARMAP v0.9.2 (Pante & Simon-Bouhet, 2013) with bathymetric data from the ETOPO1 1 Arc-Minute Global Relief Model (Amante & Eakins, 2009), and Mantel tests of IBD were performed using the R package VEGAN v2.3.0 (Dixon, 2003).

2.4 | Biophysical connectivity modelling

Physical transport and connectivity of Atlantic cod eggs and larvae was quantified using a biophysical model to explore geneflow potential and connectivity by predicting the most important sources of larvae settling along the Skagerrak coast and the Kattegat. A full description of the biophysical model is given in Jonsson, Corell, André, Svedäng, and Moksnes (2016). Briefly, the dispersal of eggs and larvae was modelled with a Lagrangian particle-tracking routine in off-line mode driven by flow fields from an ocean circulation model (BaltiX; Hordoir, Dieterich, Basu, Dietze, & Meier, 2013). The oceanographic model covers the Baltic Sea, the Kattegat, the Skagerrak and most of the North Sea with a horizontal resolution of 2 nautical miles (3.7 km) and 84 levels in the vertical, ranging from 3 m at the surface to 23 m in the deepest parts. The model has a free surface, and the atmospheric forcing is a dynamic downscaling of the ERA40 data set (Uppala et al., 2006). Freshwater run-off is forced with climatological data from a composite of databases for the Baltic Sea and the North Sea (Meier, 2007; O'Dea et al., 2014). A previous validation of the BaltiX model showed that it is able to correctly represent the sea-surface height, both tidally induced and wind driven (Hordoir et al., 2013). The velocity, temperature and salinity were updated for all grid boxes in the model domain every three hours, and the trajectory calculations were done with a 15-min time step. To simulate dispersion of cod larvae, we used an individual-based drift model with a wide range of combinations of spawning time, egg and larval drift depth, as well as pelagic larval duration time (for a detailed description see Jonsson et al., 2016). Briefly, eggs were simulated to drift at depths between 5 and 15 m and hatched after 20 days. Subsequently, the larvae drifted for another 40 or 70 days at depths between 5 and 30 m. Drifting eggs were started on the 15th of January, February, March and April in a number of spawning areas in the North Sea, Skagerrak, Kattegat and the Danish straits (Fig. S1). No mortality was included as little information about temporal and spatial differences in mortality rates is available. Larval drift simulations were repeated for 6 years (1995, 1996, 1998, 2000, 2001 and 2002), which represent negative, neutral and positive periods of the North Atlantic oscillation winter index (National Center for Atmospheric Research, 2015), as winter NAO is known to correlate well with variations in the circulation pattern (Marshall et al., 2001). To include as much variation as possible, results were based on the average of all spawning times, drift depths, drift durations and years with a total of ~100M individual drift trajectories.

Because of model domain limitations, the North Sea spawning areas did not include the Viking Bank east of Shetland. Connectivity between the spawning areas and the larval settlement areas (western and eastern Skagerrak, and Kattegat) was calculated as the proportion of eggs spawned in area *i* and settling as larvae in area *j*. Furthermore, dispersal patterns from the spawning areas to western Skagerrak fjords were also assessed. As the spatial resolution of the biophysical model is not sufficient to represent the full geomorphology of the inner fjords, only the coastal waters close to the fjord mouths were considered (Soppekilen was not included as the connectivity model cannot resolve this site from the closely situated Hellefjord). The measure of connectivity of the biophysical model only predicts the probability per egg to be transported from *i* to *j*. To obtain a relative estimate of the abundance of eggs reaching a settlement area, we also scaled the inferred connectivity with recent estimates of the spawning stock biomass (SSB, for calculations see Jonsson et al., 2016).

2.5 | Chromosomal rearrangements

The genomic architecture was examined to study the impact of large chromosomal rearrangements on population divergence and adaptation. The physical locations of SNPs within chromosomes (here: linkage groups; LGs) were inferred by mapping the flanking regions of all SNPs to the gadMor2 genome assembly (Tørresen et al., 2017) using BLAST v2.2.26+ (Camacho et al., 2009). Querying 10,913 flanking region pairs resulted in 10,804 blast hits, which were subsequently filtered according to the following quality thresholds: identity between query and hit >90%, E-value $<1.0 \times 10^{-42}$, and minimum length >100 bp. SNPs not meeting these criteria ($n = 182$) and SNPs on unplaced contigs ($n = 526$) were removed. Of the remaining SNPs, the exact positions were retrieved only for high-quality SNPs included in this study (7,783, including linked SNPs, see above). Of these, 506 SNPs could not be mapped, leaving 7,277 SNPs with known position for analysis of the chromosomal rearrangements. The R package INVERSION (Cáceres, Sindi, Raphael, Cáceres, & González, 2012) was used to approximate the start and end points of rearranged regions. A block size of 3 SNPs was used to flank each side of the breakpoint, the minimum minor allele frequency was set to 0.1, and rearrangements were scanned with fixed window sizes from 1 to 13 Mbp. All predictions with Bayesian information criterion (BIC) >0 were scored (Table S6), and breakpoints were defined as the position of the SNP closest to the mean value between breakpoint maxima. The allelic state of each individual (homozygote collinear, heterozygote or variant rearranged homozygote, as defined by nucleotide diversity in Berg et al. (2016)) was inferred using PCA as implemented in the R package ADEGENET v1.4-1 (Jombart, 2008), similar to the approach described by Ma and Amos (2012). Bootstrapping (Efron, 1979; sample size 1,000,000) of individual genotypes was used to calculate the probability of an over- or underrepresentation of the presumably rearranged allele within sampling sites and within western (Tvedestrand, Soppekilen, Hellefjord, Grenland) and eastern (Iddefjord, Gullmarsfjord, Havstensfjord) fjords under the null hypothesis that the frequency of rearranged alleles within a population corresponds to its overall frequency across all populations. Sequential Bonferroni correction was applied to correct for multiple tests (Rice, 1988).

3 | RESULTS

3.1 | Genetic differentiation

The software STRUCTURE was used to investigate population differentiation and the most likely number of clusters (*K*) by applying the admixture model in a hierarchical framework. All samples were tested for their cluster membership in up to five clusters, based on which $K = 2$ (Figure 2a) and $K = 3$ (Figure 2b) were supported as the most likely numbers of populations present (for likelihood values see Table S3). According to Evanno's ΔK statistic, an ad hoc quantity based on the rate of change of the likelihood function (Evanno, Regnaut, & Goudet, 2005), $K = 2$ received most support. In a hierarchical STRUCTURE analysis, the most differentiated clusters are excluded to allow for a more precise analysis of the remaining samples (Vähä, Erkinaro, Niemelä, & Primmer, 2007). Assuming $K = 2$, the two most differentiated clusters were composed of the English Channel (ENG), North Sea (NOR), Oslofjord (OSL) and Skagerrak (SKA) (henceforth summarized as North Sea-like group), and the Kattegat (KAT), Öresund (ORE) and Belt Sea (BEL) (from now on summarized as western Baltic-like group) (Figure 2a). Accordingly, these samples were analysed in separate runs, but no hidden substructure was detected (Fig. S2, for likelihood values see Table S3). Likewise, separate analyses of the remaining fjord sampling sites (Tvedestrand (TVE), Soppekilen (SOP), Hellefjord (HEL), Grenland (GRE), Iddefjord (IDD), Gullmarsfjord (GUL), Havstensfjord (HAV)) revealed no further substructure and resulted in very similar likelihoods for $K = 2$ and $K = 3$ (Fig. S2 and Table S3). In contrast to the well-differentiated groups, the fjord samples (except OSL, see above) consisted of either North Sea-like, or western Baltic-like individuals when $K = 2$ (Figure 2a), or a distinct third genetic cluster when $K = 3$, which was mainly present in western Skagerrak fjords, and of these predominately found in the samples Hellefjord (HEL) and Grenland (GRE) (Figure 2b). This pattern is concordant with the results of the principal component analysis (PCA), where the largest variance was found between North Sea-like and western Baltic-like groups, and the second-largest variance separated these groups from western Skagerrak fjord samples (Appendix S2 and Fig. S3). Differentiation between North Sea and Baltic-like groups was also evident based on neutral markers; however, this was not the case for the third western fjord cluster (Fig. S3). In contrast, using only diversifying SNPs, only randomly selected SNPs on larger scaffolds, or excluding the most differentiated groups had no major influence on the three-cluster pattern (Appendix S2 and Fig. S3).

All eastern and many western Skagerrak fjord individuals were found either in the North Sea-like or the western Baltic-like group, indicating a mechanical mix of individuals from different sources. To differentiate between mechanical mixture and admixture, we

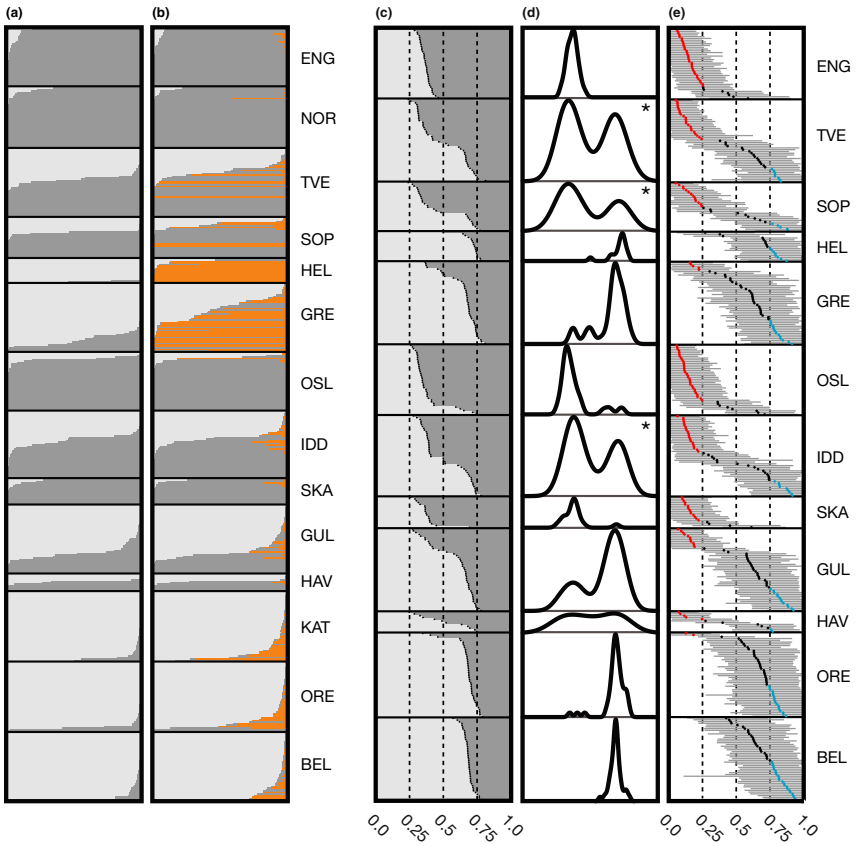

FIGURE 2 Population differentiation, admixture and ancestry analyses. (a,b) Hierarchical STRUCTURE analysis. Individual population assignment is shown by coloured and grey horizontal bars (*q*-values), black bars separate sampling locations (for sampling site abbreviation see legend Figure 1). Individuals are ordered within sampling sites according to their assignment proportions. (a) $K = 2$, (b) $K = 3$, see Supporting information for analyses in which the most differentiated groups were hierarchically excluded. (c, d) STRUCTURE ancestry analysis. (c) Inference of mechanical mixture vs. genetic admixture using the source populations North Sea (0.0) and Kattegat (1.0). (d) Kernel density estimates of (c) displaying multimodal (mechanical mixture) vs. unimodal (from one source, or admixed) patterns. Hartigans' dip test indicated three significantly multimodal sampling sites (marked with asterisks): TVE, SOP and IDD. (e) Admixture quantified as hybrid index (*H*) for each individual using BGC cline analysis with the North Sea (0.0) and the Kattegat (1.0) samples as source populations. Points represent the means of posterior distributions, indicating North Sea (red, $H \leq 0.25$), Kattegat (blue, $H \geq 0.75$) and admixed individuals (black). Grey bars indicate 95% credibility intervals

therefore applied an assignment approach as a second test in STRUCTURE, using the well-differentiated North Sea and Kattegat samples as source populations. Per location kernel density estimates showed unimodality, suggesting a single source of ancestry, for the well-differentiated populations: English Channel (ENG) (North Sea-like, *dip* 0.040, $p > .05$), Skagerrak (SKA) (North Sea-like, *dip* 0.068, $p > .05$), Oslofjord (OSL) (North Sea-like, *dip* 0.039, $p > .05$), Öresund (ORE) (western Baltic-like, *dip* 0.044, $p > .05$) and Belt Sea (BEL) (western Baltic-like, *dip* 0.031, $p > .05$) (Figure 2c,d). Significant bimodality suggesting ancestry from both source populations (NOR and KAT) was found for the western fjord sampling sites Tvedestrand (TVE) (*dip* 0.096, $p = .001$) and Soppekilen (SOP) (*dip* 0.107, $p < .01$), as well as the eastern fjord Iddefjord (IDD) (*dip* 0.095, $p = .001$) (Figure 2c,d). Nevertheless, these three sampling sites also include individuals with genotypes intermediate between the two clusters with $q \sim 0.5$ (Figure 2c). The two eastern Skagerrak fjords Gullmarsfjord (GUL) and Havstensfjord (HAV) also showed bimodal distributions; however, support for bimodality was nonsignificant (GUL: *dip* 0.050, $p > .05$; HAV: *dip* 0.083, $p > .05$). Samples from Hellefjord (HEL) and Grenland (GRE) were characterized by rather unimodal ancestry distributions, indicating a western Baltic-like origin (HEL: *dip* 0.052, $p > .05$; GRE: *dip* 0.909, $p > .05$). Whether these individuals are truly of Kattegat/western Baltic origin, or whether they originate from another nonsampled source population cannot be distinguished with this method.

To quantify genomic admixture of the two source populations within the fjord individuals by their hybrid indices (*H*), we performed Bayesian genomic cline analysis. The obtained hybrid indices largely corroborate the results of the STRUCTURE assignment approach (Figure 2e and Table S7). By applying thresholds of $H \leq 0.25$ and ≥ 0.75, individuals were classified as pure North Sea or Kattegat ancestry. Based on these thresholds, Hellefjord (HEL) and Grenland (GRE) are unique as they possess the lowest proportions of individuals with inferred pure North Sea ancestry compared to all other fjords (HEL 0%, GRE 10.6%), the largest percentages of admixed individuals (GRE 59.6%, HEL 52.9%) and the largest proportions of individuals with inferred pure Kattegat

ancestry (HEL 47.1%, GRE 29.8%) (Table S8). In general, all fjords possess admixed individuals, albeit at lower proportions in Tvedestrand (TVE 34%), Soppekilen (SOP 32.1%), Iddefjord (IDD 34.8%), Gullmarsfjord (GUL 48.9%) and Havstensfjord (HAV 41.7%). In these fjords, mechanical mixing of individuals with different ancestries seems to dominate the population structure.

Pairwise fixation indices (F_{ST}) were calculated to characterize the population structure between the different sampling sites and to assess the connectivity through isolation-by-distance (IBD) estimates. F_{ST} estimates were generally low (average pairwise F_{ST} 0.0031) but significant in almost three fourths of comparisons (Figure 3a and Table S9). Comparatively high differentiation was estimated between the North Sea (NOR) and the western Baltic (ORE, BEL) samples (F_{ST} 0.0080–0.0084), but genetic differentiation between the English Channel (ENG) and the North Sea was weak (F_{ST} 0.0005) and not significant. The largest differentiation was found between the western Skagerrak sampling site Hellefjord (HEL) and the North Sea (F_{ST} 0.0130), but Hellefjord was similarly strongly differentiated from the English Channel, Skagerrak (SKA) and Oslofjord (OSL), as well as significantly differentiated from the western Baltic (F_{ST} 0.0030–0.0033) and eastern Skagerrak fjords (F_{ST} 0.0042–0.0068). Applying multidimensional scaling (MDS) to pairwise F_{ST} distances, this separation is evident by Hellefjord being furthest off both axes (Figure 3b). The visualization of F_{ST} distances by MDS also revealed genetic distinction of the western Skagerrak fjord samples Soppekilen (SOP) and Grenland (GRE) in addition to Hellefjord (Figure 3b), whereas the eastern Skagerrak fjord samples HAV and GUL are found intermediate between North Sea and Baltic-like groups. No significant differentiation could be detected between the western Baltic and the Kattegat (KAT) samples. In the MDS plot, this high similarity is apparent by the close proximity of these three locations (Figure 3b).

Isolation by distance was assessed using a Mantel test among fjord sampling sites only, or including the reference populations, and considering either direct geographical distances between sampling coordinates or least-cost paths restricted to marine and shelf areas. However, no significant correlation was detected for any of the comparisons (Fig. S4). In summary, these results describe the presence of differentiated western Skagerrak fjord cod, and a mixed occurrence of North Sea and Kattegat cod within eastern Skagerrak fjords.

3.2 | Biophysical connectivity modelling

The biophysical model of egg and larval dispersal suggested substantial and intermediate larval supply from the spawning areas in the North Sea to the western and the eastern Skagerrak coast, respectively, but low dispersal to the Kattegat (Figure 4a, for spawning areas see Fig. S1). In contrast, the Kattegat and the small but relatively productive spawning areas in the Danish straits (belonging to the western Baltic, see Figure 1) may provide a large proportion of competent larvae along the eastern Skagerrak coast, but less dispersal to the western Skagerrak coast (Figure 4a). The Kattegat itself appeared to largely rely on local spawning areas and import from the Danish straits (Figure 4a). Similarly, local recruitment was also predicted along the western Skagerrak coast, although these values may be underestimates as the model does not resolve the complex geomorphology with high retention within fjords. No local recruitment was assumed for the eastern Skagerrak coast where spawning stocks are negligible (see Jonsson et al., 2016).

The fjords along the western Skagerrak coast received competent larvae from all considered spawning areas (Figure 4b); however, the model predicted particularly large larval supply from the North Sea to the Oslofjord (OSL). This North Sea influence varies greatly between years (indicated by the SD in Figure 4b) and is particularly strong during years with positive NAO winter index. There may also be larger connectivity of Tvedestrand (TVE) with the North Sea as compared to the Hellefjord (HEL) and Grenland (GRE). Notably, the

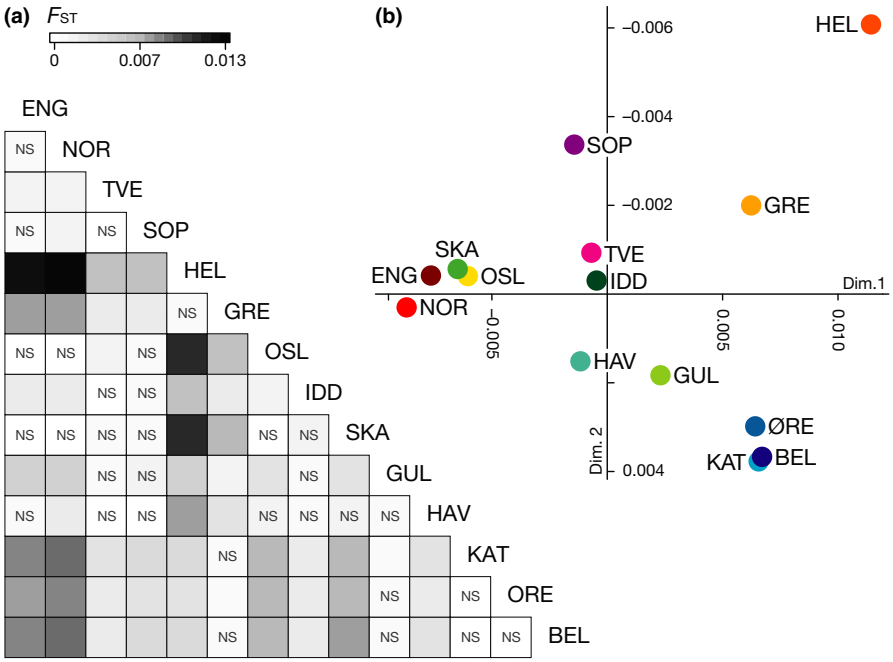

FIGURE 3 F_{ST} estimates of genetic differentiation. (a) Heat map of pairwise F_{ST} comparisons. NS, non-significant. (b) Classic multidimensional scaling (MDS) plot of pairwise F_{ST} comparisons. For sampling site abbreviations, see legend Figure 1

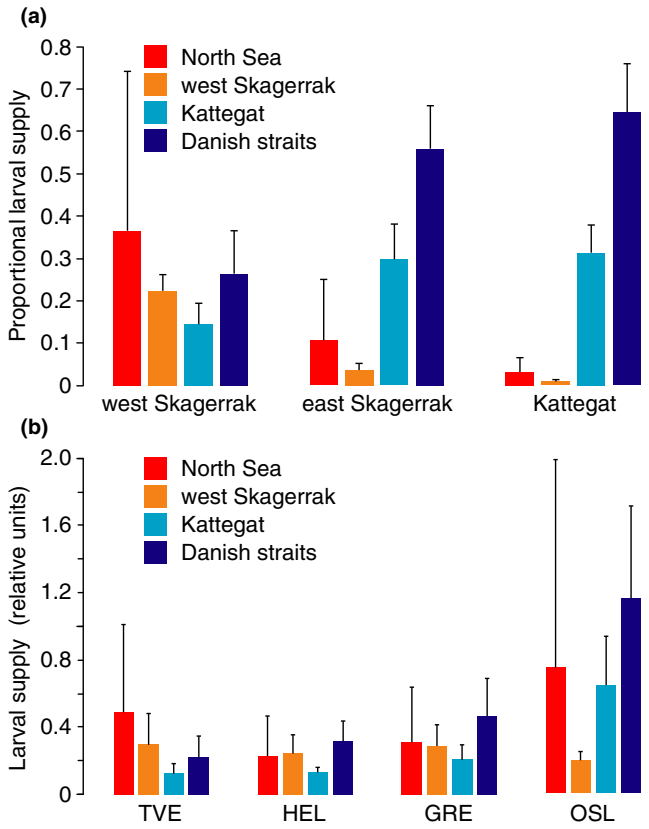

FIGURE 4 Biophysical model of larval connectivity. (a) Modelled connectivity from four spawning areas to the eastern and western Skagerrak coasts, and to the Kattegat, expressed as the proportional larval supply. Larval supply was calculated as the probability of larval dispersal from the spawning areas scaled with the respective spawning stock biomass (SSB). (b) Modelled connectivity from the same four spawning areas to western Skagerrak fjords expressed as larval supply by scaling the dispersal probability with the respective SSB, and normalized to the target area. For TVE, HEL and GRE, only the fjord mouths were included in the model. Error bars show the standard deviation of simulations for six years (1995–2002). For abbreviations of fjords see legend Figure 1

model also predicted a substantial supply of Kattegat/Danish straits larvae to all studied western Skagerrak fjords (Figure 4b). These results indicate that larval connectivity considerably influences the genetic population structure and that high connectivity and resulting gene flow may be negatively correlated with the potential for local adaptation.

3.3 | Chromosomal rearrangements

Large genomic regions exhibiting strong linkage disequilibrium (LD) on several Atlantic cod chromosomes (linkage groups; LG) have recently been reported (Berg et al., 2015, 2016; Kirubakaran et al., 2016; Sodeland et al., 2016). Likely all of these regions represent large chromosomal inversions as suggested in previous studies (Berg et al.,2016; Sodeland et al.,2016), and empirically demonstrated for the linked region on LG1 (Kirubakaran et al., 2016). As our data set was filtered for LD using a strict filtering cut-off ($r^2 > 0.1$), most SNPs within the rearranged regions were removed due to strong signals of LD, with the remaining ones not influencing the genetic structure (Fig. S5). However, as these genomic regions have been suggested to carry genes responsible for local adaptation to low salinity, temperature and oxygen levels (Berg et al., 2015; Bradbury et al., 2010), these linked SNPs were used in separate analyses to investigate the occurrence and segregation of the chromosomal rearrangements between sampling sites. Our data revealed three of the four putative inversions previously described by Berg et al. (2015): LG2 (position 18,609,260–23,660,985; ~5.05 Mbp), LG7 (position 13,622,710–23,181,520; ~9.56 Mbp) and LG12 (position 426,531–13,445,150; ~13.02 Mbp). The inversion on LG1 has so far exclusively been found in comparison with the Northeast Arctic cod (Berg et al., 2016; Kirubakaran et al., 2016), and was not detected in our data using the R package INVERSION. However, a comparison of SNPs within the linked region on LG1 in our data with the previously published data from Berg et al. (2016) revealed four heterozygous individuals (0.76%) carrying both the inverted and the collinear allele (two from OSL, one each from GRE and NOR).

Based on a bootstrap analysis, a significant overrepresentation of the rearranged allele on LG2 was detected for the western Skagerrak fjords Hellefjord (HEL, $p < .001$) and Grenland (GRE, $p < .001$), as well as for the Öresund (ORE, $p < .001$) (Figure 5a). The rearranged allele on LG7 was not found to be significantly overrepresented in any of the sampling sites (Figure 5b). However, the rearranged allele on LG12 was significantly overrepresented in the North Sea (NOR, $p < .001$), the Oslofjord (OSL, $p < .001$) and also the Skagerrak (SKA, $p < .05$; not significant after correction for multiple comparisons) (Figure 5c). In addition, the geographically most distant English Channel (ENG) exhibited a significant underrepresentation of the rearranged alleles for all three LGs ($p < .001$). Comparisons of the occurrence of the rearranged alleles in all western fjords (TVE, SOP, HEL, GRE) and all eastern fjords (IDD, GUL, HAV) revealed a significant overrepresentation of the rearranged allele on LG2 within western fjords ($p < .001$), but not within eastern fjords. As the Oslofjord clustered with the North Sea group, it was excluded from this comparison; however, the rearranged allele on LG2 was also significantly overrepresented ($p < .01$) when the Oslofjord was included within the western fjords. In summary, these findings suggest that the particular genomic architecture of Atlantic cod may contribute to the potential for local adaptation to a low salinity environment.

4 | DISCUSSION

How local adaptation can be maintained in the face of gene flow is a long-standing question in evolutionary biology, which we are now beginning to understand owing to the profound advances in sequencing technology and genomic analysis tools (Tigano & Friesen, 2016). While it is well recognized that chromosomal inversions can play an important role as drivers of evolution (reviewed in Hoffmann & Rieseberg, 2008), there are still few studies investigating the role

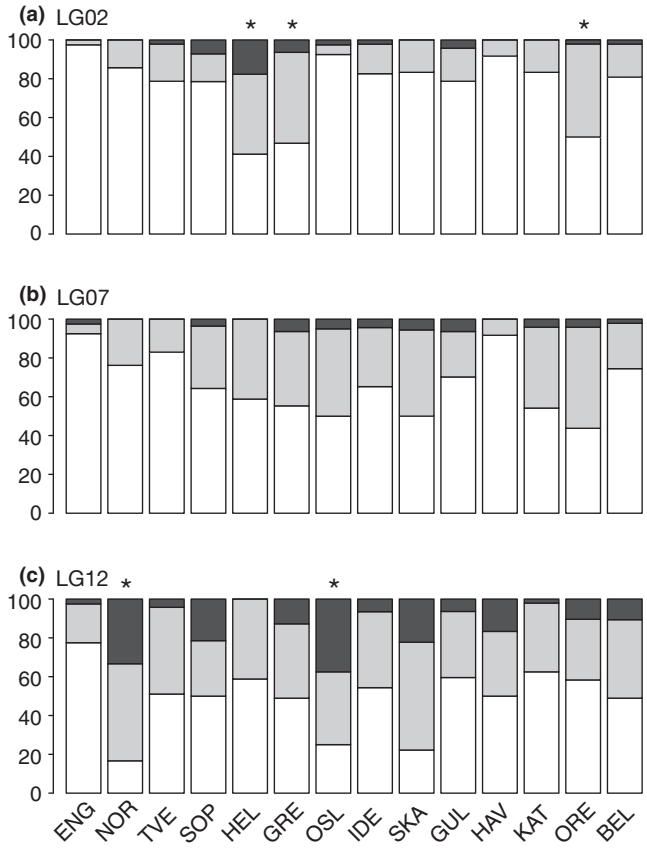

FIGURE 5 Distribution of chromosomal rearrangements. Per sampling site, individuals were scored for three chromosomal rearrangements on linkage groups (LG) 2, 7 and 12. The proportion of individuals being homozygous for the presumed collinear allele is shown in white, and proportions of individuals heterozygous or homozygous for the rearranged allele are shown in light and dark grey, respectively. Sampling sites representing a significant overrepresentation of the rearranged allele are marked with an asterisk

of chromosomal rearrangements in high geneflow species. Marine organisms provide ideal models to study this question, owing to their varied habitats and the lack of physical barriers. By combining genomic analyses of ecologically distinct Atlantic cod populations with biophysical modelling of dispersal, we were not only able to unravel cryptic population structure and detect ecologically differentiated populations, but also identified chromosomal rearrangements as a potential mechanism enabling local adaptation despite high connectivity.

4.1 | Western Skagerrak fjords possess locally differentiated Atlantic cod despite high connectivity and a mix of North Sea and Kattegat cod

The ecological peculiarity of the low-saline Baltic Sea and the transition zone connecting it with the saline North Sea have led to the evolution of unique linages (Johannesson & André, 2006). Nevertheless, based on unlinked SNPs, the overall population differentiation of Atlantic cod within this area was weak, as also shown in earlier studies and explained by large effective population sizes and high gene flow (Knutsen et al., 2011; Nielsen, Grønkjaer, Meldrup, & Paulsen, 2005). Comparatively strong differentiation was detected between North Sea/English Channel/Skagerrak and Kattegat/western Baltic samples, reflecting the geographical separation (Figure 1) as well as a separation resulting from adaptation to low salinity as shown previously for Atlantic cod, but also many other species of the eastern Baltic Sea (Berg et al., 2015; Johannesson & André, 2006; Lamichhaney et al., 2012; Sjöqvist, Godhe, Jonsson, Sundqvist, & Kremp, 2015). However, no genetic differentiation was detected within these strongly separated North Sea-like and western Baltic-like groups (Appendix S3).

Contrary to these well defined populations, the eastern Skagerrak fjords appeared to be composed of a mix between North Sea-like and western Baltic-like individuals, indicating that these fjords are part of the distributional area of the two major evolutionary units detected in this study. These fjords may experience larval recruitment through a strong influx of central North Sea water into the Skagerrak, as well as less-saline Kattegat water entering along the coast (André et al., 2016; Danielssen et al., 1997; Jonsson et al., 2016; Knutsen et al., 2004; Stenseth et al., 2006). In agreement with these predominant ocean currents, a large fraction of individuals from the eastern Skagerrak fjords appeared to be of North Sea origin (Figure 2), while our biophysical model suggested greater larval connectivity with the Kattegat and western Baltic (Figure 5). However, the model did not include the North Sea Viking bank spawning ground which has significantly increased its contribution during the last decades (Jonsson et al., 2016), suggesting that the influence of the North Sea spawning areas to the eastern Skagerrak is larger than shown in our modelling. We did not detect genetically differentiated individuals that would be indicative for a distinct fjord population in eastern Skagerrak fjords, although differentiation between Atlantic cod larvae inside and outside Gullmarsfjord was previously found (Øresland & André, 2008). It is unknown if recent reductions in abundance along the eastern Skagerrak coast (Svedäng & Bardon, 2003; Svedäng & Svenson, 2006) indicate the loss or severe decimation of a genetically differentiated population in this region.

In contrast, the western Skagerrak fjord samples included varying levels of genetically differentiated individuals that clustered neither with the North Sea-like nor the western Baltic-like group (Figure 2b), indicative of the existence of a local western Skagerrak coastal or fjord cod population(s). The existence of such local populations is also supported by the biophysical model results, which explained a large fraction of larval supply by local recruitment (Figure 4). Local fjord cod has previously also been assumed to exist at the northern Norwegian coast (Jørstad & Naevdal, 1989; Myksvoll, Jung, Albretsen, & Sundby, 2014), and differentiation between fjord, coastal or oceanic cod has been shown in two closely related gadiids, the Pacific cod (*Gadus macrocephalus*) and the polar cod (*Boreogadus saida*) (Cunningham, Canino, Spies, & Hauser, 2009; Madsen, Nelson, Fevolden, Christiansen, & Præbel, 2015).

Fjord systems represent semi-enclosed ecosystems where water exchange is restricted by a narrow connection with the outer sea, often further reduced by a tall entrance sill, thus creating an inner estuarine circulation (Howe et al., 2010). Such conditions have been shown to hamper gene flow as a result of stationary behaviour with reduced adult migration and restricted egg and larval dispersal (Bergstad, Jørgensen, Knutsen, & Berge, 2008; Ciannelli et al., 2010; Espeland et al., 2007, 2008; Jung et al., 2012; Knutsen et al., 2007; Rogers et al., 2014). Consequently, the strongest genetic differentiation and the largest fraction of local western Skagerrak fjord individuals was found in the particularly isolated Hellefjord (Molvær, Green, & Baalsrud, 1978) and Grenland fjord (Danielssen & Føyn, 1973) (Figure 2b). Although the differentiation of the Hellefjord sample might be overestimated due to the small sample size and collection of juveniles, these results were strongly supported by the Grenland fjord sample, consisting of a large sample of adults collected during both spawning and nonspawning periods. However, weaker genetic differentiation was estimated for the Tvedestrand and Soppekilen samples, which may be attributed to bathymetric and temporal differences (Appendix S4).

Interestingly, the majority of the Oslofjord individuals were assigned a North Sea origin in the ancestry analysis (Figure 2e), a pattern largely supported by the biophysical model (Figure 4b). However, strong contribution from the Kattegat/western Baltic was also predicted by the model but was not as evident in the genetic results, possibly indicating the lack of the North Sea Viking bank spawning ground in the model. In contrast to the Oslofjord, all western Skagerrak fjords showed a lower percentage of individuals with North Sea origin and about one quarter were assigned Kattegat/western Baltic origin. This result supports the suggestion that spawning areas in the Danish straits and especially in the Öresund may constitute an important source of Atlantic cod larvae for both the eastern and the western Skagerrak (Jonsson et al., 2016).

4.2 | Do chromosomal rearrangements facilitate ecological adaptation of Atlantic cod?

Atlantic cod can be found in a variety of different habitats, ranging from the relatively warm waters in the Bay of Biscay, from small sheltered coastal and fjord ecosystems, to low-saline seas like the Baltic Sea, and to open oceanic environments and very cold waters in the Barents Sea (Lilly et al., 2008), an environmental flexibility that likely required the acquisition of locally adaptive traits. It has recently been described that such adaptations, especially in highly connected organisms like oceanic fish, can arise through the segregation of chromosomal rearrangements, where recombination is suppressed and important functional genes are inherited together (Feder, Egan, & Nosil, 2012; Thompson & Jiggins, 2014; Tigano & Friesen, 2016). While empirical evidence for this theory is still scarce, it is well supported by studies on stickleback (Jones et al., 2012; Roesti et al., 2015). Recently, haplotype blocks associated with ecological adaptation were also detected in the Atlantic herring, but it is unclear if inversions are the causative mechanism (Lamichhaney et al., 2017; Martinez-Barrio et al., 2016). In contrast, a series of recent studies employing genomewide data to dissect Atlantic cod population differentiation, discovered exceptionally large chromosomal rearrangements that are likely to be inversions on several linkage groups (LGs), which were suggested to play a major role for the adaptive abilities of Atlantic cod (Barney et al., 2017; Berg et al., 2015, 2016; Bradbury et al., 2013, 2014; Hemmer-Hansen et al., 2013; Kirubakaran et al., 2016; Sodeland et al., 2016). These recent studies, including this study, therefore contribute remarkable examples in the marine environment to a growing body of literature identifying chromosomal rearrangements and inversions as an important mechanism to maintain contrasting ecotypes in intermixing populations (Cheng et al., 2012; Hoffmann & Rieseberg, 2008; Joron et al., 2011; Lowry & Willis, 2010).

For example, adaptation to low-saline and hypoxic environments as occurring in the Baltic Sea strongly depends on the ability for osmoregulation and effective oxygen management (Andersen et al., 2009; Berg et al., 2015). Berg et al. (2015) compared North and Baltic Sea cod and found several SNPs within genes important for salinity and oxygen regulation, of which the majority reside within a rearranged region on LG2, implicating an essential role of this rearranged region for the Atlantic cod's ability to adapt to the environmental conditions in the Baltic Sea. Such genetic–environment correlations may also be due to intrinsic genetic incompatibilities that merely coincide with ecological barriers (Bierne, Welch, Loire, Bonhomme, & David, 2011). However, similar patterns of genes involved in oxygen- or osmoregulation were also associated with salinity clines in studies of Atlantic herring (Limborg et al., 2012; Martinez-Barrio et al., 2016), indicating the presence of true local adaptation.

Remarkably, fjord ecosystems have notable similarities with the Baltic Sea: both originated by glacial retreat, represent enclosed estuaries with high freshwater input and restricted exchange with saline oceanic water leading to estuarine circulations, and both feature deep basins with mostly hypoxic conditions (Harff, Björck, & Hoth, 2011; Howe et al., 2010). Thus, similar adaptations may be required for successful colonization of the Baltic Sea and fjord ecosystems. Indeed, our ancestry analyses showed that local western Skagerrak fjord individuals are genetically more similar to the Kattegat/western Baltic population (an area discussed as a transition zone between the North Sea and the eastern Baltic Sea (Nielsen, Hansen, Ruzzante, Meldrup, & Grønkjaer, 2003)) than to the North Sea population. In addition, we found a significant overrepresentation of the rearranged LG2 allele in the Hellefjord and Grenland fjord samples (Figure 5a), an allelic shift that has recently also been described between oceanic and coastal cod groups (Sodeland et al., 2016). Both fjords have high freshwater influx, causing a low-saline surface layer above oceanic water with 25–30‰ salinity (Danielssen & Føyn, 1973; Molvær et al., 1978), comparable to salinity gradients in the Kattegat/western Baltic (Madsen & Højerslev, 2009). As an adaptation to low-saline conditions, Atlantic cod inhabiting the Baltic Sea produce highly hydrated eggs that are neutrally buoyant between ~14‰ (eastern Baltic Sea) and ~21‰ (Danish straits) (Nissling &

Westin, 1997; for a recent review see Hüssy, 2011), a mechanism that for example prevents lethal sinking of the eggs to the hypoxic deeper layers in the Baltic Sea. In contrast, the eggs of marine Atlantic cod populations are neutrally buoyant at salinities of ~33‰ (Thorsen, Kjesbu, Fyhndr, & Solemdal, 1996). Similar to Baltic cod, eggs of fjord cod are neutrally buoyant in the low-saline water layers of fjords, which not only prevents sinking of the eggs to hypoxic layers, but also retains the eggs inside the sheltered fjord area (Ciannelli et al., 2010; Espeland et al., 2007; Jung et al., 2012; Knutsen et al., 2007). Egg buoyancy can be regulated by the in- and efflux of solutes (Reading et al., 2012), and many SNPs in or close to genes coding for membrane trafficking proteins have been identified within the rearranged region on LG2 (Berg et al., 2015). This accumulation of adaptive variation could be explained by diversifying selection shaping the rearranged region in the likely absence of recombination between the alleles. In ecosystems where regulation of egg buoyancy provides an evolutionary advantage, an increase in the frequency of the rearrangement might be expected.

In addition to our samples from Hellefjord and Grenland fjord, our Öresund sample from the western Baltic also shared a significant overrepresentation of the rearranged allele on LG2, which occurs at very high frequency in eastern Baltic cod (Berg et al., 2015). However, our Belt Sea and Kattegat samples did not show an increased occurrence of the rearranged LG2 allele although the genetic structure analyses suggested genetic similarity between the Kattegat and western Baltic samples, indicative for additional adaptive variation outside the large rearrangements. Interestingly, the rearranged LG12 allele was found to be significantly overrepresented in our North Sea and Oslofjord samples, with high occurrences also in the eastern Skagerrak sample (Figure 5c). Concordantly, this allele was recently found to occur at higher frequency in oceanic compared to coastal Atlantic cod populations and was suggested to play a role in ecological adaptation (Sodeland et al., 2016). It has previously also been associated with an adaptation to temperature (Berg et al., 2015; Bradbury et al., 2010), which could thus be relevant with regard to survival and abundance of Atlantic cod in the face of global warming (Drinkwater, 2005). However, similar to the Kattegat/western Baltic samples, which shared most genetic variation but showed a distinct pattern in the occurrence of the rearranged LG2 allele, the North Sea, Oslofjord, Skagerrak and English Channel samples were not distinguishable based on SNPs outside the rearranged regions, but showed a distinct distribution of the rearranged LG12 allele. This contrast between the genomewide profile that rather reflects connectivity and geography, and the chromosomal rearrangements that seem to cluster according to environment, indicates that despite the high gene flow between Atlantic cod populations important genes under adaptive divergent selection likely reside within rearranged regions.

4.3 | Significance and summary of the study

Because of their relatively higher fitness in their native habitat compared to introduced populations, locally adapted populations are often irreplaceable once vanished (Kawecki & Ebert, 2004; Reiss, Hoarau, Dickey-Collas, & Wolff, 2009). Human activity has led to the collapse of several fish stocks (Myers, Hutchings, & Barrowman, 1996; Pinsky, Jensen, Ricard, & Palumbi, 2011) and populations of Atlantic cod regionally suffer from overexploitation and population decline (Bartolino et al., 2012; Bonanomi et al., 2015; Svedäng & Bardon, 2003; Svedäng & Svenson, 2006), causing predator-prey shifts and imbalance of sensible ecosystems (Baden, Emanuelsson, Pihl, Svensson, & Åberg, 2012; Östman et al., 2016). Thus, priorities are high to clarify the potential and occurrence of local adaptation in such high gene flow species, as well as to improve our understanding of the genetic mechanism for adaptation to conserve genetic resources in a globally changing world.

Our study showed that: 1.) the here described North Sea, Kattegat/western Baltic and western Skagerrak fjord cod genotypes most likely correspond to the previously identified oceanic and coastal ecotypes, respectively, thus shedding light on the long-standing question whether local fjord ecotypes exist and 2.) western Skagerrak fjord cod, despite high connectivity with the North Sea, may possess adaptations facilitating a life in a low salinity environment similar to Atlantic cod from the Baltic Sea. The genes encoding these adaptations are suggested to partially reside in large chromosomal rearrangements, regions that due to their reduced recombination are known to promote adaptive population divergence (Feder & Nosil, 2009; Kirkpatrick & Barton, 2006; Thompson & Jiggins, 2014).

In contrast, no locally differentiated fjord cod was detected in the eastern Skagerrak fjords, supporting the absence or suspected loss of local populations along the Swedish coast (Svedäng & Bardon, 2003). We thus emphasize the importance of taking genome architecture into account when characterizing ecological adaptation, particularly for species characterized by high gene flow.

ACKNOWLEDGEMENTS

We thank Mariann Arnyasi, Matthew P. Kent and Sigbjørn Lien (Norwegian University of Life Sciences, CIGENE) for SNP genotyping, and Michael M. Hansen, Daniel Ruzzante and two anonymous reviewers for valuable input that greatly helped to improve the manuscript. Initial sequencing for SNP identification was provided by the Norwegian Sequencing Centre. JMIB thanks Michael Matschiner for valuable input to the manuscript and careful proofreading, Trond Reitan for support with statistical analyses, and the Centre for Ecological and Evolutionary Synthesis (CEES) at the University of Oslo (UiO) for funding. This work was performed on the Abel Cluster owned by the UiO and the Norwegian metacenter for High Performance Computing (NOTUR) and operated by the UiO Department for Research Computing, and was supported by funds of the Interreg projects "CodS—restoration and management of cod populations in Skagerrak-Kattegat" (#168975) and "MarGen" (#175806), and by the Centre for Marine Evolutionary Biology at the University of Gothenburg (CeMEB).

DATA ACCESSIBILITY

All SNPs are referred to by their database of single nucleotide polymorphisms (dbSNP) Accession numbers, available from: http://www.ncbi.nlm.nih.gov/SNP. Individual genotype data are available from the Dryad Digital Repository: https://doi.org/10.5061/dryad.3f1c8. The nomenclature of linkage groups in this study follows Hubert, Higgins, Borza, and Bowman (2010).

AUTHOR CONTRIBUTION

The study was conceived and designed by C.A., J.M.I.B., P.R.B., J.H.H., K.S.J., S.J., K.J., P.E.J., H.K., P.M., B.S., N.C.S., H.S. Assessment of genotypes and data quality was done by J.M.I.B., P.R.B., S.B., J.H.H. Genomic analyses were performed by J.M.I.B. Oceanographic modelling was carried out by H.C., P.R.J., P.M. Samples were provided by C.A., J.H.H., S.J., H.K., H.S. The manuscript was written by J.M.I.B. with contributions from P.R.J. All authors read and revised the manuscript.

REFERENCES

Allendorf, F. W., Hohenlohe, P. A., & Luikart, G. (2010). Genomics and the future of conservation genetics. *Nature Reviews Genetics*, *11*, 697–709.

Amante, C., & Eakins, B. W. (2009). ETOPO1 1 arc-minute global relief model: procedures, data sources and analysis. NOAA Technical Memorandum, NESDIS NGDC-24.

Andersen, Ø. (2012). Hemoglobin polymorphisms in Atlantic cod - A review of 50 years of study. *Marine Genomics*, *8*, 59–65.

Andersen, Ø., Wetten, O. F., De Rosa, M. C., Andre, C., Carelli Alinovi, C., Colafranceschi, M., … Colosimo, A. (2009). Haemoglobin polymorphisms affect the oxygen-binding properties in Atlantic cod populations. *Proceedings of the Royal Society B*, *276*, 833–841.

André, C., Svedäng, H., Knutsen, H., Dahle, G., Jonsson, P., Ring, A.-K., … Jorde, P. E. (2016). Population structure in Atlantic cod in the eastern North Sea-Skagerrak-Kattegat: early life stage dispersal and adult migration. *BMC Research Notes*, *9*, 63.

Baden, S., Emanuelsson, A., Pihl, L., Svensson, C. J., & Åberg, P. (2012). Shift in seagrass food web structure over decades is linked to overfishing. *Marine Ecology Progress Series*, *451*, 61–73.

Barney, B. T., Munkholm, C., Walt, D. R., & Palumbi, S. R. (2017). Highly localized divergence within supergenes in Atlantic cod (*Gadus morhua*) within the Gulf of Maine. *BMC Genomics*, *18*, 271.

Bartolino, V., Cardinale, M., Svedäng, H., Linderholm, H. W., Casini, M., & Grimwall, A. (2012). Historical spatiotemporal dynamics of eastern North Sea cod. *Canadian Journal of Fisheries and Aquatic Sciences*, *69*, 833–841.

Beacham, T. D., Brattey, J., Miller, K. M., Le, K. D., & Withler, R. E. (2002). Multiple stock structure of Atlantic cod (*Gadus morhua*) off Newfoundland and Labrador determined from genetic variation. *ICES Journal of Marine Science*, *59*, 650–665.

Benjamini, Y., & Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *The Annals of Statistics*, *29*, 1165–1188.

Berg, P. R., Jentoft, S., Star, B., Ring, K. H., Knutsen, H., Lien, S., … André, C. (2015). Adaptation to low salinity promotes genomic divergence in Atlantic cod (*Gadus morhua* L.). *Genome Biology and Evolution*, *7*, 1644–1663.

Berg, P. R., Star, B., Pampoulie, C., Sodeland, M., Barth, J. M. I., Knutsen, H., … Jentoft, S. (2016). Three chromosomal rearrangements promote genomic divergence between migratory and stationary ecotypes of Atlantic cod. *Scientific Reports*, *6*, 23246.

Bergstad, O. A., Jørgensen, T., Knutsen, J. A., & Berge, J. A. (2008). Site fidelity of Atlantic cod *Gadus morhua* L. as deduced from telemetry and stable isotope studies. *Journal of Fish Biology*, *72*, 131–142.

Bernatchez, L. (2016). On the maintenance of genetic variation and adaptation to environmental change: considerations from population genomics in fishes. *Journal of Fish Biology*, *89*, 2519–2556.

Bierne, N., Welch, J., Loire, E., Bonhomme, F., & David, P. (2011). The coupling hypothesis: why genome scans may fail to map local adaptation genes. *Molecular Ecology*, *20*, 2044–2072.

Bonanomi, S., Therkildsen, N. O., Retzel, A., Hedeholm, R. B., Pedersen, M. W., Meldrup, D., … Nielsen, E. E. (2016). Historical DNA documents long-distance natal homing in marine fish. *Molecular Ecology*, *25*, 2727–2734.

Bonanomi, S., Pellissier, L., Therkildsen, N. O., Hedeholm, R. B., Retzel, A., Meldrup, D., … Nielsen, E. E. (2015). Archived DNA reveals fisheries and climate induced collapse of a major fishery. *Scientific Reports*, *5*, 15395.

Bradbury, I. R., Bowman, S., Borza, T., Snelgrove, P. V. R., Hutchings, J. A., Berg, P. R., …Bentzen, P. (2014). Long distance linkage disequilibrium and limited hybridization suggest cryptic speciation in Atlantic cod. *PLoS ONE*, *9*, e106380.

Bradbury, I. R., Hubert, S., Higgins, B., Borza, T., Bowman, S., Paterson, I. G., … Bentzen, P. (2010). Parallel adaptive evolution of Atlantic cod on both sides of the Atlantic Ocean in response to temperature. *Proceedings of the Royal Society B*, *277*, 3725–3734.

Bradbury, I. R., Hubert, S., Higgins, B., Bowman, S., Borza, S., Paterson, I.G., … Bentzen, P. (2013). Genomic islands of divergence and their consequences for the resolution of spatial structure in an exploited marine fish. *Evolutionary Applications*, *6*, 450–461.

Cáceres, A., Sindi, S. S., Raphael, B. J., Cáceres, M., & González, J. R. (2012). Identification of polymorphic inversions from genotypes. *BMC Bioinformatics*, *13*, 28.

Camacho, C., Coulouris, G., Avagyan, V., Ma, N., Papadopoulos, J., & Bealer, K., & Madden, T. L. (2009). BLAST+: architecture and applications. *BMC Bioinformatics*, *10*, 421.

Cheng, C., White, B. J., Kamdem, C., Mockaitis, K., Costantini, C., Hahn, M. W., & Besansky, N. J. (2012). Ecological genomics of *Anopheles gambiae* along a latitudinal cline: a population-resequencing approach. *Genetics*, *190*, 1417–1432.

Ciannelli, L., Knutsen, H., Olsen, E. M., Espeland, S. H., Asplin, L., Jelmert, A., … Stenseth, N. C. (2010). Small-scale genetic structure in a marine population in relation to water circulation and egg characteristics. *Ecology*, *91*, 2918–2930.

Clarke, L. M., Munch, S. B., Thorrold, S. R., & Conover, D. O. (2010). High connectivity among locally adapted populations of a marine fish (*Menidia menidia*). *Ecology*, *91*, 3526–3537.

Cunningham, K. M., Canino, M. F., Spies, I. B., & Hauser, L. (2009). Genetic isolation by distance and localized fjord population structure in Pacific cod (*Gadus macrocephalus*): limited effective dispersal in the northeastern Pacific Ocean. *Canadian Journal of Fisheries and Aquatic Sciences*, *66*, 153–166.

Danielssen, D. S., Edler, L., Fonselius, S., Hernroth, L., Ostrowski, M., Svendsen, E., & Talpsepp, L. (1997). Oceanographic variability in the Skagerrak and Northern Kattegat, May-June, 1990. *ICES Journal of Marine Science*, *54*, 753–773.

Danielssen, D. S., & Føyn, L. (1973). Frierfjorden - en vurdering av fjordsystemets vannutskiftning. *Fisken og Havet*, *6*, 1–19.

DeWoody, J. A., & Avise, J. C. (2000). Microsatellite variation in marine, freshwater and anadromous fishes compared with other animals. *Journal of Fish Biology*, *56*, 461–473.

Dixon, P. (2003). VEGAN, a package of R functions for community ecology. *Journal of Vegetation Science*, *14*, 927–930.

Dobzhansky, T. (1937). *Genetics and the origin of species*. New York, NY: Columbia University Press.

Drinkwater, K. F. (2005). The response of Atlantic cod (*Gadus morhua*) to future climate change. *ICES Journal of Marine Science*, *62*, 1327–1337.

Efron, B. (1979). Bootstrap methods: another look at the jackknife. *The Annals of Statistics*, *7*, 1–26.

Espeland, S. H., Gundersen, A. F., Olsen, E. M., Knutsen, H., Gjøsæter, J., & Stenseth, N. C. (2007). Home range and elevated egg densities within an inshore spawning ground of coastal cod. *ICES Journal of Marine Science*, *64*, 920–928.

Espeland, S. H., Olsen, E. M., Knutsen, H., Gjøsæter, J., Danielssen, D., & Stenseth, N. C. (2008). New perspectives on fish movement: kernel and GAM smoothers applied to a century of tagging data on coastal Atlantic cod. *Marine Ecology Progress Series*, *372*, 231–241.

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

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

Falush, D., Stephens, M., & Pritchard, J. K. (2003). Inference of population structure using multilocus genotype data: linked loci and correlated allele frequencies. *Genetics*, *164*, 1567–1587.

Feder, J. L., Egan, S. P., & Nosil, P. (2012). The genomics of speciation-with-gene-flow. *Trends in Genetics*, *28*, 342–350.

Feder, J. L., & Nosil, P. (2009). Chromosomal inversions and species differences: when are genes affecting adaptive divergence and reproductive isolation expected to reside within inversions? *Evolution*, *63*, 3061–3075.

Foll, M., & Gaggiotti, O. (2008). A genome-scan method to identify selected loci appropriate for both dominant and codominant markers: a Bayesian perspective. *Genetics*, *180*, 977–993.

Gompert, Z., & Buerkle, C. A. (2012). bgc: Software for Bayesian estimation of genomic clines. *Molecular Ecology Resources*, *12*, 1168–1176.

Harff, J., Björck, S., & Hoth, P. (2011). The Baltic Sea Basin. In J. Harff, S. Björck, & P. Hoth (Eds.), *Central and eastern european development studies*. Berlin, Heidelberg, Germany: Springer-Verlag.

Hartigan, J. A., & Hartigan, P. M. (1985). The dip test of unimodality. *The Annals of Statistics*, *13*, 70–84.

Hemmer-Hansen, J., Nielsen, E. E., Therkildsen, N. O., Taylor, M. I., Ogden, R., Geffen, A. J., … Carvalho, G. R. (2013). A genomic island linked to ecotype divergence in Atlantic cod. *Molecular Ecology*, *22*, 2653–2667.

Hoffmann, A. A., & Rieseberg, L. H. (2008). Revisiting the impact of inversions in evolution: from population genetic markers to drivers of adaptive shifts and speciation? *Annual Review of Ecology, Evolution, and Systematics*, *39*, 21–42.

Hordoir, R., Dieterich, C., Basu, C., Dietze, H., & Meier, H. E. M. (2013). Freshwater outflow of the Baltic Sea and transport in the Norwegian current: a statistical correlation analysis based on a numerical experiment. *Continental Shelf Research*, *64*, 1–9.

Howe, J. A., Austin, W. E. N., & Forwick, M. Paetzel, M., Harland, R., & Cage, A. G. (2010). Fjord systems and archives: a review. In J. A. Howe, W. E. N. Austin, M. Forwick & M. Paetzel (Eds.), *Fjord systems and archives*, 344 (pp. 5–15). London: Geological Society, Special Publications.

Hubert, S., Higgins, B., Borza, T., & Bowman, S. (2010). Development of a SNP resource and a genetic linkage map for Atlantic cod (*Gadus morhua*). *BMC Genomics*, *11*, 191.

Hüssy, K. (2011). Review of western Baltic cod (*Gadus morhua*) recruitment dynamics. *ICES Journal of Marine Science*, *68*, 1459–1471.

Johannesson, K., & André, C. (2006). Life on the margin: genetic isolation and diversity loss in a peripheral marine ecosystem, the Baltic Sea. *Molecular Ecology*, *15*, 2013–2029.

Jombart, T. (2008). adegenet: a R package for the multivariate analysis of genetic markers. *Bioinformatics*, *24*, 1403–1405.

Jones, F. C., Grabherr, M. G., Chan, Y. F., Russell, P., Mauceli, E., Johnson, J., … Kingsley, D. M. (2012). The genomic basis of adaptive evolution in threespine sticklebacks. *Nature*, *484*, 55–61.

Jonsson, P. R., Corell, H., André, C., Svedäng, H., & Moksnes, P. (2016). Recent decline in cod stocks in the North Sea–Skagerrak–Kattegat shifts the sources of larval supply. *Fisheries Oceanography*, *25*, 210–228.

Jorde, P. E., Knutsen, H., Espeland, S. H., & Stenseth, N. C. (2007). Spatial scale of genetic structuring in coastal cod *Gadus morhua* and geographic extent of local populations. *Marine Ecology Progress Series*, *343*, 229–237.

Joron, M., Frezal, L., Jones, R. T., Chamberlain, N. L., Lee, S. F., Haag, C. R., … Ffrench-Constant, R. H. (2011). Chromosomal rearrangements maintain a polymorphic supergene controlling butterfly mimicry. *Nature*, *477*, 203–206.

Jørstad, K. E., & Naevdal, G. (1989). Genetic variation and population structure of cod, *Gadus morhua* L, in some fjords in northern Norway. *Journal of Fish Biology*, *35*, 245–252.

Jung, K.-M., Folkvord, A., Kjesbu, O. S., Agnalt, A. L., Thorsen, A., & Sundby, S. (2012). Egg buoyancy variability in local populations of Atlantic cod (*Gadus morhua*). *Marine Biology*, *159*, 1969–1980.

Karlsen, B. O., Klingan, K., Emblem, Å., Jørgensen, T. E., Jueterbock, A., Furmanek, T., … Moum, T. (2013). Genomic divergence between the migratory and stationary ecotypes of Atlantic cod. *Molecular Ecology*, *22*, 5098–5111.

Kawecki, T. J., & Ebert, D. (2004). Conceptual issues in local adaptation. *Ecology Letters*, *7*, 1225–1241.

Keenan, K., McGinnity, P., Cross, T. F., Crozier, W. W., & Prodöhl, P. A. (2013). diveRsity: an R package for the estimation and exploration of population genetics parameters and their associated errors. *Methods in Ecology and Evolution*, *4*, 782–788.

Kirkpatrick, M., & Barton, N. (2006). Chromosome inversions, local adaptation and speciation. *Genetics*, *173*, 419–434.

Kirubakaran, T. G., Grove, H., Kent, M. P., Sandve, S. R., Baranski, M., Nome, T., … Andersen, Ø. (2016). Two adjacent inversions maintain genomic differentiation between migratory and stationary ecotypes of Atlantic cod. *Molecular Ecology*, *25*, 2130–2143.

Knutsen, H., André, C., Jorde, P. E., Skogen, M. D., Thuróczy, E., & Stenseth, N. C. (2004). Transport of North Sea cod larvae into the Skagerrak coastal populations. *Proceedings of the Royal Society B*, *271*, 1337–1344.

Knutsen, H., Jorde, P. E., André, C., & Stenseth, N. C. (2003). Fine-scaled geographical population structuring in a highly mobile marine species: the Atlantic cod. *Molecular Ecology*, *12*, 385–394.

Knutsen, H., Olsen, E. M., Ciannelli, L., Espeland, S. H., Knutsen, J. A., Simonsen, J. H., … Stenseth, N. C. (2007). Egg distribution, bottom topography and small-scale cod population structure in a coastal marine system. *Marine Ecology Progress Series*, *333*, 249–255.

Knutsen, H., Olsen, E. M., Jorde, P. E., Espeland, S. H., André, C., & Stenseth, N. C. (2011). Are low but statistically significant levels of genetic differentiation in marine fishes 'biologically meaningful'? A case study of coastal Atlantic cod. *Molecular Ecology*, *20*, 768–783.

Lamichhaney, S., Fuentes-Pardo, A. P., Rafati, N., Ryman, N., McCracken, G. R., Bourne, C., … Andersson, L. (2017). Parallel adaptive evolution of geographically distant herring populations on both sides of the North Atlantic Ocean. *Proceedings of the National Academy of Sciences of the United States of America*, *114*, E3452–E3461.

Lamichhaney, S., Martinez-Barrio, A., Rafati, N., Sundström, G., Rubin, C.-J., Gilbert, E. R., … Andersson, L. (2012). Population-scale sequencing reveals genetic differentiation due to local adaptation in Atlantic

herring. *Proceedings of the National Academy of Sciences of the United States of America*, *109*, 19345–19350.

Lilly, G. R., Wieland, K., Rothschild, B. J., Sundby, S., Drinkwater, K. F., Brander, K., … Vazquez, A. (2008). Decline and recovery of Atlantic cod (*Gadus morhua*) stocks throughout the North Atlantic. In G. H. Kruse, K. Drinkwater, J. N. Ianelli, J. S. Link, D. L. Stram, V. Wespestad, & D. Woodby (Eds.), *Resiliency of gadid stocks to fishing and climate change* (pp. 39–66). Anchorage, Alaska: University of Alaska Fairbanks, Alaska Sea Grant.

Limborg, M. T., Helyar, S. J., De Bruyn, M., Taylor, M. I., Nielsen, E. E., Ogden, R., … Bekkevold, D. (2012). Environmental selection on transcriptome-derived SNPs in a high gene flow marine fish, the Atlantic herring (*Clupea harengus*). *Molecular Ecology*, *21*, 3686–3703.

Lischer, H. E. L., & Excoffier, L. (2012). PGDSpider: an automated data conversion tool for connecting population genetics and genomics programs. *Bioinformatics*, *28*, 298–299.

Lowry, D. B., & Willis, J. H. (2010). A widespread chromosomal inversion polymorphism contributes to a major life-history transition, local adaptation, and reproductive isolation. *PLoS Biology*, *8*, e1000500.

Ma, J., & Amos, C. I. (2012). Investigation of inversion polymorphisms in the human genome using principal components analysis. *PLoS ONE*, *7*, e40224.

Mächler, M. (2014). *diptest v0.75-6*. Retrieved from https://cran.r-project.org/web/packages/diptest

Madsen, K. S., & Højerslev, N. K. (2009). Long-term temperature and salinity records from the Baltic Sea transition zone. *Boreal Environment Research*, *14*, 125–131.

Madsen, M. L., Nelson, R. J., Fevolden, S. E., Christiansen, J. S., & Præbel, K. (2015). Population genetic analysis of Euro-Arctic polar cod *Boreogadus saida* suggests fjord and oceanic structuring. *Polar Biology*, *39*, 969–980.

Marshall, J., Kushnir, Y., Battisti, D., Chang, P., Czaja, A., Dickson, R., … Visbeck, M. (2001). North Atlantic climate variability: phenomena, impacts and mechanisms. *International Journal of Climatology*, *21*, 1863–1898.

Martinez-Barrio, A., Lamichhaney, S., Fan, G., Rafati, N., Pettersson, M., Zhang, H., … Andersson, L. (2016). The genetic basis for ecological adaptation of the Atlantic herring revealed by genome sequencing. *elife*, *5*, e12081.

Mayr, E. (1942). *Systematics and the origin of species from the viewpoint of a zoologist*. New York, NY: Columbia University Press.

Meier, H. E. M. (2007). Modeling the pathways and ages of inflowing salt- and freshwater in the Baltic Sea. *Estuarine, Coastal and Shelf Science*, *74*, 610–627.

Milano, I., Babbucci, M., Cariani, A., Atanassova, M., Bekkevold, D., Carvalho, G. R., … Bargelloni, L. (2014). Outlier SNP markers reveal fine-scale genetic structuring across European hake populations (*Merluccius merluccius*). *Molecular Ecology*, *23*, 118–135.

Moller, D. (1966). Genetic differences between cod groups in the Lofoten area. *Nature*, *212*, 824.

Molvær, J., Green, N., & Baalsrud, K. (1978). Orienterende hydrokjemisk og biologisk undersøkelse av Hellefjorden, Kragerø. *Norsk Institutt for vannforsning (NIVA)*, *1037*, 1–49.

Myers, R. A., Hutchings, J. A., & Barrowman, N. J. (1996). Hypotheses for the decline of cod in the North Atlantic. *Marine Ecology Progress Series*, *138*, 293–308.

Myksvoll, M. S., Jung, K.-M., Albretsen, J., & Sundby, S. (2014). Modelling dispersal of eggs and quantifying connectivity among Norwegian coastal cod subpopulations. *ICES Journal of Marine Science*, *71*, 957–969.

National Center for Atmospheric Research Staff (Eds). (2015). *The Climate Data Guide: Hurrell North Atlantic Oscillation (NAO) Index (PC-based)*. Retrieved from https://climatedataguide.ucar.edu/climate-data/hurrell-north-atlantic-oscillation-nao-index-pc-based.

Neuenfeldt, S., Righton, D., Neat, F., Wright, P. J., Svedäng, H., Michalsen, K., … Metcalfe, J. (2013). Analysing migrations of Atlantic cod *Gadus morhua* in the north-east Atlantic Ocean: then, now and the future. *Journal of Fish Biology*, *82*, 741–763.

Nielsen, E. E., Grønkjaer, P., Meldrup, D., & Paulsen, H. (2005). Retention of juveniles within a hybrid zone between North Sea and Baltic Sea Atlantic cod (*Gadus morhua*). *Canadian Journal of Fisheries and Aquatic Sciences*, *62*, 2219–2225.

Nielsen, E. E., Hansen, M. M., Ruzzante, D. E., Meldrup, D., & Grønkjaer, P. (2003). Evidence of a hybrid-zone in Atlantic cod (*Gadus morhua*) in the Baltic and the Danish Belt Sea revealed by individual admixture analysis. *Molecular Ecology*, *12*, 1497–1508.

Nielsen, E. E., Hemmer-Hansen, J., Poulsen, N. A., Loeschcke, V., Moen, T., Johansen, T., … Carvalho, G. R. (2009). Genomic signatures of local directional selection in a high gene flow marine organism; the Atlantic cod (*Gadus morhua*). *BMC Evolutionary Biology*, *9*, 276.

Nissling, A., & Westin, L. (1997). Salinity requirements for successful spawning of Baltic and Belt Sea cod and the potential for cod stock interactions in the Baltic Sea. *Marine Ecology Progress Series*, *152*, 261–271.

O'Dea, E. J., Arnold, A. K., Edwards, K. P., Furner, R., Hyder, P., Martin, M. J., … Liu, H. (2014). An operational ocean forecast system incorporating NEMO and SST data assimilation for the tidally driven European North-West shelf. *Journal of Operational Oceanography*, *5*, 3–17.

Olsen, E. M., Knutsen, H., Gjøsæter, J., Jorde, P. E., Knutsen, J. A., & Stenseth, N. C. (2004). Life-history variation among local populations of Atlantic cod from the Norwegian Skagerrak coast. *Journal of Fish Biology*, *64*, 1725–1730.

Øresland, V., & André, C. (2008). Larval group differentiation in Atlantic cod (*Gadus morhua*) inside and outside the Gullmar Fjord. *Fisheries Research*, *90*, 9–16.

Östman, Ö., Eklöf, J., Eriksson, B. K., Olsson, J., Moksnes, P., & Bergström, U. (2016). Top-down control as important as nutrient enrichment for eutrophication effects in North Atlantic coastal ecosystems. *Journal of Applied Ecology*, *53*, 1138–1147.

Pante, E., & Simon-Bouhet, B. (2013). marmap: a package for importing, plotting and analyzing bathymetric and topographic data in R. *PLoS ONE*, *8*, e73051.

Pinsky, M. L., Jensen, O. P., Ricard, D., & Palumbi, S. R. (2011). Unexpected patterns of fisheries collapse in the world's oceans. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 8317–8322.

Pinsky, M. L., & Palumbi, S. R. (2014). Meta-analysis reveals lower genetic diversity in overfished populations. *Molecular Ecology*, *23*, 29–39.

Pogson, G. H., Taggart, C. T., Mesa, K. A., & Boutilier, R. G. (2001). Isolation by distance in the Atlantic cod, *Gadus morhua*, at large and small geographic scales. *Evolution*, *55*, 131–146.

Porras-Hurtado, L., Ruiz, Y., Santos, C., Phillips, C., Carracedo, Á., & Lareu, M. V. (2013). An overview of STRUCTURE: applications, parameter settings, and supporting software. *Frontiers in Genetics*, *4*, 98.

Pritchard, J. K., Stephens, M., & Donnelly, P. (2000). Inference of population structure using multilocus genotype data. *Genetics*, *155*, 945–959.

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A. R., Bender, D., … Sham, P. C. (2007). PLINK: a tool set for whole-genome association and population-based linkage analyses. *American Journal of Human Genetics*, *81*, 559–575.

R Core Team, R Foundation for Statistical Computing (2016). *R: A language and environment for statistical computing*. Retrieved from https://www.r-project.org/

Rambaut, A., Suchard, M. A., Xie, D., & Drummond, A. J. (2014). *Tracer v1.6*. Retrieved from http://beast.bio.ed.ac.uk/Tracer

Reading, B. J., Chapman, R. W., Schaff, J. E., Scholl, E. H., Opperman, C. H., & Sullivan, C. V. (2012). An ovary transcriptome for all maturational stages of the striped bass (*Morone saxatilis*), a highly advanced perciform fish. *BMC Research Notes*, *5*, 111.

Reiss, H., Hoarau, G., Dickey-Collas, M., & Wolff, W. J. (2009). Genetic population structure of marine fish: mismatch between biological and fisheries management units. *Fish and Fisheries*, *10*, 361–395.

Reusch, T. B. H. (2014). Climate change in the oceans: evolutionary versus phenotypically plastic responses of marine animals and plants. *Evolutionary Applications*, *7*, 104–122.

Rice, W. R. (1988). Analyzing tables of statistical tests. *Evolution*, *43*, 223–225.

Roesti, M., Kueng, B., Moser, D., & Berner, D. (2015). The genomics of ecological vicariance in threespine stickleback fish. *Nature Communications*, *6*, 8767.

Rogers, L. A., Olsen, E. M., Knutsen, H., & Stenseth, N. C. (2014). Habitat effects on population connectivity in a coastal seascape. *Marine Ecology Progress Series*, *511*, 153–163.

Ross, S. D., Behrens, J. W., Brander, K., Methling, C., & Mork, J. (2013). Haemoglobin genotypes in cod (*Gadus morhua* L): their geographic distribution and physiological significance. *Comparative Biochemistry and Physiology, Part A*, *166*, 158–168.

Savolainen, O., Lascoux, M., & Merilä, J. (2013). Ecological genomics of local adaptation. *Nature Reviews Genetics*, *14*, 807–820.

Schwander, T., Libbrecht, R., & Keller, L. (2014). Supergenes and complex phenotypes. *Current Biology*, *24*, R288–R294.

Sick, K. (1961). Haemoglobin polymorphism in fishes. *Nature*, *192*, 894–696.

Sick, K. (1965). Haemoglobin polymorphism of cod in the North Sea and the North Atlantic Ocean. *Hereditas*, *54*, 49–69.

Sjöqvist, C., Godhe, A., Jonsson, P. R., Sundqvist, L., & Kremp, A. (2015). Local adaptation and oceanographic connectivity patterns explain genetic differentiation of a marine diatom across the North Sea-Baltic Sea salinity gradient. *Molecular Ecology*, *24*, 2871–2885.

Skjæraasen, J. E., Meager, J. J., Karlsen, Ø., Hutchings, J. A., & Fernö, A. (2011). Extreme spawning-site fidelity in Atlantic cod. *ICES Journal of Marine Science*, *68*, 1427–1477.

Sodeland, M., Jorde, P. E., Lien, S., Jentoft, S., Berg, P. R., Grove, H., … Knutsen, H. (2016). "Islands of Divergence" in the Atlantic cod genome represent polymorphic chromosomal rearrangements. *Genome Biology and Evolution*, *8*, 1012–1022.

Star, B., Nederbragt, A. J., Jentoft, S., Grimholt, U., Malmstrøm, M., Gregers, T. F., … Jakobsen, K. S. (2011). The genome sequence of Atlantic cod reveals a unique immune system. *Nature*, *477*, 207–210.

Stenseth, N. C., Jorde, P. E., Chan, K.-S., Hansen, E., Knutsen, H., André, C., … Lekve, K. (2006). Ecological and genetic impact of Atlantic cod larval drift in the Skagerrak. *Proceedings of the Royal Society B*, *273*, 1085–1092.

Storey, J. D., Taylor, J. E., & Siegmund, D. (2004). Strong control, conservative point estimation and simultaneous conservative consistency of false discovery rates: a unified approach. *Journal of the Royal Statistical Society: Series B*, *66*, 187–205.

Svedäng, H., André, C., Jonsson, P., Elfman, M., & Limburg, K. E. (2010). Migratory behaviour and otolith chemistry suggest fine-scale sub-population structure within a genetically homogenous Atlantic cod population. *Environmental Biology of Fishes*, *89*, 383–397.

Svedäng, H., & Bardon, G. (2003). Spatial and temporal aspects of the decline in cod (*Gadus morhua* L.) abundance in the Kattegat and eastern Skagerrak. *ICES Journal of Marine Science*, *60*, 32–37.

Svedäng, H., Righton, D., & Jonsson, P. (2007). Migratory behaviour of Atlantic cod *Gadus morhua*: natal homing is the prime stock-separating mechanism. *Marine Ecology Progress Series*, *345*, 1–12.

Svedäng, H., & Svenson, A. (2006). Cod *Gadus morhua* L. populations as behavioural units: inference from time series on juvenile abundance in the eastern Skagerrak. *Journal of Fish Biology*, *69*, 151–164.

Therkildsen, N. O., Hemmer-Hansen, J., Als, T. D., Swain, D. P., Morgan, M. J., Trippel, E. A., … Nielsen, E. E. (2013). Microevolution in time and space: SNP analysis of historical DNA reveals dynamic signatures of selection in Atlantic cod. *Molecular Ecology*, *22*, 2424–2440.

Thompson, M. J., & Jiggins, C. D. (2014). Supergenes and their role in evolution. *Heredity*, *113*, 1–8.

Thorsen, A., Kjesbu, O. S., Fyhndr, H. J., & Solemdal, P. (1996). Physiological mechanisms of buoyancy in eggs from brackish water cod. *Journal of Fish Biology*, *48*, 457–477.

Tigano, A., & Friesen, V. L. (2016). Genomics of local adaptation with gene flow. *Molecular Ecology*, *25*, 2144–2164.

Tørresen, O. K., Star, B., Jentoft, S., Reinar, W. B., Grove, H., Miller, J. R., … Nederbragt, A. J. (2017). An improved genome assembly uncovers prolific tandem repeats in Atlantic cod. *BMC Genomics*, *18*, 95.

Uppala, S. M., Kållberg, P. W., Simmons, A. J., Andrae, U., Da Costa Bechtold, V., Fiorino, M., … Woollen, J. (2006). The ERA-40 re-analysis. *Quarterly Journal of the Royal Meteorological Society*, *131*, 2961–3012.

Vähä, J.-P., Erkinaro, J., Niemelä, E., & Primmer, C. R. (2007). Life-history and habitat features influence the within-river genetic structure of Atlantic salmon. *Molecular Ecology*, *16*, 2638–2654.

Vavrek, M. J. (2011). fossil: palaeoecological and palaeogeographical analysis tools. *Palaeontologia Electronica*, *14*, 1T:16.

Via, S., Gomulkiewicz, R., De Jong, G., Scheiner, S. M., Schlichting, C. D., & Van Tienderen, P. H. (1995). Adaptive phenotypic plasticity: consensus and controversy. *Trends in Ecology & Evolution*, *10*, 212–217.

Waples, R. S., & Gaggiotti, O. (2006). What is a population? An empirical evaluation of some genetic methods for identifying the number of gene pools and their degree of connectivity. *Molecular Ecology*, *15*, 1419–1439.

Weir, B. S., & Cockerham, C. C. (1984). Estimating F-statistics for the analysis of population structure. *Evolution*, *38*, 1358–1370.

Wright, S. (1931). Evolution in Mendelian populations. *Genetics*, *16*, 97–159.

Yeaman, S., & Whitlock, M. C. (2011). The genetic architecture of adaptation under migration-selection balance. *Evolution*, *65*, 1897–1911.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

How to cite this article: Barth JMI, Berg PR, Jonsson PR, et al. Genome architecture enables local adaptation of Atlantic cod despite high connectivity. *Mol Ecol.* 2017;26:4452–4466. https://doi.org/10.1111/mec.14207