Genomic stability through time despite decades of exploitation in cod on both sides of the Atlantic

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The mode and extent of rapid evolution and genomic change in response to human harvesting are key conservation issues. Although experiments and models have shown a high potential for both genetic and phenotypic change in response to fishing, empirical examples of genetic responses in wild populations are rare. Here, we compare whole-genome sequence data of Atlantic cod (*Gadus morhua*) that were collected before (early 20th century) and after (early 21st century) periods of intensive exploitation and rapid decline in the age of maturation from two geographically distinct populations in Newfoundland, Canada, and the northeast Arctic, Norway. Our temporal, genome-wide analyses of 346,290 loci show no substantial loss of genetic diversity and high effective population sizes. Moreover, we do not find distinct signals of strong selective sweeps anywhere in the genome, although we cannot rule out the possibility of highly polygenic evolution. Our observations suggest that phenotypic change in these populations is not constrained by irreversible loss of genomic variation and thus imply that former traits could be reestablished with demographic recovery.

fisheries-induced evolution | population genomics | genetic diversity | selective sweeps | historical DNA

As anthropogenic activities rapidly transform the environment, a fundamental question is whether wild populations have the capacity to adapt and evolve fast enough in response (1–3). Phenotypic change can result from phenotypic plasticity, but emerging examples of genomic change over only a few generations have made clear that rapid evolution is also possible (4–6). In the literature, one of the most dramatic and widely cited cases involves the declining age and size at maturation of Atlantic cod (*Gadus morhua*) following several generations of high fishing pressure (3, 7–10). Fisheries produce some of the fastest rates of phenotypic change ever observed in wild populations (2, 11), but the extent to which fisheries-induced evolution has occurred in the wild and the degree to which it is reversible remain strongly debated (12).

The hypothesis that evolution underlies these phenotypic changes is supported by a range of observations. For example, theory on the selective nature of many fisheries reveals that higher rates of harvesting will—with only a few exceptions—favor earlier sexual maturation, greater investment in reproduction, and slower growth (13). In addition, experiments in the laboratory that selectively remove large or small individuals from a population reveal rapid evolution of body size and maturation time in only a few generations, as well as substantial impacts on fishery yields (14–16). Fisheries-induced evolution experiments in the laboratory also reveal selective sweeps through dramatic shifts in allele frequencies, loss of genetic diversity, and increases in linkage disequilibrium at specific locations in the genome (15, 17, 18).

However, translating these findings to wild populations has been substantially more difficult. One concern is that phenotypic plasticity, gene flow, or spatial shifts in populations can also explain the substantial phenotypic and limited genotypic changes reported from the wild to date (10, 13, 19–23). The magnitude and rate of fisheries-induced evolution may also be quite small in the wild (19). While theory provides strong evidence that fishing can be a potent driver of evolutionary changes, a clear empirical demonstration of fisheries-induced evolution would require evidence that the observed change is genetic (13). Whether and to what extent the widespread genomic reorganization observed in experiments also occurs in wild-harvested populations therefore remain unknown.

Genomic analyses of temporal samples before and after selective events have provided key opportunities to test for rapid adaptive evolution from standing genetic variation in wild populations by

Significance

Both theory and experiments suggest that fishing can drive the evolution of an earlier maturation age. However, determining whether changes in the wild are the result of fisheries-induced evolution has been difficult. Temporal, genome-wide datasets can directly reveal responses to selection. Here, we investigate the genomes of two wild Atlantic cod populations from samples that pre- and postdate periods of intensive fishing. Although phenotypic changes suggest fisheries-induced evolution, we do not find evidence for any strong genomic change or loss of genetic diversity. While evolution could have occurred through undetectable frequency changes at many loci, the irreversible loss of late-maturing genotypes appears unlikely. Instead, we suggest that recovery of former phenotypes is possible with reduced fishing pressure.

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identifying unusually strong shifts in allele frequencies over time (4, 5). In addition, the history of genomic research with Atlantic cod (24, 25) provides a unique opportunity to test for genomic signatures of fisheries-induced evolution in particular. Archival samples collected by fisheries scientists decades or even centuries ago represent a valuable source of historical genomic material that can provide rare insight into the genetic patterns of the past (26). Here, we obtained whole-genome sequence data from well-preserved archives of Atlantic cod scales and otoliths (ear bones) that were originally collected from two populations on either side of the Atlantic Ocean: the northeast Arctic population sampled near Lofoten, Norway in 1907 and the Canadian northern cod population sampled near Twillingate, Newfoundland in 1940 (Fig. 1*A* and *SI Appendix*, Table S1). The Canadian northern population collapsed from overfishing in the early 1990s, while the northeast Arctic population experienced high fishing rates but smaller declines in biomass (10, 27, 28). Both populations have shown marked reductions in age at maturation, though with slight increases in maturation age in northeast Arctic cod after 2005 (Fig. 1*B*). We compared these historical genomes with modern data from the same locations (Fig. 1*A* and *SI Appendix*, Table S2). In total, we analyzed 113 individual genomes (*Methods*) from these two unique populations that had independently experienced intensive fishing during the last century (7, 10). We found a marked lack of large genomic changes or selective sweeps through time, suggesting instead that phenotypic plasticity or, potentially, highly polygenic evolution can explain the observed changes in phenotype.

Genomic Stability through Time

We analyzed over 10.9 billion sequencing reads, obtaining an average of 8.1-fold nuclear coverage for the historical ($n = 43$; *SI Appendix*, Table S1) and 9.4-fold coverage for the modern samples ($n = 70$; *SI Appendix*, Table S2). The historical samples showed excellent potential for whole-genome resequencing with high proportions of endogenous DNA (average 0.48) and fragmentation and sequence damage patterns (increases in C>T and G>A transitions) that are expected from authentic, degraded DNA (*SI Appendix*, Figs. S1 and S2). We mapped all reads to a chromosome-scale reference genome assembly from a northeast Arctic individual (25) and—following an extensive set of quality-filtering steps (*SI Appendix*, *Materials and Methods* and Fig. S3)—we analyzed 346,290 single-nucleotide polymorphisms (SNPs) in 113 individuals using approaches based on hard (called) genotypes and genotype likelihoods. Principal-component analysis (PCA) and model-based admixture analysis (*SI Appendix*, *Materials and Methods*) showed support for two genetic groups matching the two geographic locations (Fig. 1 *C* and *D* and *SI Appendix*, Fig. S4). We note that the slight shift of a few historical Canadian samples toward the northeast Arctic population (Fig. 1*C*) could indicate preferential mapping of short historical reads that match the reference genome (reference bias), though further tests did

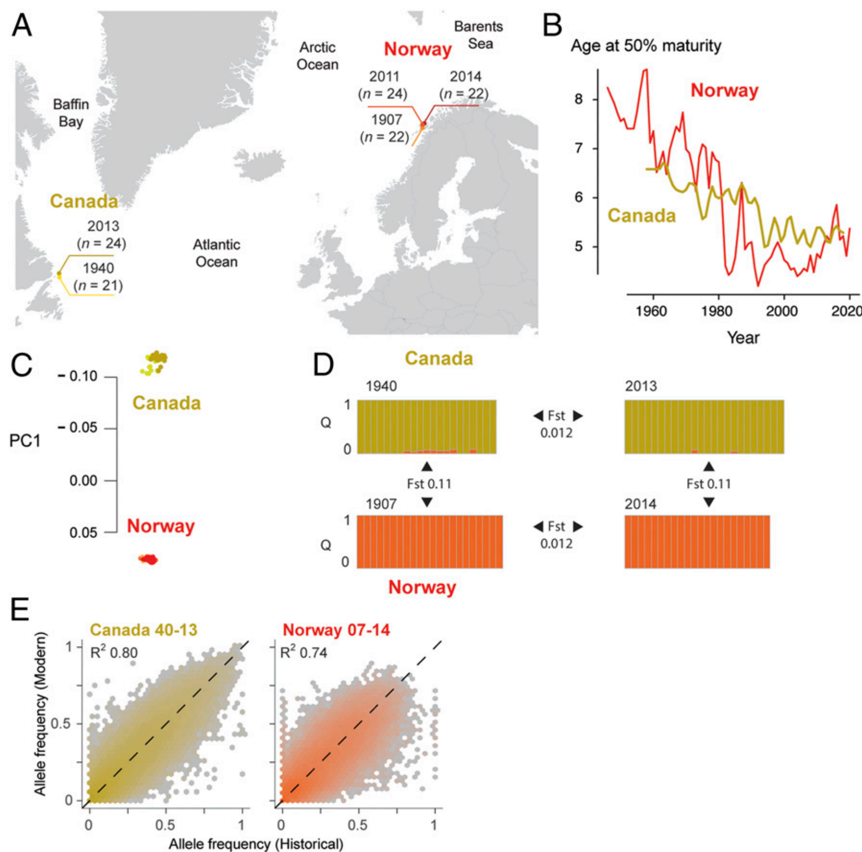

Fig. 1. Spatiotemporal population structure based on genome-wide data in Atlantic cod. (*A*) In total, 113 modern and historical specimens were analyzed from northern cod collected in Newfoundland, Canada (1940, yellow; 2013, dark yellow) and from northeast Arctic cod collected in the Lofoten archipelago, Norway (1907, orange; modern: 2011, red; 2014, dark red). (*B*) Age at 50% maturity over time in each population. (*C*) PCA as implemented in PCAngsd. Velicier's minimum average partial (MAP) test identified a single significant PC and only one PC is shown. Individuals are colored according to *A*. (*D*) Model-based ADMIXTURE ancestry components for historical (1907, 1940) and modern (2013, 2014) populations ($k = 2$; NGSadmix). Each individual is represented by a column colored to show the proportion of each ancestry component for Canada (dark yellow) and Norway (orange). Population differentiation based on pairwise weighted F_{ST} is also shown. (*E*) The correlation between the allele frequencies in historical and modern populations. Colors reflect the relative density of points, from darker (more density) to lighter (less density). R^2, coefficient of correlation.

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not suggest such bias (*SI Appendix*, *Materials and Methods* and Fig. S5). Levels of trans-Atlantic genetic differentiation of F_{ST} = 0.11 (Fig. 1*D* and *SI Appendix*, Fig. S4) agreed with earlier estimates (29). Between historical and modern specimens from the same location, F_{ST} differences were an order of magnitude lower, $F_{ST} \leq 0.012$ (Fig. 1*D* and *SI Appendix*, Fig. S4), and allele frequencies in temporal comparisons were highly correlated (Fig. 1*E* and *SI Appendix*, Fig. S6). Replicated samples from the modern northeast Arctic population (2011 and 2014) have a correlation to each other similar to that in the temporal Canadian 1940 and 2013 comparison (Fig. 1*E* and *SI Appendix*, Fig. S6). The higher temporal correlation among the Canadian samples suggested that reference bias was not a major concern. Together, the genetic clustering of historical individuals with their colocated modern individuals and the high correlation of allele frequencies through time support a genetic continuity at each location, allowing the identification of unusually strong shifts in allele frequency resulting from natural selection in these data.

Genome-wide estimates of temporal frequency change suggested a large harmonic-mean effective population size (N_e) for the time periods covered, consistent with previous estimates in Atlantic cod that suggest drift is very weak (21, 30–32). Our estimates were 10,098 [95% CI 4,757 to 115,586] for northeast Arctic cod and 35,760 [8,206 to 824,430] for Canadian northern cod. In contrast to meta-analyses of fisheries impacts and laboratory experiments (17, 33), levels of genome-wide diversity (π) remained stable through time without exhibiting a decline in either population (Table 1). Genome-wide Tajima's *D* values also did not reveal strong changes through time (Table 1). However, the Canadian northern cod population does reveal other signals of a recent population decline, including elevated linkage disequilibrium and excess heterozygosity (32).

We then conducted a series of scans for selective sweeps by testing if specific regions (50-kb windows with 10-kb step size) of the genome significantly changed in allele frequency, genetic diversity (π), Tajima's *D*, or linkage disequilibrium compared with the genome-wide expectation. Calculating divergence between historical and contemporary samples in both Norway and Canada revealed some regions with F_{ST} up to 0.85, but only for regions with few (two or three) SNP loci, as would be expected from stochastic sampling (Fig. 2 and *SI Appendix*, Fig. S7). All of these peaks were consistent with a null model that randomized F_{ST} values across the observed SNP locations in the genome, thereby testing for any regions that were unusually diverged (Fig. 2 and *SI Appendix*, *Materials and Methods* and Fig. S7). The smallest genome-wide *P* values were 0.1 (*SI Appendix*, Fig. S8 and Table S4). Similarly, changes in diversity (π; *SI Appendix*, Fig. S9), Tajima's *D* (*SI Appendix*, Fig. S10), and linkage disequilibrium (*SI Appendix*, Fig. S11) between early and late samples—all of which are also signals of selective sweeps (34)—revealed no statistically significant ($P < 0.05$) outlier regions (*SI Appendix*, Figs. S12 and S13). Power analyses suggested that the F_{ST} regional outlier tests would be most likely to detect loci experiencing selection coefficients $s \geq 1$ in large populations ($N_e \geq 10{,}000$) (*SI Appendix*, Fig. S14). Overall, these windowed, temporal analyses therefore yielded no statistical support for a strong selective sweep that affected the genome.

Four regions of the genome on LG10, LG11, LG14, and LG20 had unusually high (99th percentile) F_{ST} values in Canadian northern cod, in northeast Arctic 1907 and 2011, and in northeast Arctic 1907 and 2014 comparisons (Fig. 2 and *SI Appendix*, Figs. S7 and S15 and Table S4). Under an assumption of independence between populations, the number of shared outlier regions was higher than expected between Canadian northern cod and northeast Arctic 1907 to 2011 (binomial test, two-sided $P = 4 \times 10^{-7}$, n = 9,509 genomic regions) and between Canadian northern cod and northeast Arctic 1907 to 2014 (two-sided P = 0.0026, n = 9,509 regions). However, three (on LG10, LG11, and LG14) of the four regions were sections of the genome with low SNP density, suggesting these were sampling noise or bioinformatic errors rather than selective sweeps (*SI Appendix*, Fig. S15). The LG11 region was also the F_{ST} outlier region with the lowest *P* value (*SI Appendix*, Fig. S15 and Table S4). The remaining region on LG20 included part of the integrin beta (itgbl1) gene, which is differentially expressed in guppies between male and female brains and is in an integrin-mediated signaling pathway (35).

We further investigated if individual SNPs (rather than genomic regions) revealed signatures of selection, but we found similarly little evidence. Across the genome, F_{ST} values for individual SNPs were generally low, with higher values spread evenly across the genome without distinct outlier clusters (*SI Appendix*, Fig. S16). Comparison against simulations from a Wright–Fisher neutral model identified three loci in northeast Arctic cod with a false detection rate (FDR)-corrected *P* value of 0.13 and one locus in Canadian northern cod at an FDR of 0.2, which were the smallest values found (*SI Appendix*, Table S4). The locus in northeast Arctic cod on LG11 was within one of the four outlier regions shared with Canadian northern cod, though this was also a region with notably low SNP density (*SI Appendix*, Fig. S15).

We also used a principal component-based test for selection that detects unusual divergence of individual SNPs relative to the genome-wide average covariance among individuals (36). The principal-component test suggested that no SNPs were unusually diverged in northeast Arctic cod but that nine loci in Canadian northern cod had an FDR-corrected *P* value below 0.05, none of which overlapped with loci identified by the Wright–Fisher null model (*SI Appendix*, Fig. S17 and Table S4). The potential outlier loci were largely singletons, without clear signals of elevated allele frequency changes at linked loci in the nearby vicinity (*SI Appendix*, Fig. S15). Two outlier loci in Canada co-occurred on LG18 about 32 kbp apart in an intron and in an intergenic region near the phosphatidylethanolamine *N*-methyltransferase (PEMT) gene without raising linkage disequilibrium significantly (*SI Appendix*, Fig. S15). PEMT is involved in phospholipid synthesis, is up-regulated in fasting fish (37), and was previously identified as an outlier region between North Sea and fjord-type cod (38). Power analyses suggested that the principal-component tests would be most likely to detect selection in smaller populations ($N_e \leq 1{,}000$) in which drift was able to drive substantial genome-wide divergence

Table 1. Summary statistics for Atlantic cod samples

Population	Year	*N*	Π	*D*
Canadian northern	1940	21	0.000823 (0.000759, 0.000896)	0.0244 (0.0221, 0.0280)
Canadian northern	2013	24	0.000828 (0.000764, 0.000899)	0.0266 (0.0243, 0.0302)
Northeast Arctic	1907	22	0.000731 (0.000683, 0.000772)	0.0163 (0.0131, 0.0182)
Northeast Arctic	2011	24	0.000759 (0.000701, 0.000815)	0.0197 (0.0183, 0.0217)
Northeast Arctic	2014	22	0.000745 (0.000700, 0.000789)	0.0172 (0.0154, 0.0183)

Columns include the number of individuals (*N*) and estimates for genome-wide pairwise genetic diversity per site (π) and Tajima's *D* with bootstrapped 95% CIs.

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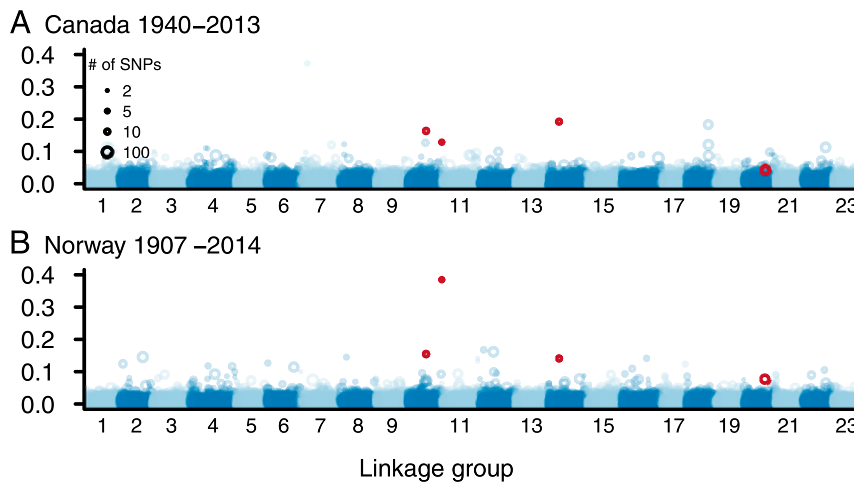

Fig. 2. F_{ST} between temporal samples across the genome for (*A*) Canadian northern cod 1940 to 2013, and (*B*) northeast Arctic cod 1907 to 2014. F_{ST} was calculated in nonoverlapping 50-kb windows. The linkage group is labeled on the *x* axis. Point size indicates the number of SNPs in each window, and color indicates the linkage group. Four regions that are in the highest 99th percentile in the Canadian northern cod and all historical with contemporary northeast Arctic cod comparisons are marked in red. See *SI Appendix*, Fig. S7 for the comparisons involving the northeast Arctic cod 2011 sample.

between historical and modern samples but had high false positive rates for $N_e = 30{,}000$ similar to the cod populations in our study (*SI Appendix*, Fig. S18).

Finally, we examined the quality of the SNPs that came closest to being identified as outliers. We found that the potential outlier SNPs and regions had significantly lower coverage, more missing data, and significantly lower genotype quality, particularly in historical samples (*SI Appendix*, Fig. S19). Those SNPs closest to being identified as under selection were therefore also associated with lower-quality genomic regions that can lead to erroneous genotype calls. While stricter quality filtering would have eliminated these regions, doing so had to be balanced against the potential for removing true signals of selection. We also checked for preferential mapping of historical reads with the reference allele, which could drive apparent outliers. However, we found that only 5 of the 10 potential Canadian outlier loci had a higher frequency of the reference allele in the historical population (as would be expected by chance), and the same was true for only 2 of the 3 potential Norwegian outlier loci.

Discussion

By analyzing temporal, genome-wide data obtained from two exploited Atlantic cod populations from either side of the Atlantic Ocean, we found little evidence for outlier loci suggestive of rapid evolution. In comparison, temporal genomic approaches in terrestrial vertebrates such as rabbit and chipmunk have yielded substantially higher rates of outlier loci that were clustered together, with multiple loci supporting genetic change in specific genomic regions (4, 6). The few outliers that we observed in Atlantic cod are predominantly singletons, with no classic patterns of a genomic sweep affecting the nearby genomic regions. Compared with similar studies, the outlier patterns we observe here are therefore comparatively weak. We interpret this handful of loci with evidence of selection cautiously given the substantial risk of false positives from many selection tests (39, 40), the lack of corroboration among independent methods for identifying outliers, the association of outliers with significantly lower quality genotype calls, and the lack of congruent changes among adjacent loci in the genome. Preferential mapping of short historical sequencing reads that match the reference genome could also produce false positives (41, 42), though we did not find evidence for this reference bias here.

The most striking finding is the contrast between our results from wild populations and similar results from experimental fisheries-induced evolution. Rather than substantial allele frequency changes at hundreds of loci and at large blocks of tightly linked genes, as observed in experiments (15, 17, 18), we find large effective population sizes, no strong signals of selective sweeps, and no loss of diversity in the wild despite decades of intense fishing pressure. These results suggest substantial differences in the response to fishing in the wild and in the laboratory, despite similar phenotypic patterns between wild and experimental populations. Wild populations may have responded largely through phenotypic plasticity rather than genetic evolution, and recent estimates of density-dependent growth in cod show that observed plasticity is sufficient to explain phenotypic changes previously attributed to fisheries-induced evolution (8). Alternatively, evolution may have occurred through subtle allele frequency changes at many loci (43). Our results cannot exclude the possibility of low-intensity or polygenic selection because subtle allele frequency changes are unlikely to have been detected without dramatically larger sample sizes. We also cannot exclude the possibility of evolution in the highly repetitive regions of the cod genome that remain difficult to genotype (25). Major differences between laboratory and wild populations include dramatically larger population sizes in the wild, substantially lower rates of harvest, less dramatic fishery selectivity on life-history traits, multiple sources of selection on traits, and the potential for gene flow from adjacent populations (12, 19, 44). These factors likely help explain why laboratory experiments are not complete models for the complex changes that occur in the wild.

Much of the concern about fisheries-induced evolution relates to impaired recovery even if fishery mortality is reduced (12, 45, 46). Loss of alleles during a selective sweep, for example, might lock a population for an extended period of time in a state of low biomass and maturation at young ages and small sizes. However, our genome-wide scans suggest that such sweeps and loss of adaptive diversity have not occurred in Atlantic cod. In contrast, rapid phenotypic changes due to phenotypic plasticity, small allele frequency changes at many loci, or a combination of the two will preserve the genetic basis for phenotypic reversal and the potential for recovery of previous traits after the population recovers toward unfished biomass. The northeast Arctic cod population may be displaying the initial stages of such a phenotypic reversal, though ongoing low abundance of Canadian

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northern cod may be impeding such a reversal under current conditions (47).

Our genomic findings complement conclusions from literature reviews and evolutionary modeling that, from a management perspective, the direct impacts of fisheries on population abundances and ecosystems are a more pressing concern than the effects of fisheries-induced evolution (12, 19). Avoidance of overfishing and reduction of fishing pressure when population abundances become low therefore remain a key management strategy.

Rapid evolution in response to human predation has been inferred from phenotypic change in a wide range of species (2), but genomic evidence from the wild has been substantially more limited (13). Here, we tested for rapid evolution from standing genetic variation in the widely cited case of Atlantic cod. The evidence suggested no loss of standing genetic variation and a lack of major genomic change in the wild, in strong contrast to the genomic responses observed in laboratory experiments. Our results highlight the necessity of continued focus on understanding how, when, and for which species evolutionary rescue and rapid evolution in the wild do or do not occur.

Methods

We genotyped historical otoliths and scales of Atlantic cod (*G. morhua*) collected during fisheries management surveys in 1940 from the northern cod population in region 2J3KL of Canada near Twillingate, Newfoundland ($n = 21$) and in 1907 from the migratory northeast Arctic stock near Lofoten Island, Norway ($n = 22$; Fig. 1 and *SI Appendix*, *Materials and Methods* and Table S1). Samples had been preserved in research collections. We also genotyped modern tissue samples collected from the same locations in 2013 (Canada; $n = 24$) and in 2011 and 2014 (Norway; $n = 46$). Whole-genome sequencing libraries for the historical samples were prepared in the historical DNA facility at the Natural History Museum in Oslo, Norway following established protocols (48, 49), while modern libraries were prepared at the Department of Biosciences, University of Oslo. Sequencing was performed on an Illumina 2000/2500 using read lengths of 100, 125, and 150 bp (*SI Appendix*, *Materials and Methods*). Reads were mapped to the chromosome-scale gadMor2 Atlantic cod genome assembly (25), and SNP allele frequencies were estimated using ANGSD 0.931 with custom filtering to avoid mapping errors and historical DNA damage patterns (*SI Appendix*, *Materials and Methods*) (50).

To reconstruct phenotypic changes, we fit logistic regressions to the proportion of fish mature in each age class and interpolated the age at which 50% of fish were mature in each year. We used data from the Canadian northern cod 2J3KL stock assessment (27) and the northeast Arctic cod stock assessment (51).

For the genomic analysis, we first used principal-component analysis, admixture, and F_{ST} calculated in ANGSD and NGSAdmix (52) to verify that Canadian northern cod and northeast Arctic cod samples each came from consistent populations through time. We then calculated genetic diversity (π) and Tajima's *D* with ANGSD, identified unlinked loci with ngsLD (53), and calculated effective population size (N_e) with the Jorde–Ryman estimator (54).

Finally, we conducted four types of tests for selective sweeps in the cod genome (see *SI Appendix*, *Materials and Methods* for full details). The first analysis tested for unusually large changes in regions of the genome that would be consistent with a sweep. Specifically, we tested whether any 50-kb region of the genome had larger allele frequency changes, larger declines in diversity (π), larger increases in linkage among loci, or larger changes in Tajima's *D* than would be expected given the distribution of such changes elsewhere in the genome. We generated a null model for the changes in each region by shuffling the temporal pairs of unlinked SNP allele frequencies across the unlinked SNP positions in the genome, recalculating the windowed F_{ST} and π, *D*, and linkage disequilibrium changes from the shuffled values, and calculating a genome-wide *P* value for each region from the null distribution of expected maximum F_{ST} or other changes across the genome. We used the empirical distribution of changes across the genome in order to avoid parametric assumptions about the evolutionary history of the populations that bias many tests for selection (55).

The second analysis tested for an unusually large number of shared genomic regions that had high F_{ST} in pairs of the Canadian northern cod, northeast Arctic 1907 and 2011, and northeast Arctic 1907 and 2014 comparisons. We identified genomic regions that were in the highest 99th percentile for each pair of comparisons and then conducted an exact binomial test for the hypothesis that the number of shared outlier regions was simply a binomial sample from all genomic regions with probability equal to the product of the probabilities of sampling an outlier in each comparison.

The third selective sweep analysis tested for unusual divergence among individuals at particular SNPs using the genome scan method proposed by Galinsky et al. (36) and implemented in PCAngsd 0.982 (56). For this, we removed the individual BM_115 because it was closely related to BM_111. We then applied a false detection rate correction (57).

The fourth analysis compared the allele frequency change at each SNP against a null model that simulated the amount of allele frequency change expected from genetic drift and sampling variance. We used a forward Wright–Fisher neutral simulation based on the empirical N_e and elapsed number of generations in the Canadian northern cod (8) and northeast Arctic cod (11) populations. The number of generations was calculated from the average age of parents weighted by the number of offspring at each age. We calculated a locus-specific *P* value from the null distribution of expected changes and applied an FDR correction. Full details are available in *SI Appendix*, *Materials and Methods*.

In addition, we conducted a power analysis based on selective sweep simulations in SLiM 3.3.2 (58). Each simulation considered 21 chromosomes of 30 Mb with a recombination rate of 3.11×10^{-8} (25, 59). We initialized each simulation with a coalescent burn-in, ran 100 generations of neutral forward simulations to regularize the evolutionary patterns, and then applied positive selection to a SNP near the middle of one chromosome that had a relatively low allele frequency (0.05 or 0.2). We used sample sizes of 22 diploid individuals and an 11-generation timespan between our historical and modern samples to be consistent with the numbers and period covered by our samples.

Data Availability. Analysis scripts and associated data reported in this article are archived as a Git repository through Zenodo at https://doi.org/10.5281/zenodo.4554375. Raw sequencing reads for the historical and modern samples reported in this article are available at the European Nucleotide Archive (project no. PRJEB41431).

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