

Whole genome sequences reveal substantial inbreeding in Sierra Nevada red fox

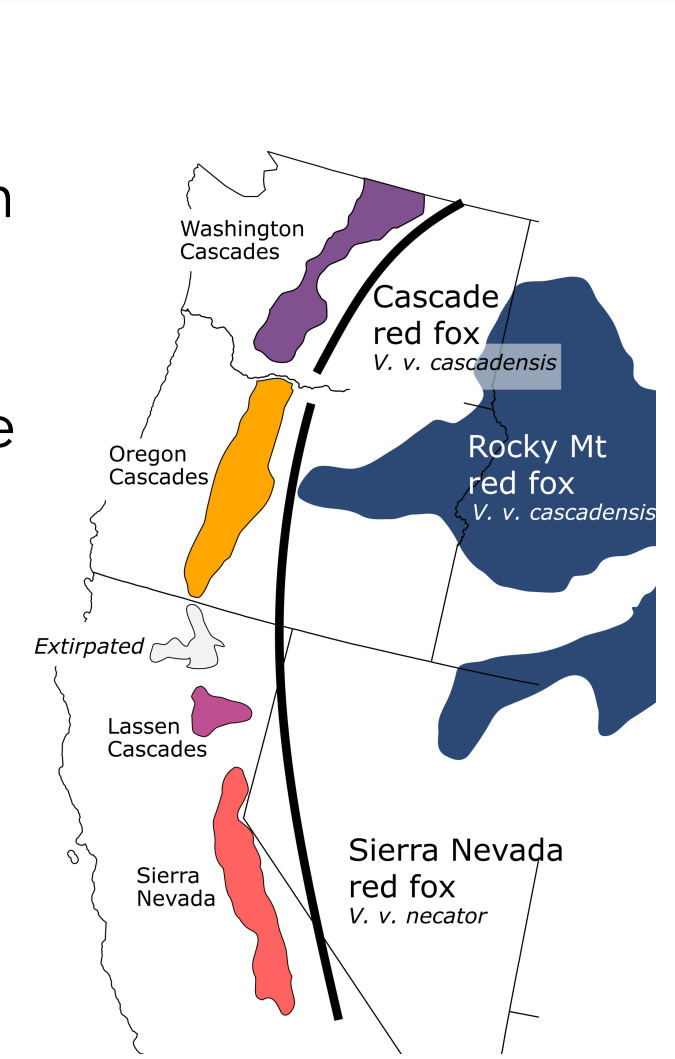
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Background

Conservation of native western red foxes has been hindered by a deficiency of basic population data, particularly estimates of abundance. However, sparse occurrence data suggest 20th century range contractions, the most dramatic of which occurred in the Pacific mountains (Cascades and Sierra Nevada)¹. Low microsatellite genetic diversity combined with an absence of clear contemporary stressors² raise the possibility that inbreeding depression could be contributing to a sluggish recovery of Pacific mountain populations^{3,4}.



Questions

- Is inbreeding depression a risk factor to be mitigated in western red fox populations?
- If genetic rescue is warranted, which populations should serve as translocation sources?

Approach

We re-sequenced whole genomes of 31 red foxes to an average depth of coverage of 17x (5–51x), yielding 16.9 million SNPs.

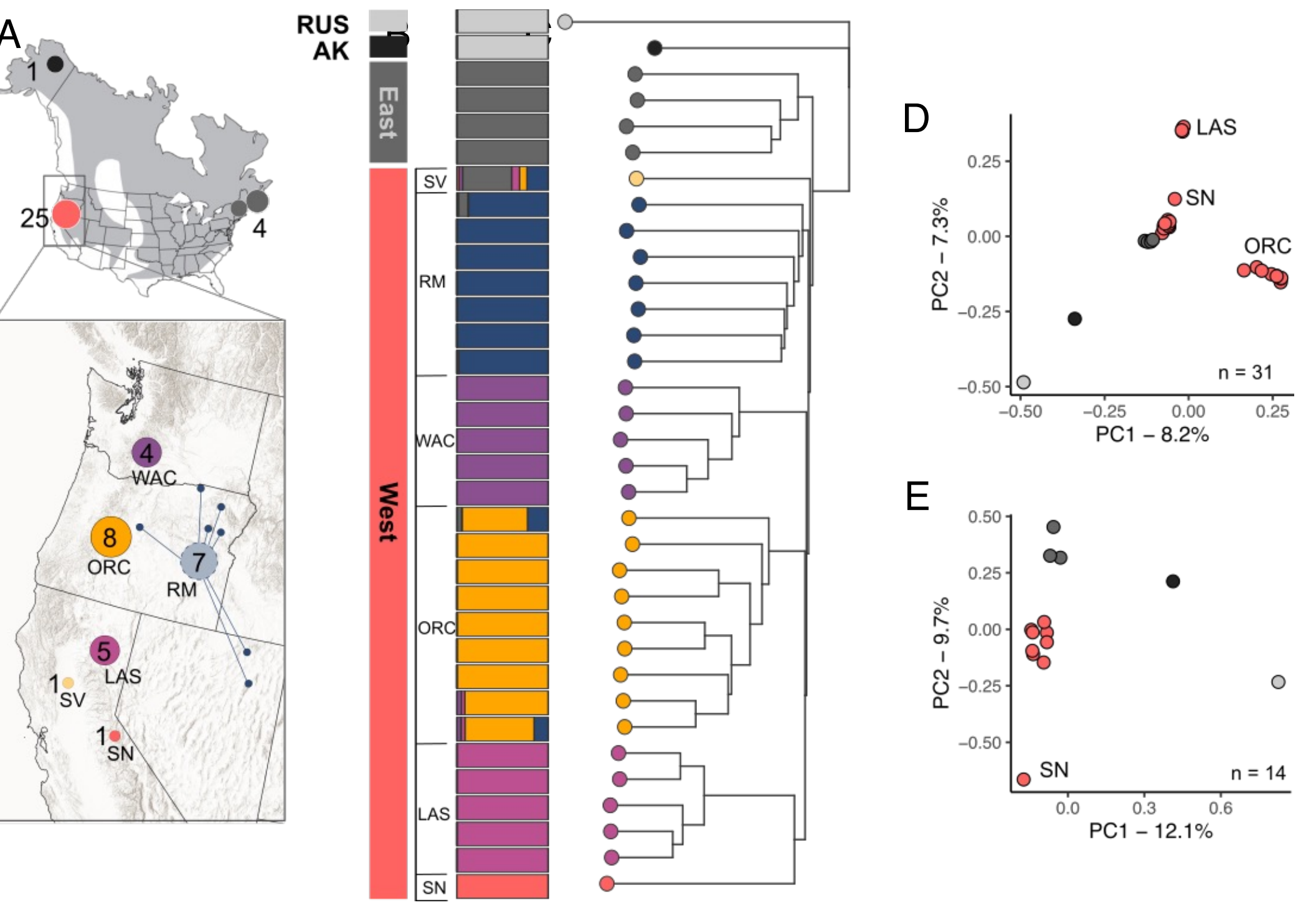


Fig. 1 Red fox sampling and population structure. (A) Localities of 31 red foxes selected for whole-genome resequencing, including Russia (B) Genetic clustering inferred from ADMIXTURE⁵ at K = 7 (C) Neighbor-joining dendrogram based on identity-by-state. (D) PCA of all sequenced samples and (E) PCA for sample set reduced to ≤2 individuals per population.

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Findings

1. Long-term demographic history

Western red foxes share a long-term history:

- large N_e at the Last Glacial Maximum
- trend toward fragmentation in the Holocene

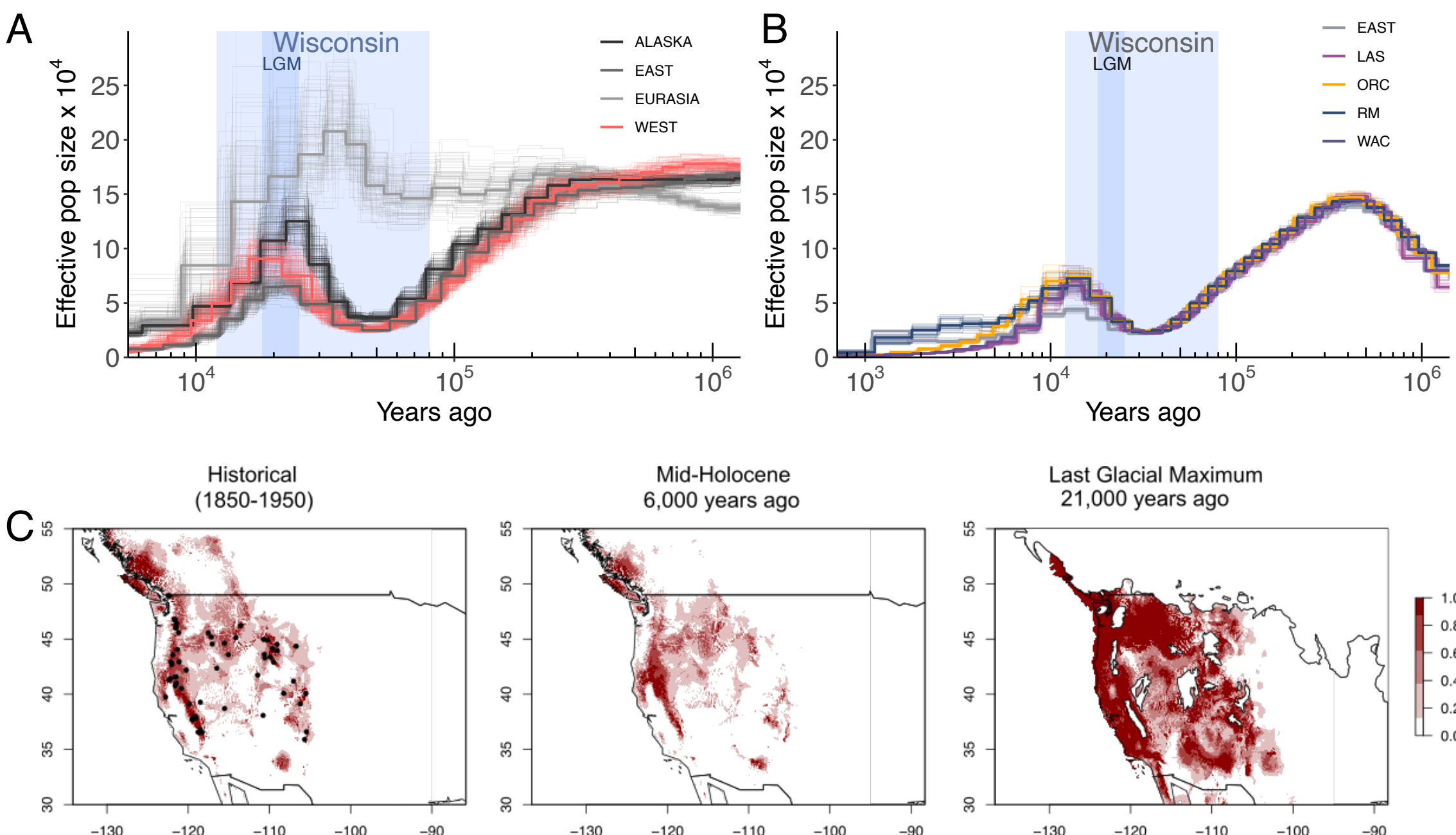


Fig. 2 Long-term demographic history. Inferred changes in effective population size over time using (A) PSMC⁶, based on a single representative for each genetic group and (B) MSMC2⁷, based on 2 samples per group. Both approaches assumed a generation time of 2 years and a per-generation mutation rate of 4.5×10^{-9} . (C) Maxent projections of suitable red fox climatic niche modeled from the location of 60 museum specimen collected before 1950.

2. Recent demographic history

Western red foxes differ in their short-term history

- 21–57% of genomes in runs of homozygosity (ROH)
- Most variation due to differing amounts of long ROH originating in the last 35 years

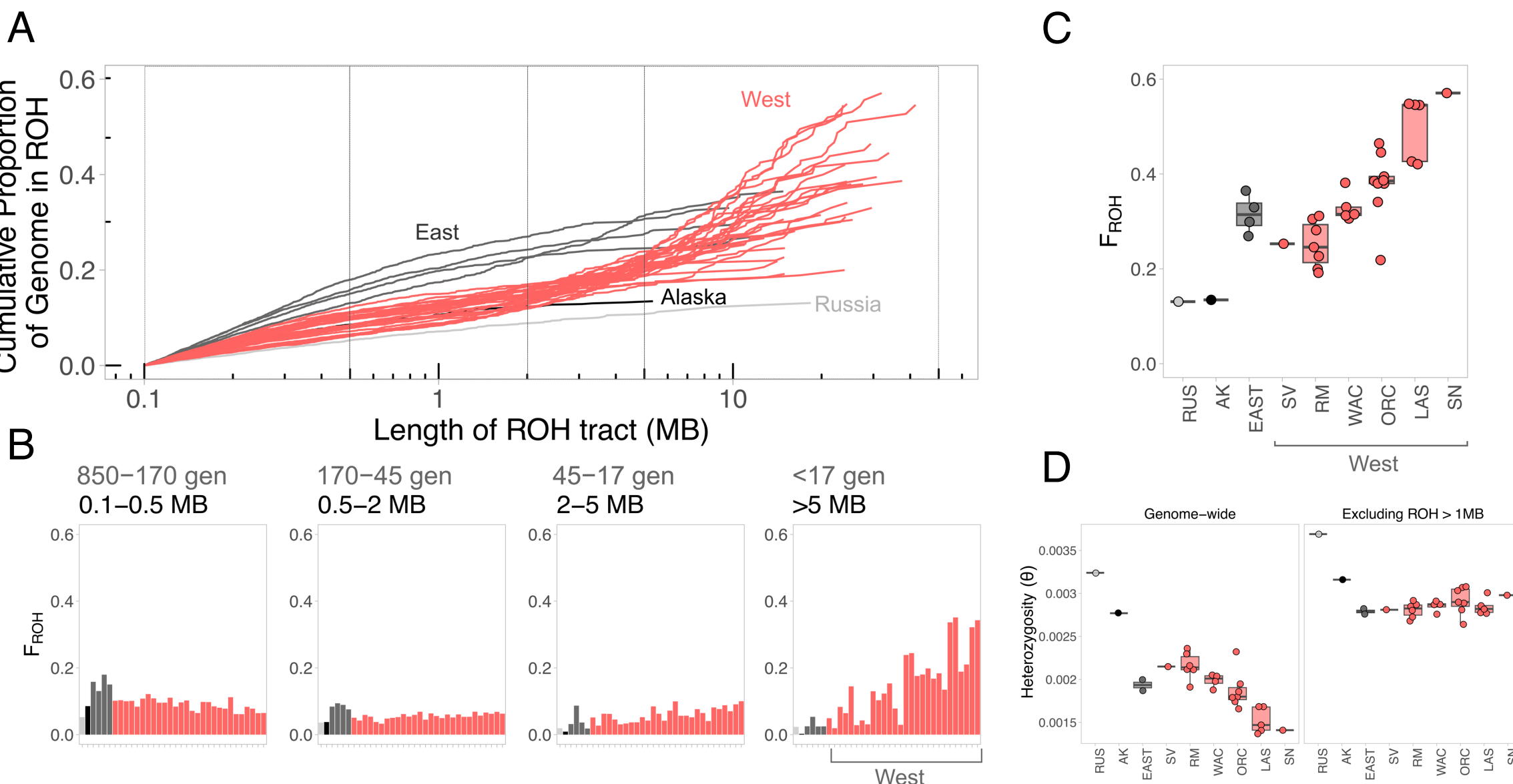


Fig. 3 Inbreeding and genome-wide diversity. (A) Proportion of the genome in runs of homozygosity (ROH) at least 100 KB long. (B) Cumulative proportion of the genome in ROH (top), with the contribution of different length classes shown as bar plots (bottom). (C) Estimates of heterozygosity genome-wide and after excluding ROH >1 MB in length.

3. Deleterious Variation

Total genetic loads are similar among western populations but realized loads differ

- drift and selection may have slightly altered the number and average frequency of deleterious mutations
- expression is chiefly driven by recent inbreeding

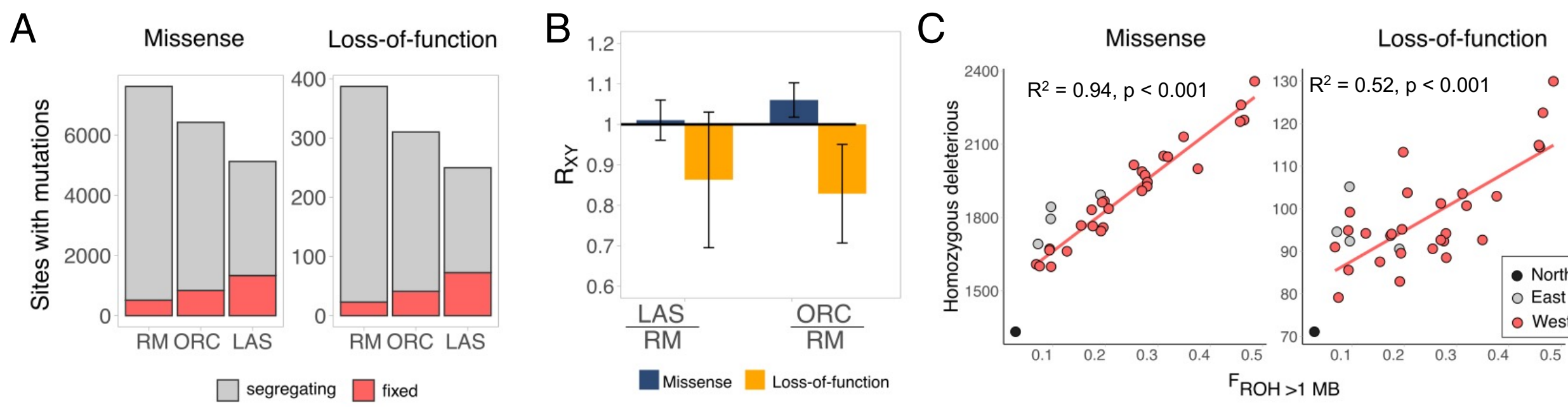


Fig. 4 Genetic load. (A) Segregating and fixed sites with deleterious mutations (B) Frequency of deleterious mutations in population X relative to population Y (R_{XY}); error bars represent ± 2 SE. (C) Relationship between inbreeding and expression of deleterious alleles under a recessive model.

4. Optimal source selection

Genetic rescue is currently being considered for the Lassen (LAS) population² with several candidate donor populations

- Oregon Cascades (ORC) would minimize introduction of novel deleterious variation
- Rocky Mountains (RM) would minimize co-ancestry of donors

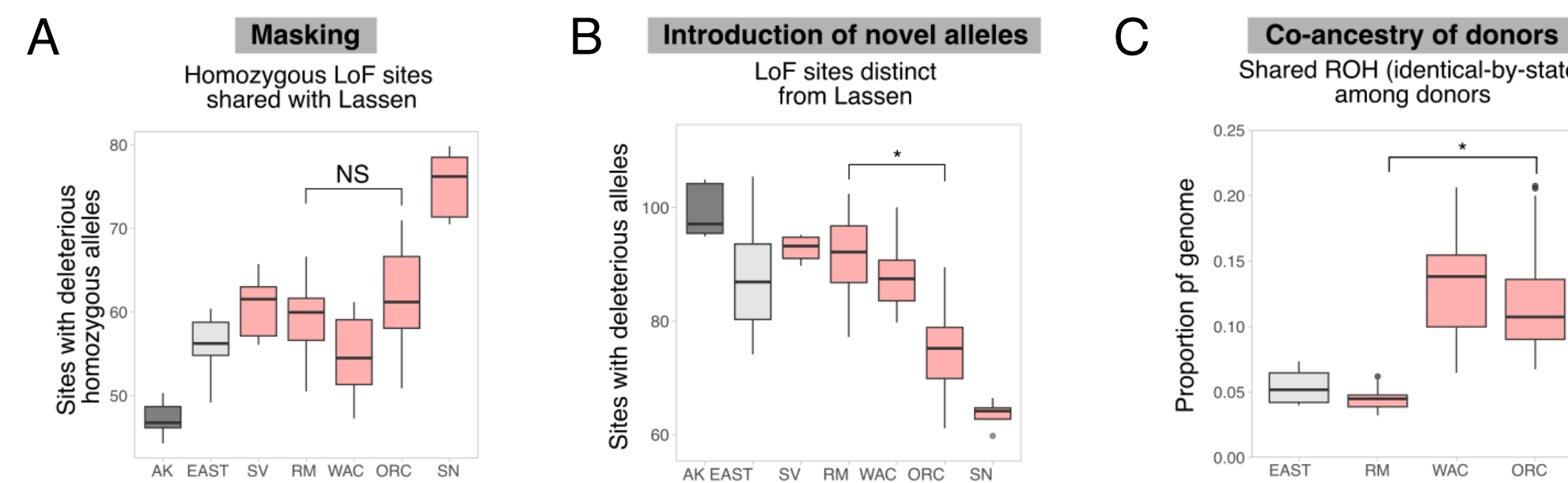


Fig. 5 Optimal source selection for planned genetic rescue of the Lassen population. Distribution of individual pairwise comparisons for (A) number of sites in which both donor and recipient share homozygous deleterious alleles, (B) number of sites where donor introduces a novel deleterious allele not present in recipient genotype, and (C) p two donor individuals.

Conclusions

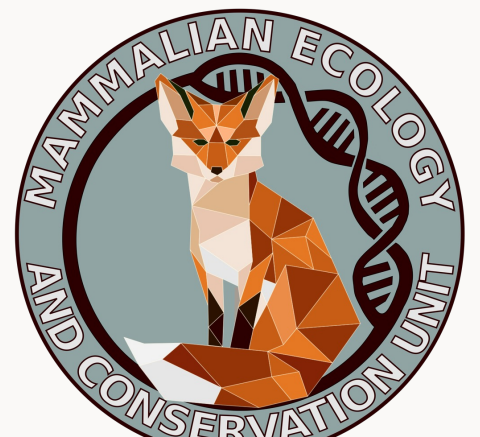
- Pacific mountain populations are likely experiencing reduced fitness due to anthropogenic bottlenecks.
- The recency of declines and similarity of deleterious burdens broadly support deliberate translocations as an appropriate tool for genetic restoration.
- Tradeoffs between the co-ancestry and genetic load suggest the optimal source population for genetic rescue of the Lassen population will depend on its current and projected demographic trajectory.



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