Uncovering Human Adaptations in the Last 400 Years

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1. Limited Insight into Recent Human Adaptations

Urbanization, industrialization, and modern lifestyles have reshaped human traits over the past 400 years. But are these shifts purely cultural and environmental, or ***has natural selection played a role?*** *No genomic method can yet detect selection over this timescale*, as allele frequencies change too slowly. To uncover recent adaptations, we need new genomic signatures.

2. An Alternative Signature of Recent Selection

Stabilizing and directional selection favor chromosomes with a mix of trait-increasing (+) and trait-decreasing (-) alleles. This mix creates negative covariance between like-effect alleles, reducing genetic variance, known as the ***Bulmer effect*** (Bulmer 1971). Thus, ***negative covariance in sampled genomes hints at recent selection***.

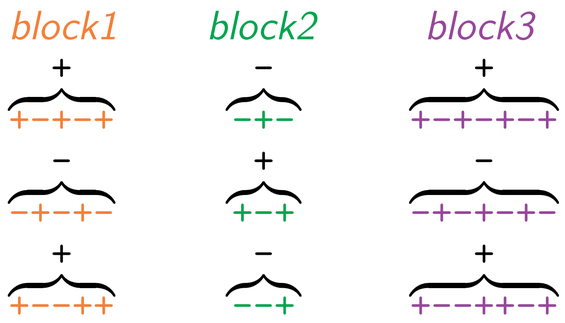
Chromosome	Phenotype
++++	large
−−−−	small
+−+−	intermediate
−+−+	
++−−	
−−++	

3. Uncertainty in Assigning +/- Alleles

Under selection, (+) and (-) alleles ***counteract*** each other, leading to underestimated allelic effect sizes in genome-wide association studies and reducing the power to detect selection.

4. BULMER: A Novel Statistical Genomic Method

Our new method is based on the insight that negative correlations between like-effect alleles also result in negative correlations between ***like-effect linkage disequilibrium (LD) blocks***.

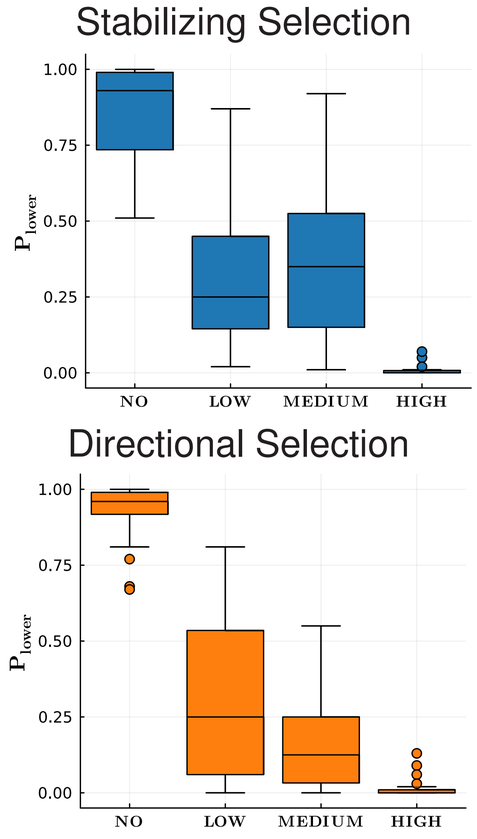


We use the most significant loci from each block in a multivariate regression to estimate the net effects of individual blocks. This reduces the number of loci analyzed, lowering the required sample size.

5. Confounding & Correction

- *Genetic drift* creates correlation with ***random sign***. We use ***randomization*** to test the hypothesis of selection against drift.
- *Population subdivision* ***masks*** the Bulmer effect; we correct for it using a ***clustering*** approach.

6. BULMER Detects Recent Selection



P-values from 30 downsampled bootstrap replicates using forward simulations with SLiM. BULMER detects selection ***within the last 400 years*** (15 generations, $\sim$ 27 years/generation) in large biobank datasets, ***even under population subdivision***.

7. Conclusions

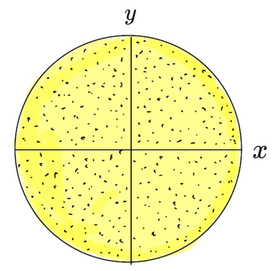
- The Bulmer effect is sensitive to recent stabilizing and directional selection.
- The new method corrects for population subdivision.
- Simulations show selection is detectable in the last 400 years.

8. Future Work

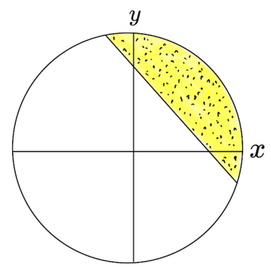
- Differentiate between stabilizing and directional selection.
- Separate recent from ongoing selection.
- Analyze anthropometric, molecular, and life-history traits in the UK Biobank.

Appendix: The Bulmer Effect

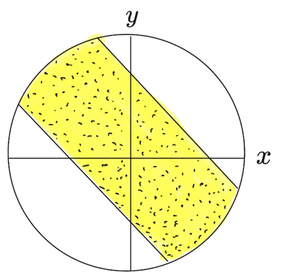
Consider a quantitative trait, such as height, determined by two loci (x & y), whose effects combine ***additively***.



The yellow circle shows all possible heights under neutrality. ***All heights*** have ***equal fitness***. $Cov(x, y) = 0$



Taller heights in yellow strip have ***higher fitness*** under directional selection. $Cov(x, y) < 0$



Intermediate heights in yellow strip have ***higher fitness*** under stabilizing selection. $Cov(x, y) < 0$

Acknowledgements

This work was supported by NSF, and by the Center for High Performance Computing at the University of Utah.

Scan Me!!

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