hapbin: An efficient program for performing haplotype based scans for positive selection in large genomic datasets.

Citation for published version:
Maclean, CA, Chue Hong, N & Prendergast, J 2015, 'hapbin: An efficient program for performing haplotype based scans for positive selection in large genomic datasets.' Molecular Biology and Evolution, vol. 32, no. 11, pp. 3027. DOI: 10.1093/molbev/msv172

Digital Object Identifier (DOI):
10.1093/molbev/msv172

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Molecular Biology and Evolution

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
hapbin: An Efficient Program for Performing Haplotype-Based Scans for Positive Selection in Large Genomic Datasets

Colin A. Maclean,1 Neil P. Chue Hong,1,† and James G.D. Prendergast*,•,‡

1EPCC, School of Physics and Astronomy, University of Edinburgh, Edinburgh, Scotland, United Kingdom
2Roslin Institute, University of Edinburgh, Scotland, United Kingdom
†These authors contributed equally to this work.
*Corresponding author: E-mail: prenderj@gmail.com.
Associate editor: Nicole Soranzo

Abstract

Understanding how the genome is shaped by selective processes forms an integral part of modern biology. However, as genomic datasets continue to grow larger it is becoming increasingly difficult to apply traditional statistics for detecting signatures of selection to these cohorts. There is therefore a pressing need for the development of the next generation of computational and analytical tools for detecting signatures of selection in large genomic datasets. Here, we present hapbin, an efficient multithreaded implementation of extended haplotype homzygosity-based statistics for detecting selection, which is up to 3,400 times faster than the current fastest implementations of these algorithms.

Key words: selection, iHS, EHH, XP-EHH, software.

As a selected allele is swept through a population the haplotype on which it resides will increase in frequency faster than recombination can break it down. As a result alleles under positive selection will be expected to reside upon unusually long haplotypes given their frequency, and such extended haplotype homozygosity (EHH) (Sabeti et al. 2002) forms the basis of a number of the most popular tests of selection including the integrated haplotype score (iHS) (Voight et al. 2006) and the cross-population EHH (XP-EHH) statistic (Sabeti et al. 2007). These haplotype-based methods of detecting selection have a number of advantages over other tests; for example their ability to detect partial or incomplete sweeps (Vitti et al. 2013), short-term balancing selection (Vitti et al. 2013) and their comparative insensitivity to background selection (reduced neutral variation as a result of purifying selection at linked deleterious sites) that can otherwise confound studies of adaptive evolution (Enard et al. 2014). However with sequencing costs falling faster than computational speeds are increasing (Check Hayden 2014), as genomic datasets grow larger it is becoming increasingly difficult to apply these statistics to contemporary cohorts.

Recently an improved implementation of these statistics was made available within the selscan program (Szpiech and Hernandez 2014), demonstrated to be two times faster at calculating iHS than the next fastest algorithm, rehh (Gautier and Vitalis 2012). However even with this improved implementation of these statistics the calculation of iHS across 100 whole human genomes, the approximate average size of a 1000 genomes (1000 Genomes Project Consortium et al. 2010) population cohort, is still expected to take over 2 months when run on a single core on a standard desktop machine. For these algorithms to be widely used, there is a requirement for the development of new, faster, and more efficient, computational approaches to improve the speed at which EHH-based selection scans can be carried out. As a result, allowing for the analysis of whole-genome sequencing datasets of ever increasing size to be processed in reasonable timeframes and on non-specialist hardware.

Here, we introduce hapbin that utilizes a new computational approach (see Supplementary methods, Supplementary Material online) to calculate the EHH, iHS, and XP-EHH statistics. We show that this implementation is up to 3,400 times faster than even selscan, allowing iHS to be calculated across 100 fully sequenced human genomes in ~3 h, as opposed to over 2 months, when run on a single core on a standard desktop machine.

To assess the performance of hapbin, it was first benchmarked alongside selscan on two different hardware architectures. An Amazon c3.8xlarge EC2 Ubuntu instance (32 CPUs) as well as on ARCHER, the UK National Supercomputer. Importantly hapbin will equally run on a standard desktop machine but the use of these resources allowed us to assess its scalability while also enabling other users to repeat these analyses. Performance was characterized using various subsets of data from chromosome 22 of the 1000 genomes project (1000 Genomes Project Consortium et al. 2010) cohort (phase 1 version 3) and both programs were run with default parameters (an EHH decay cutoff of 0.05 and minimum minor allele frequency of 5%).

As shown in figures 1A–C, Supplementary figure S1 and table S1, Supplementary Material online, hapbin is from 88 to 3,400 times quicker than selscan at calculating the iHS, depending on the hardware used and the number of variants and individuals in the input dataset. With an input cohort of 50 individuals hapbin processed all 489,301 genetic variants...
on chromosome 22 in 37 s when run across one core on ARCHER. In comparison, selscan took 35 h. As shown in figure 1D, this speedup comes with no loss of accuracy.

A further advantage of hapbin is that while selscan requires a further program to produce standardized iHS from the unstandardized values it outputs, hapbin produces both by default. As a result all selscan timings presented here are the times taken to calculate unstandardized iHS only, while those for hapbin are for the calculation of both standardized and unstandardized values. Hapbin’s relative speedup at calculating XP-EHH with respect to selscan are more modest than those observed when calculating iHS but order of magnitude speedups are still observed (Supplementary fig. S1, Supplementary Material online).

The hapbin program can be downloaded from https://github.com/evotools/hapbin (last accessed August 10, 2015). Hapbin can be applied to datasets from any meiotically recombinant species and takes phased genotypes in IMPUTE format (Howie et al. 2009), as produced by the popular phasing algorithm SHAPEIT2 (O’Connell et al. 2014). To accompany the program, we have also exploited the speed of hapbin to calculate iHS genome-wide for all 26 populations in the recently released, phased, 1000 genomes phase 3 cohort (Delaneau et al. 2014). These can be downloaded from http://dx.doi.org/10.7488/ds/214 (last accessed August 10, 2015) or viewed at the UCSC genome browser (Supplementary figs. S2 and S3, Supplementary Material online).
**Supplementary Material**

Supplementary methods, figures S1–S3, and table S1 are available at *Molecular Biology and Evolution* online (http://www.mbe.oxfordjournals.org/).

**Acknowledgments**

This work was supported by a UK Biotechnology and Biological Sciences Research Council (BBSRC) Fellowship (to J.G.D.P.) and a UK Engineering and Physical Sciences Research Council (EPSRC) Grant (EP/H043160/1 for the UK Software Sustainability Institute to N.P.C.H.).

**References**


