Efficient identification of SNPs in high linkage disequilibrium in large genotype and sequence datasets

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Introduction

High density SNP & sequence data have:

- Many SNPs
- High co-linearity between loci due to high LD

=> A lot of redundant loci

Introduction

Reduced co-linearity by pruning SNPs based on LD:

- Ideally involves evaluating r^2 (LD) for all pairs of SNPs
- Which is too demanding for (very) large datasets
- So, r^2 are typically only evaluated for a sliding window

Objective

Develop an algorithm to prune for pairwise LD that does *not* require computation of all pairwise r^2 values

Algorithm for an r^2 threshold of 1

- r^2 can only be 1 when minor allele frequencies (MAF) of two loci are *the same*

- So, only r^2 values between pairs of SNPs with *the same MAF* need to be computed

Algorithm for an r^2 threshold of *close to* 1

- r^2 can only be close to 1 when minor allele frequencies (MAF) of two loci are *similar*
- So, only r^2 values between pairs of SNPs with *similar MAF* need to be computed

Software SNPrune

- Sorts loci based on MAF
- Implements the algorithms:
  - for an r^2 threshold of 1
  - for an r^2 threshold of *close to* 1
- Outputs list of removed SNPs & pruned data

- Input can be:
  - Allele counts (0,1,2)
  - Phased alleles (e.g. 0,1)

Data & analysis

Simulated sequence data:

- 10,812,225 segregating SNPs on 2500 individuals
- Phase assumed to be known

Prune data with $r^2 > 0.99$ using:

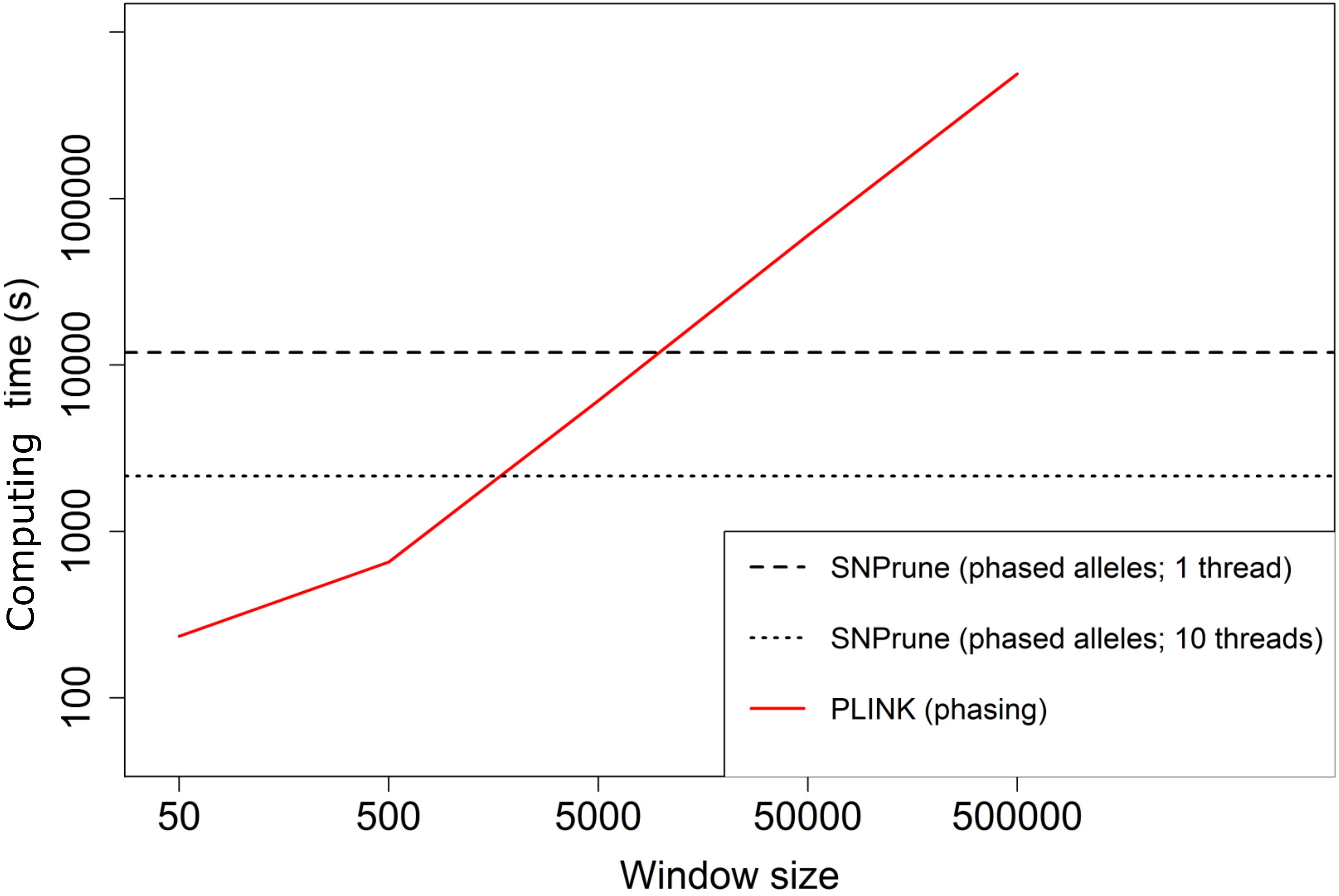
- SNPrune
- PLINK (v1.90 beta)
  - Different windows: 50-500,000 SNPs

Results – numbers of removed SNPs

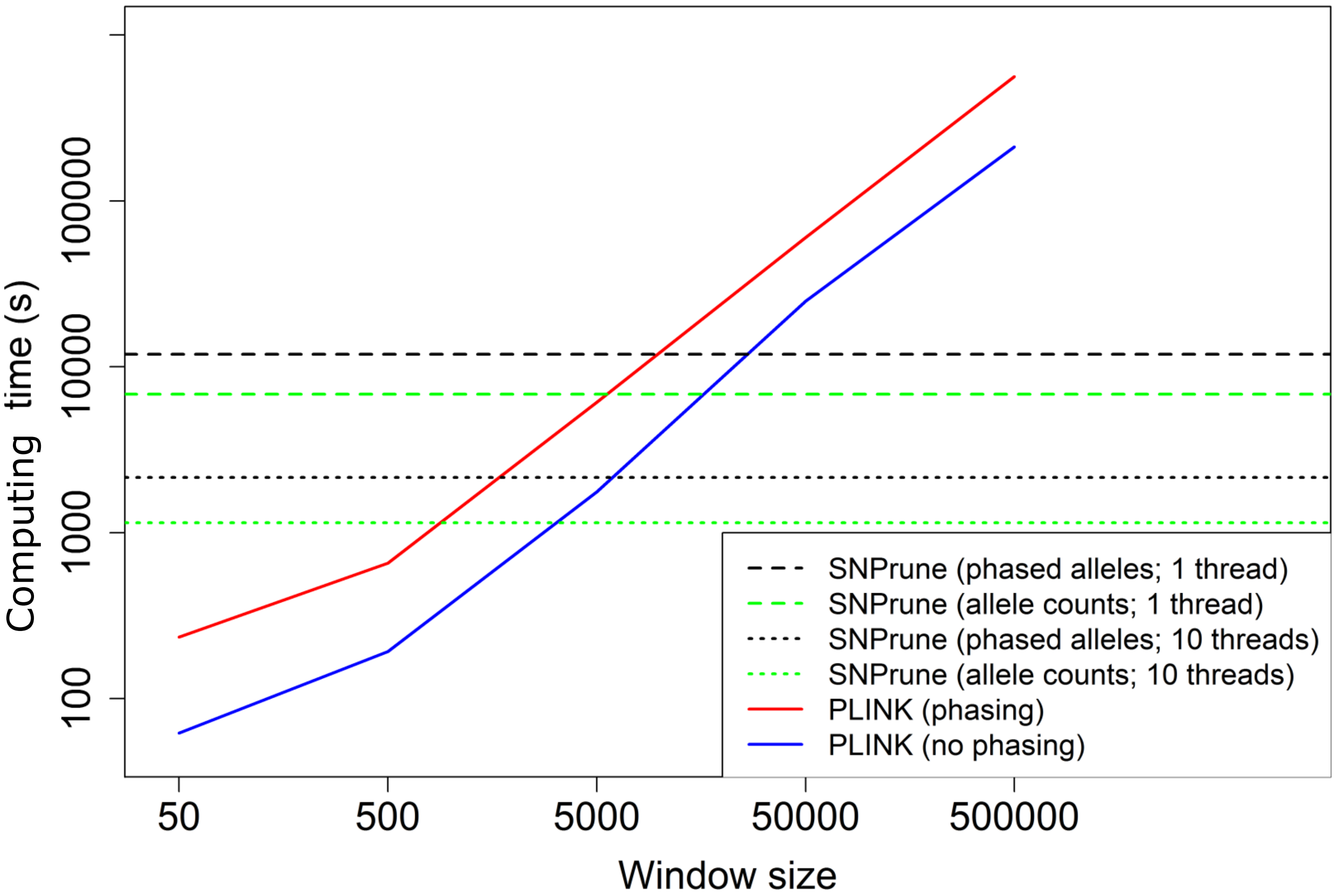
		#SNPs removed	
Software	Window size	Phased alleles	Allele counts
SNPrune	10 812 225	7 796 412	7 796 048
PLINK	500 000	7 752 485	7 752 008
PLINK	50 000	7 751 008	7 750 558
PLINK	5 000	7 741 279	7 740 937
PLINK	500	7 543 234	7 547 118
PLINK	50	5 401 527	5 401 197

- Large redundancy in sequence data
- Results are very similar with and without phasing
- SNPrune computed only 0.06% of all pairwise r^2 values

Results – computing time



Results – computing time



Conclusions

SNPrune is:

- Able to efficiently prune for LD across the genome
- By reducing the number of computed r^2 values
- Therefore feasible for (large) sequence datasets

Thank you!

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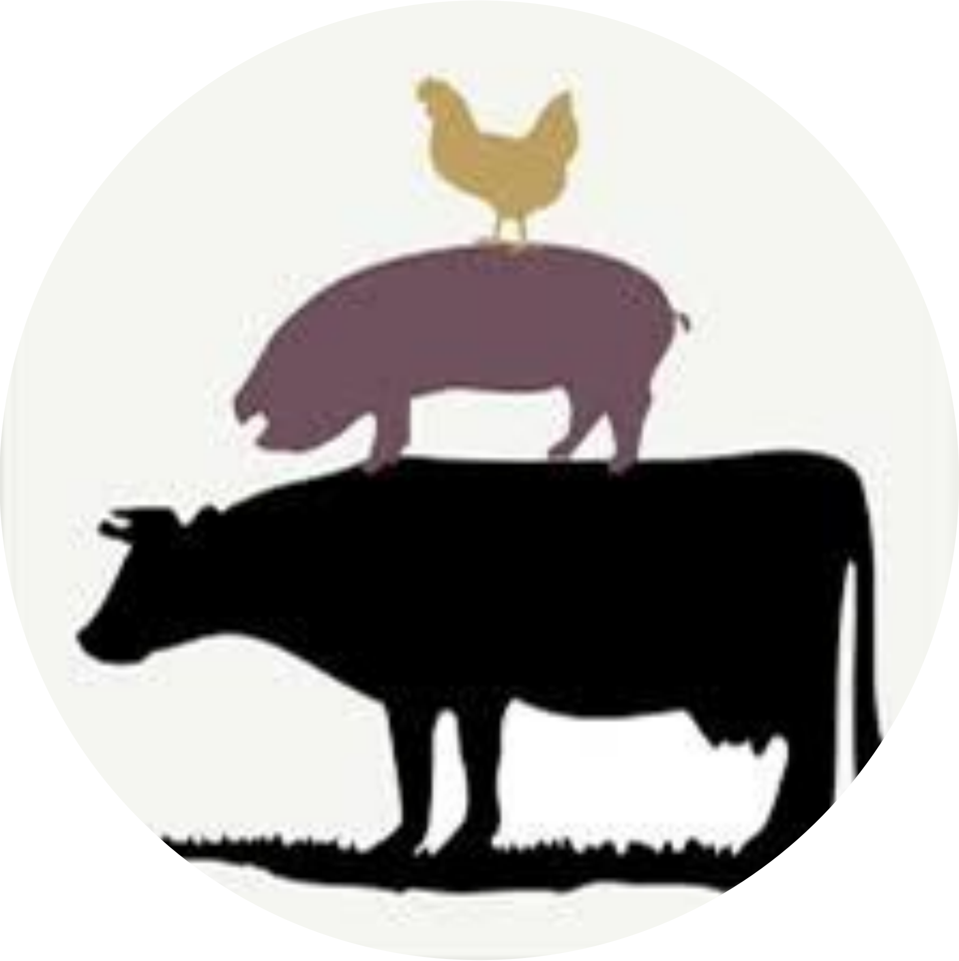

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