Fast Epistasis Detection in Large-Scale GWAS for Intel Xeon Phi Clusters

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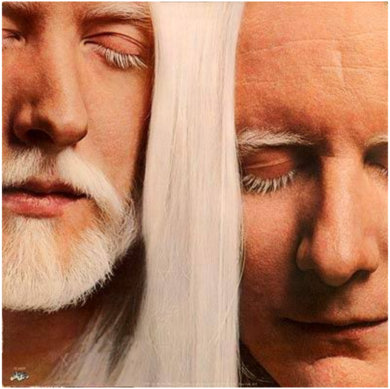
Introduction
Epistasis

Epistasis is the interaction of genes to determine a trait.

Example: albinism (recessive epistasis)

Right: Albino brothers (and famous musicians) Edgar and Johnny Winter (*Source: Edgar Winter*)



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A **quantitative trait** is a phenotype that is expressed as a quantity (e.g., height, weight).

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A **Genome-Wide Association Study (GWAS)** is a statistical association of single nucleotide polymorphisms (SNPs) with phenotypes (observable traits).

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Testing for pairwise epistasis is computationally expensive, requiring a large number of individuals, and $\mathcal{O}(n^2)$ pairwise genetic marker tests.

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- serial optimizations
- improved data distribution for better load balancing and to allow execution using an arbitrary number of MPI processes
- shared-memory parallelism to reduce memory footprint and further improve load balancing
- port to the Intel Xeon Phi coprocessor

Results (average speedup vs. original EPISNPmpi):

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Serial Optimizations

Serial Optimizations
Data Type Changes

Some advantages of using smaller data types for arrays:

- Less main memory usage
- More efficient cache utilization
- SIMD instructions can operate on more data elements per instruction.

Main changes to epiSNP:

- SNP genotypes stored in 1-byte integer instead of 4-byte integer
- Phenotype values can be stored in single precision instead of double (customizable at compile time)

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Serial Optimizations

Dead Code Elimination

A computationally-expensive p-value calculation (accounting for 45% of the original EPISNPmpi run time) was performed for all pairs of SNPs, but this value was not output.

This p-value was recalculated and output for SNPs with the most significant interaction effects.

Compilers try to detect and eliminate *dead code*, but it was too difficult in this case.

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Serial Optimizations

Loop Optimization and Vectorization

Branching (IF statements) inside of loops is bad for performance:

- Inhibits vectorization
- Xeon Phi lacks branch prediction hardware

Code was restructured to remove IF statements from loops where possible.

Serial Optimizations
CDFLIB

epiSNP uses a third-party library of cumulative distribution functions (CDFLIB).

- Replacing *cdft()* with *cumt()* improved performance
- Declaring *cumt()* as `elemental` in an interface block further improved performance
- Using equivalent CDFLIB90 subroutine (*cum_t()*) resulted in severe performance regression, despite claims of improved performance of CDFLIB90 over CDFLIB

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EPISNPmpi Data Distribution

The data distribution used by EPISNPmpi has two limitations:

- Load imbalance: some ranks compute $5n^2$ pairwise tests, while others compute $3n + \frac{5n(n-1)}{2} = \frac{5}{2}n^2 + \frac{1}{2}n$ pairwise tests
- Number of MPI processes used (P) limited to $P \in \{1, 1+2, 1+2+3, ...\}$

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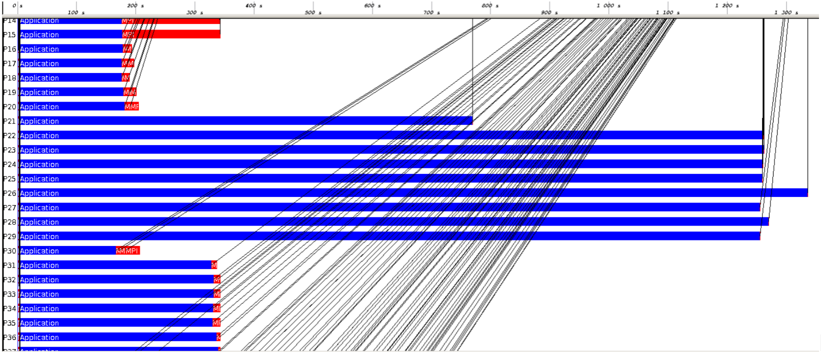
EPISNPmpi Load Imbalance



Intel Trace Analyzer Event Timeline for EPISNPmpi ranks 14-37 (out of 56) Each horizontal bar is an MPI process (blue: program execution; red: MPI communication). Black lines connect communicating processes.

MPI

Improved Load Balancing

Example: $N = 10$ SNPs, $P = 4$ MPI processes

SNP_1 \ SNP_2	1	2	3	4	5	6	7	8	9	10	
1											rank 1
2											rank 2
3											rank 3
4											rank 4
5											rank 4
6											rank 3
7											rank 2
8											rank 1
9											rank 1

MPI

Improved Load Balancing

This improved load balancing method:

- Alleviates most load imbalance
- Allows the use of an arbitrary number of MPI ranks, allowing a flexible number of nodes/cores/Xeon Phi coprocessors
- Facilitates OpenMP parallelization

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OpenMP was used to implement shared-memory parallelism in epiSNP

- Facilitates more efficient load balancing
- Allows MPI rank 0 to read input data faster, using multiple threads
- Reduces MPI communication
- Reduces memory footprint by sharing data structures that would otherwise be replicated
- Required to fully utilize Intel Xeon Phi coprocessor due to per-process memory constraints

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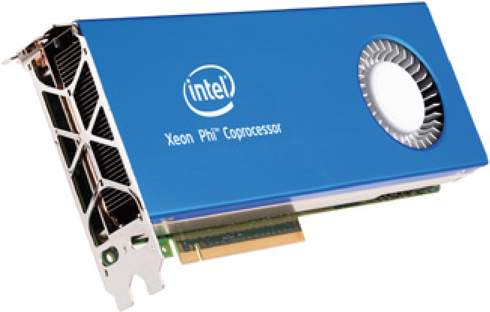

Figure: The Intel Xeon Phi coprocessor (aka MIC)

MIC
epiSNP on Accelerators

epiSNP was a good candidate for porting to an accelerator due to several characteristics:

- Abundant parallelism in computationally-intensive portions of the code
- Relatively small memory footprint in new hybrid MPI+OpenMP version
- Little data movement relative to computation

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MIC
Specifications

The Intel Xeon Phi (MIC) "Knights Corner" generation features:

- Over 1 teraFLOPS double-precision peak performance
- Up to 3 times the performance per watt vs. Intel Xeon E5-2697v2
- 57 - 61 processor cores
- 1.1 - 1.238 GHz
- 4 threads per core
- 512-bit vector registers
- 6GB - 16GB memory

MIC
MIC vs. GPU

The Intel Xeon Phi coprocessor (MIC) has a couple advantages over NVIDIA GPUs as an accelerator target for epiSNP:

- Allows the use of the same programming language (Fortran)
- Optimized epiSNP could run as-is on the MIC with reasonable performance (approx. 1.5X faster than host Xeon CPUs)

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Programming Models

An MPI application can be run on the MIC using one of three execution modes (*native*, *offload*, *symmetric*).

Symmetric mode (MPI processes run on both hosts and coprocessors) was chosen for epiSNP

- simplicity: no code modification required (initially)
- flexibility: arbitrary numbers of host processors and MIC coprocessors

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Load Balancing Host and MIC

Problem: host processors and MIC coprocessors don't have the same performance characteristics.

- This leads to load imbalance when MPI processes execute on both the host and MIC.

Solution: Allow user to specify a *MIC Performance Factor* (F) so that additional comparisons would be assigned to the faster processes.

- Implemented as an environment variable (`EPISNP_MIC_PERF_FACTOR`)

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Benchmarking

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Benchmark data set:

- 1,634 individuals (Angus sired cattle)
- 774,660 SNPs
- 45 traits (fatty acid content)

Since epiSNP scales linearly with the number of traits, a single trait (stearic acid content) was chosen for benchmarking.

Environment

Stampede

Source: Texas Advanced Computing Center

Environment

Compute node specs

- 2×8-core Intel Xeon E5-2680 2.7GHz CPUs
- 32 GB DDR3-1600MHz memory
- 1 or 2×61-core Xeon Phi SE10P 1.1GHz coprocessors

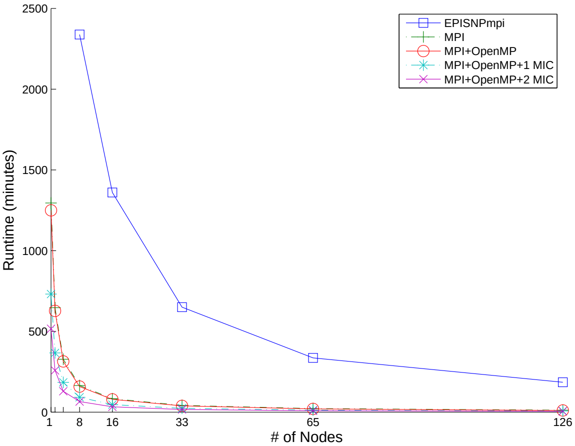
Software Environment

- Intel Fortran 14.0.1.106
- Intel MPI 4.1 Update 1[a]

[a] MVAPICH2 2.0b was used for original EPISNPmpi when run on 16 nodes

Results

Runtime



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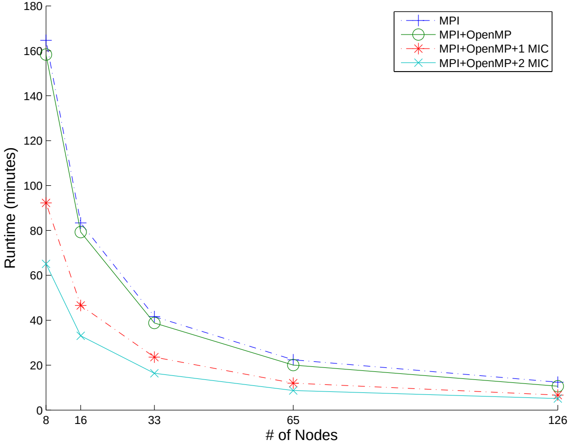
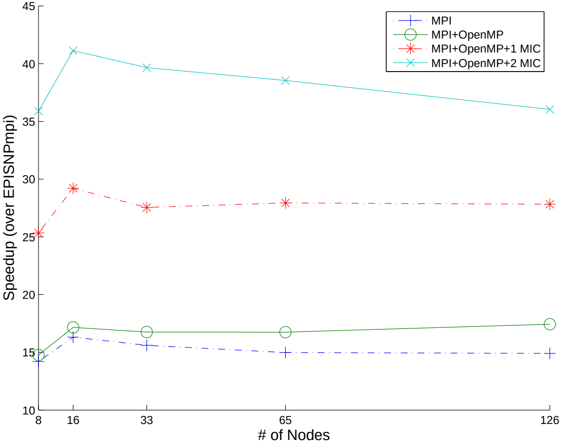
Runtime (without original EPISNPmpi)



Results

Speedup (over EPISNPmpi)



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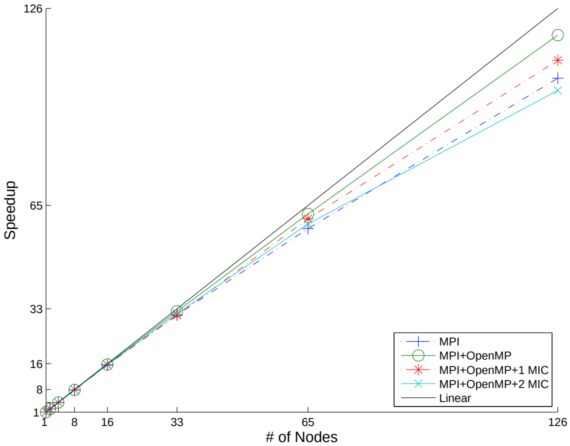

Results
Node Hours

nodes	EPISNPmpi	MPI	MPI + OpenMP	MPI + OpenMP 1 MIC	MPI + OpenMP 2 MIC
1		21.58	20.82	12.19	8.61
2		21.55	20.90	12.21	8.61
4		21.84	20.91	12.30	8.62
8	311.78	21.96	21.11	12.30	8.69
16	362.68	22.22	21.14	12.42	8.82
33	357.46	22.91	21.33	12.97	9.01
65	363.65	24.27	21.71	13.01	9.44
126	388.50	26.06	22.28	13.97	10.77

Conclusions

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Acknowledgment

Yang Da

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Questions

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