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Automated Genotypic Imputation of PAGE II Data using Scientific Workflows

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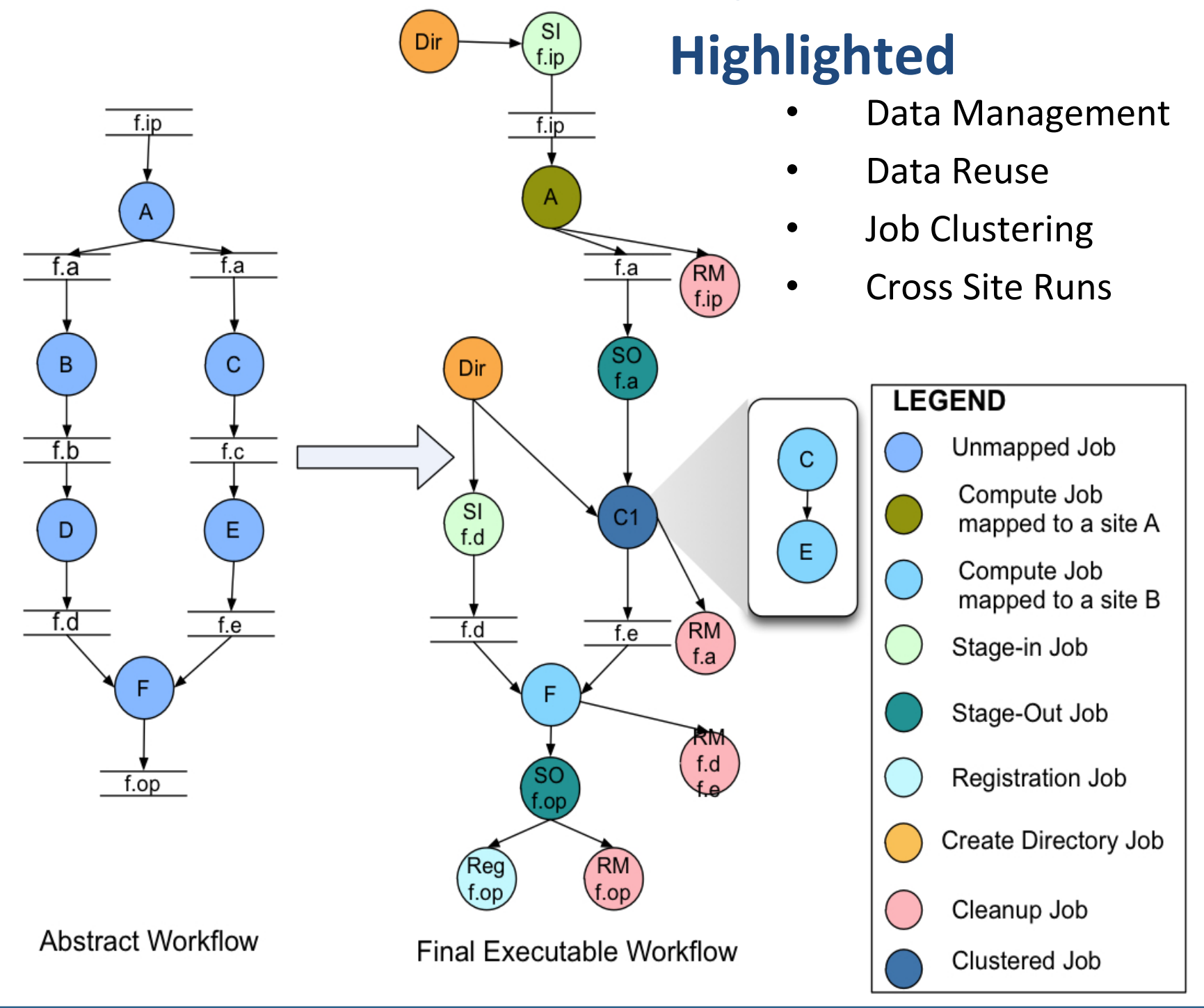
Background

- PAGE II (Population Architecture using Genomics and Epidemiology) study has genotyped 50,000 samples using MEGA, an Illumina high density consortium-built array array.
- We are also imputing an additional 50,000 subjects genotyped in 20 different GWAS studies.
- Imputation is done using SHAPEIT and IMPUTE2 with 1000 Genomes Project Reference Panel.
- Imputation can be parallelized by chromosome to reduce total processing time.
- We decided to use the Pegasus Workflow Management System to do runs on the Rutgers Genetics Cluster.

A Scientific Workflow

- Allows users to easily express multi-step computational tasks.
- Describes the dependencies among the tasks.
- Manages data flow.



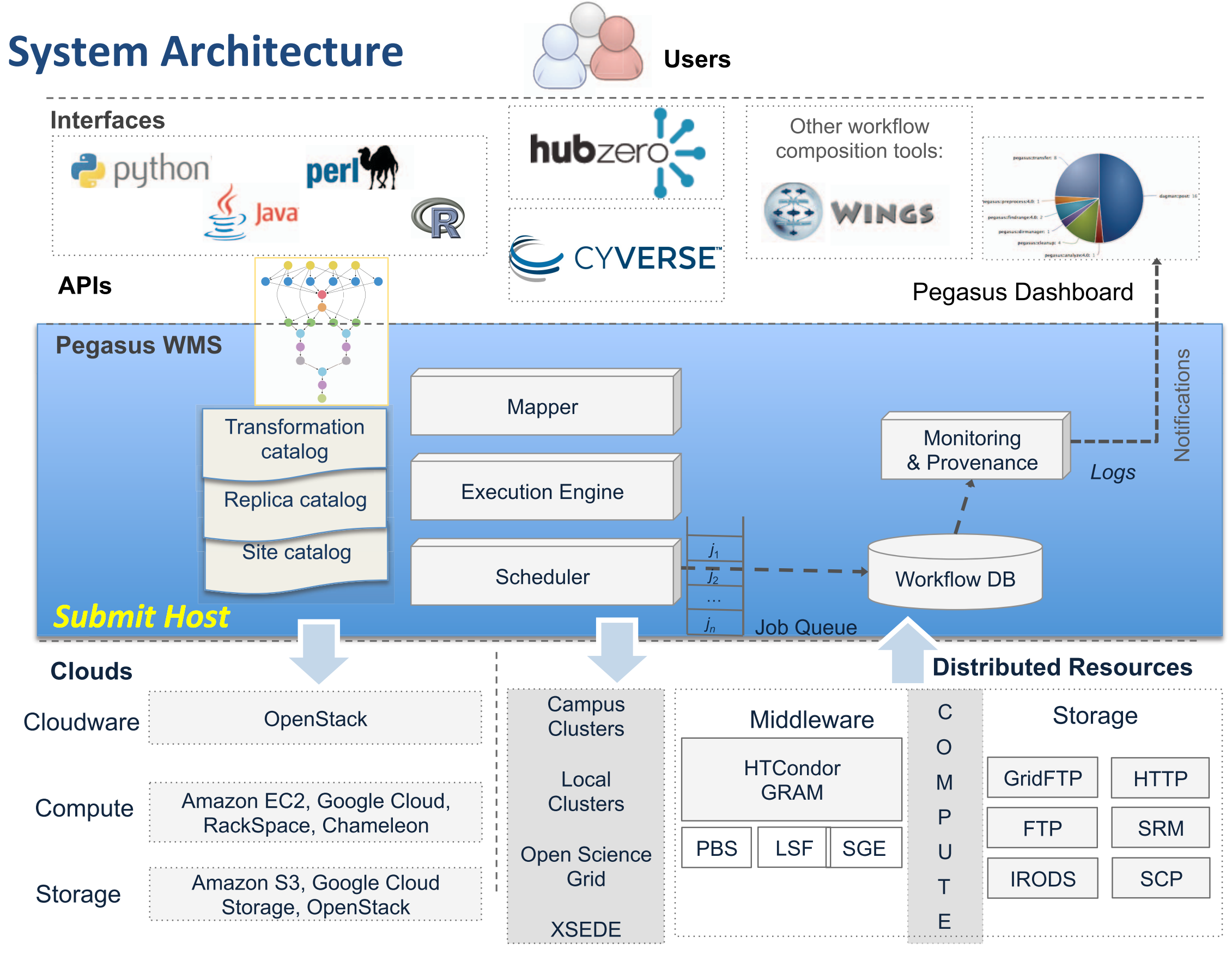
Capabilities Highlighted

- Data Management
- Data Reuse
- Job Clustering
- Cross Site Runs

Pegasus Workflow Management System

- General, open source solution for describing and executing workflows on laptops, clusters and clouds.
- Provides Python, Java, and Perl APIs for workflow creation.
- Provides portability, reliability, performance.

System Architecture



Documentation
http://pegasus.isi.edu

Applications
https://pegasus.isi.edu/application-showcase/

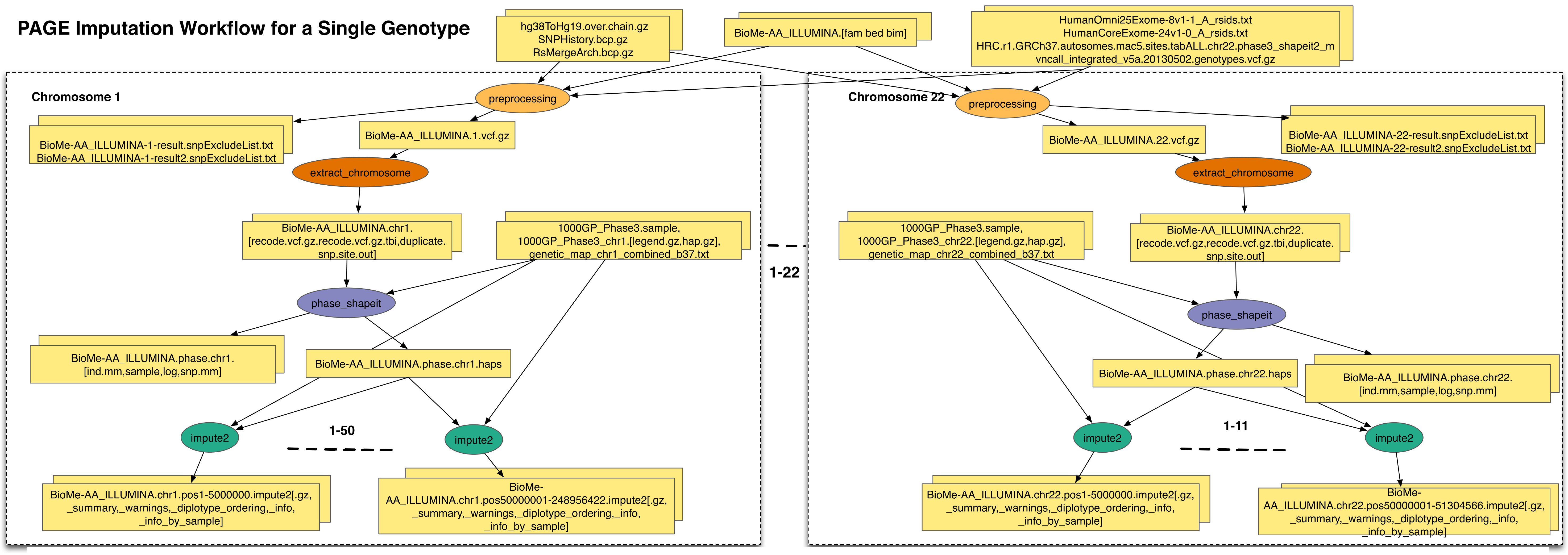
User Support
pegasus-users@isi.edu

Can handle workflows with millions of tasks, TB's of data.

- Can optimize the workflow from the point of view of performance, can handle data management across local and wide area networks, leveraging parallel file systems and object stores.
- Used in a number of domains: astronomy, bioinformatics, earthquake science, helioseismology, gravitational-wave physics, seismology, etc.

PAGE II Imputation Pipeline

PAGE Imputation Workflow for a Single Genotype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SNPHistory.bcp.gz
RsMergeArch.bcp.gz
BioMe-AA_ILLUMINA.[fam bed bim]
HumanOmni25Exome-8v1-1_A_rsids.txt
HumanCoreExome-24v1-0_A_rsids.txt
HRC.r1.GRCh37.autosomes.mac5.sites.tabALL.chr22.phase3_shapeit2_mvncall_integrated_v5a.20130502.genotypes.vcf.gz
Chromosome 1
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BioMe-AA_ILLUMINA-1-result2.snpExcludeList.txt
BioMe-AA_ILLUMINA.1.vcf.gz
extract_chromosome
BioMe-AA_ILLUMINA.chr1.[recode.vcf.gz,recode.vcf.gz.tbi,duplicate.snp.site.out]
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phase_shapeit
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BioMe-AA_ILLUMINA.phase.chr1.haps
impute2
1-50
impute2
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1-22
Chromosome 22
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BioMe-AA_ILLUMINA-22-result2.snpExcludeList.txt
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BioMe-AA_ILLUMINA.phase.chr22.[ind.mm,sample,log,snp.mm]
impute2
1-11
impute2
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BioMe-AA_ILLUMINA.chr22.pos50000001-51304566.impute2[.gz,_summary,_warnings,_diplotype_ordering,_info,_info_by_sample]

Pipeline available at **https://github.com/pegasus-isi/page-imputation**

- Many resources have been put into dense genotyping - we want to maximize the utility of that data.
- Multi-center consortia have heterogenous collections of GWAS array data.

Tools used

- Plink
- liftOver
- LiftRsNumber.py
- HRC-check-bim.pl
- vcftools
- SHAPEIT
- IMPUTE2

Inputs

- 53536 samples across 17 studies (71MB to 2.6GB)

Outputs

- Range from 21GB to 204GB
- Made available via the PAGE FTP Server

Benefits of Pegasus Workflows for Imputation

- Imputation results offer a common data framework, but the heterogeneity of the inputs can present difficulties.
- Future updates to imputation reference panels mean that the entire process may need to be repeated.
- This workflow is agnostic as to array, strand, and build of the input data
- If components of the imputation fail (in our case, usually because of our heterogeneous compute cluster), PEGASUS can automatically resume the required components while not repeating the completed components.
- Pegasus keeps the many component files distinct and prevents filename collisions.
- Once constructed, the workflow requires almost no analyst effort - literally a few minutes per dataset.
- To re-impute with a new panel therefore also requires almost no analyst effort.

Workflow Tracking and Error Reporting

- Workflow progress can be monitored through the pegasus dashboard, or the user can wait for workflow completion email notification.
- Generates an error report when things go wrong.
- Error reports indicate the source of error and what tasks failed.

Failure Reasons

- Jobs failed because of incorrect memory estimates or low memory available on nodes.
- Input data not clean. Some allele names are recorded as 0, scripts were modified to use PLINK to generate cleaned datasets from the bim files.

Recovery Semantics

- Ability to recover and resubmit pipeline from point of last failure.
- Automatic job retries.
- If everything else failed, memory requirements were increased and workflow was submitted again, pruning the jobs that were successfully executed part of the previous failed run.
- **For the largest study, impute jobs took about 42GB of memory.**

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