Sequence-based Association, Interpretation, Visualization using EPACTS

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Sequence Analysis Workshop

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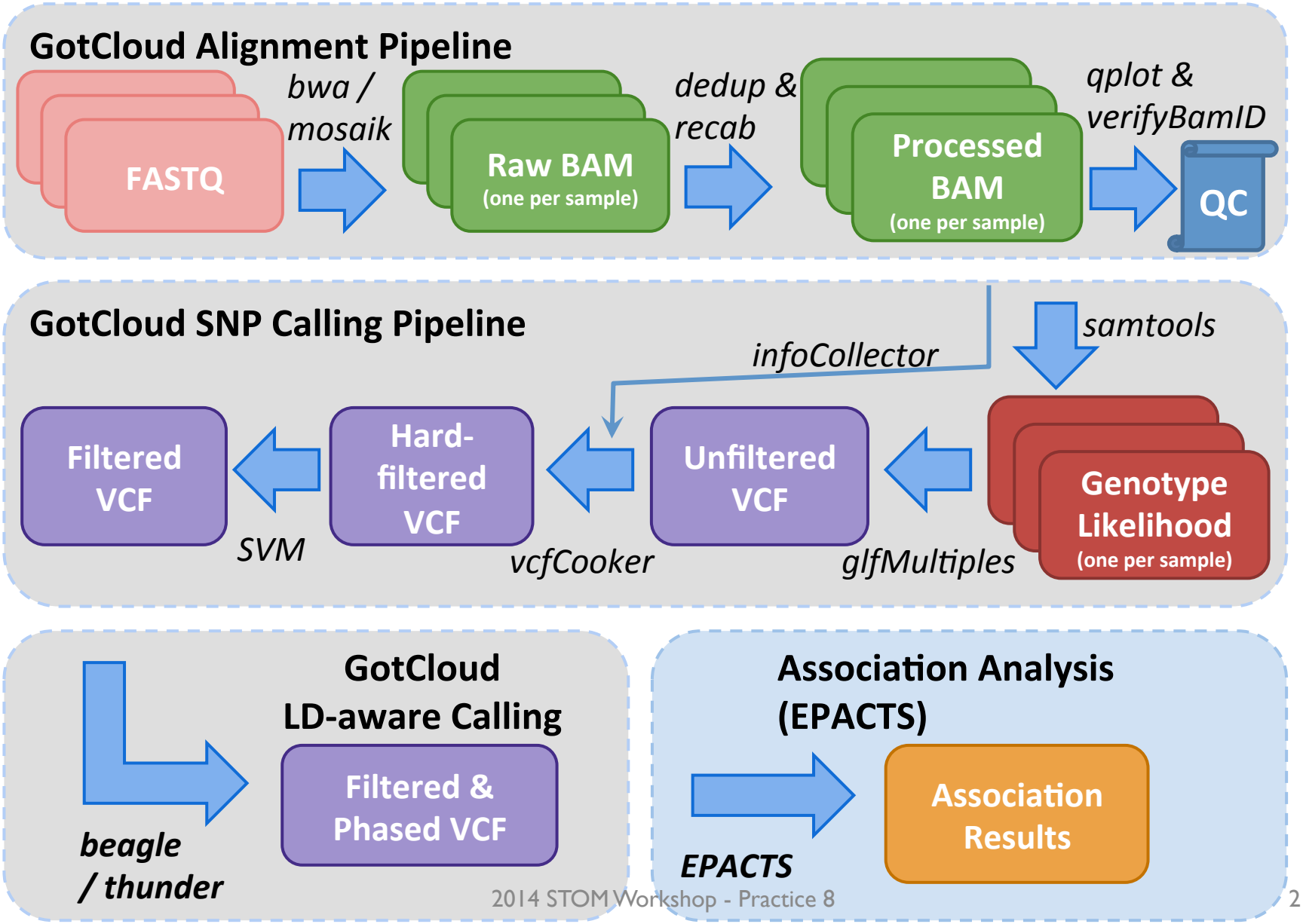
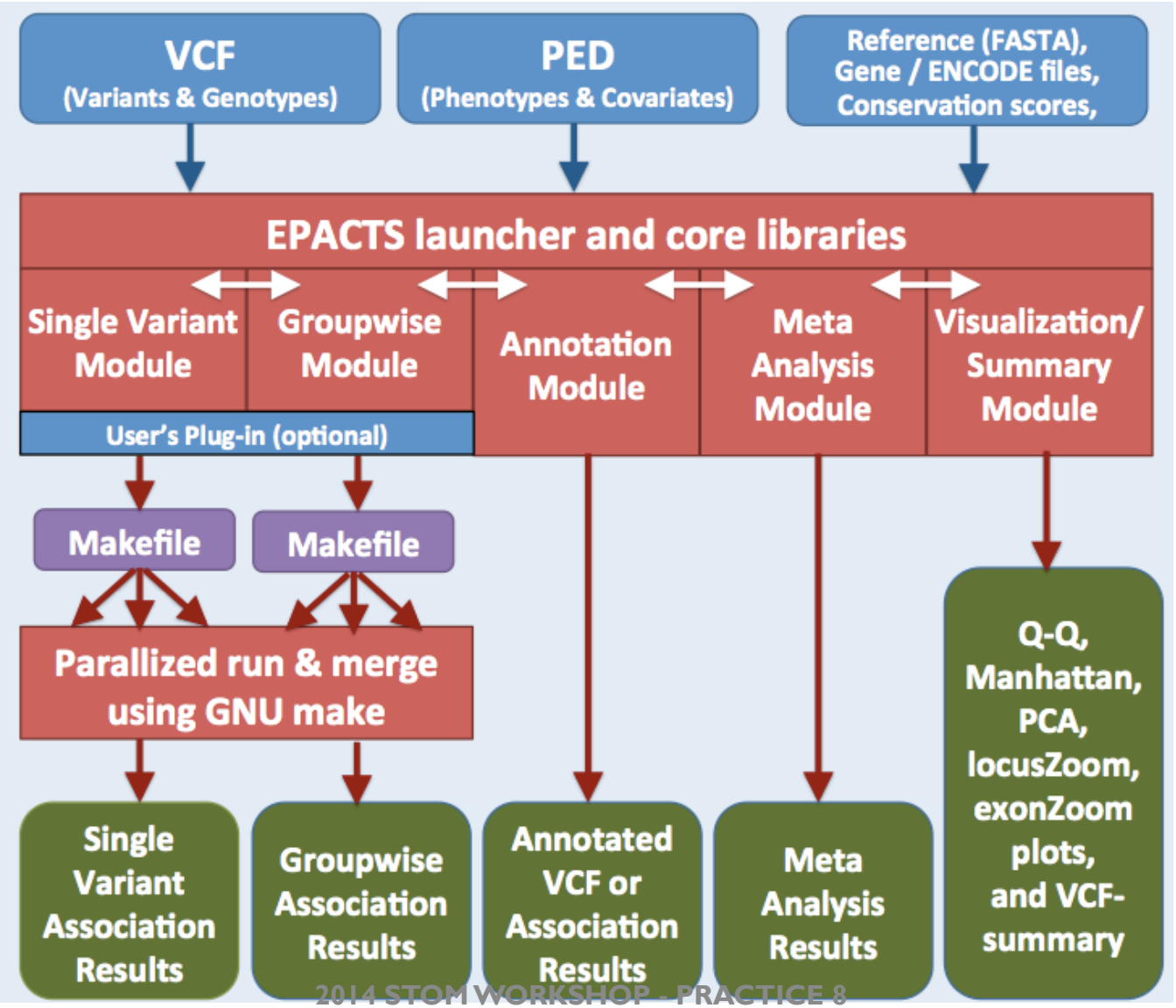
EPACTS Association Analysis Pipeline



OVERVIEW OF EPACTS FRAMEWORK



CHALLENGES IN SEQUENCE-BASED ASSOCIATION

- Much larger (10~100x) data size
  - Efficient and parallel computation is important

- Complex representation of variants and genotypes
  - SNPs, Indels, structural variations with multi-allelic variants
  - Genotypes with uncertainty across different depth and quality
  - Efficient implementation VCF (Variant Call Format) files is not simple

- Many methods are published, but only a few are usefully implemented.
  - Software implementation is becoming a major bottleneck
  - Need tools to transform “methods” to “software”

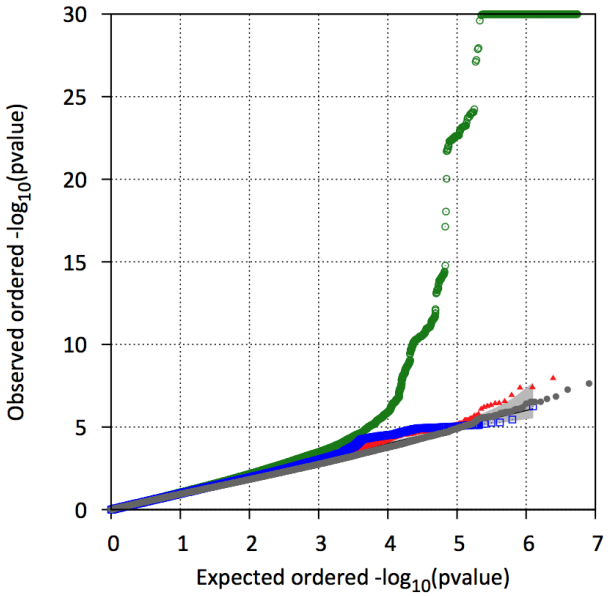
KEY FEATURES OF EPACTS

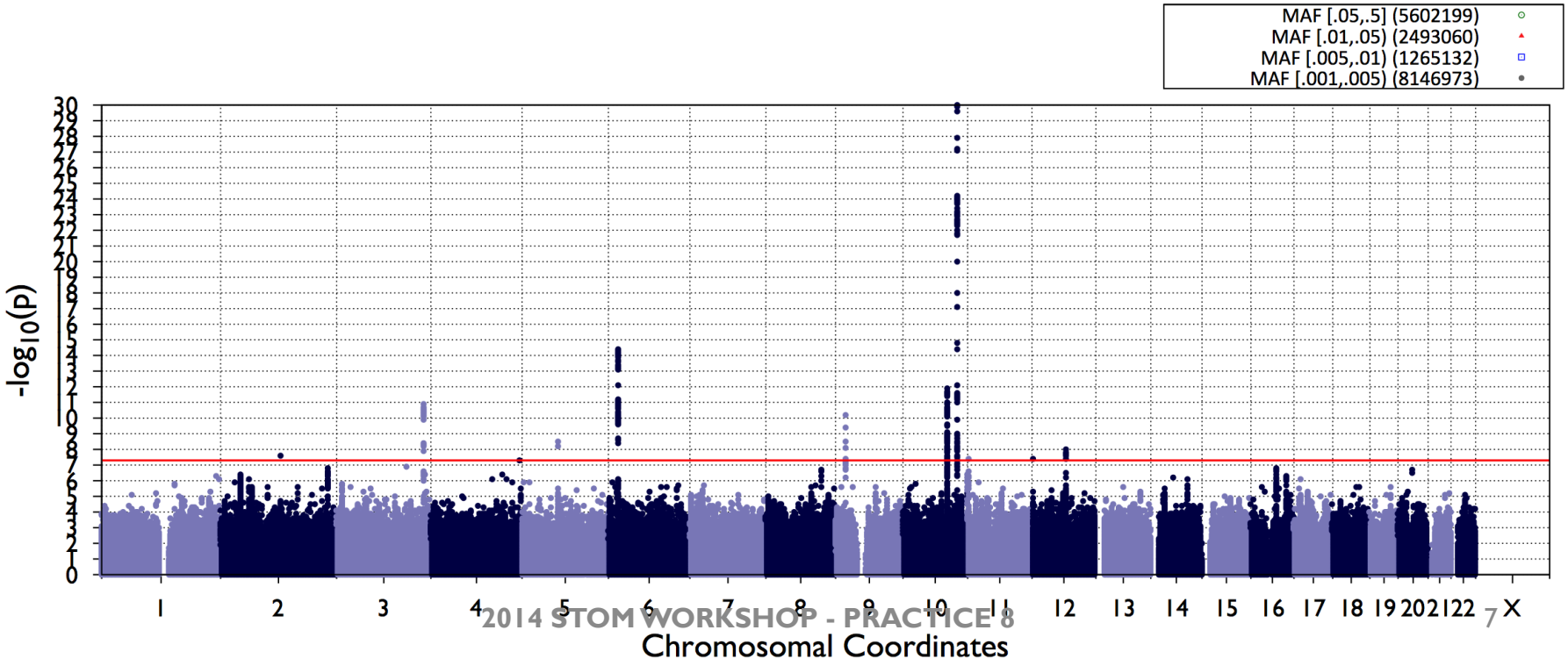
- Convenient and **dynamic plug-in** of user-defined statistical tests
  - Facilitate interaction between method developers and users
- **Efficient and parallel access of VCF** files
- **Fault-tolerant pipeline** structure based on GNU make
- Support of **a variety of single variant and groupwise tests**
- **Convenient** to run
  - All you need is just VCF and phenotype (PED) file
- **Automated visualization** of association signals and QC metrics
  - QQ-plot, Manhattan plot, PCA plot, LocusZoom plot
- Automated **annotation** of coding and noncoding variants
- Under **active development** more features are in progress (e.g. eQTL)

STATISTICAL TESTS AVAILABLE

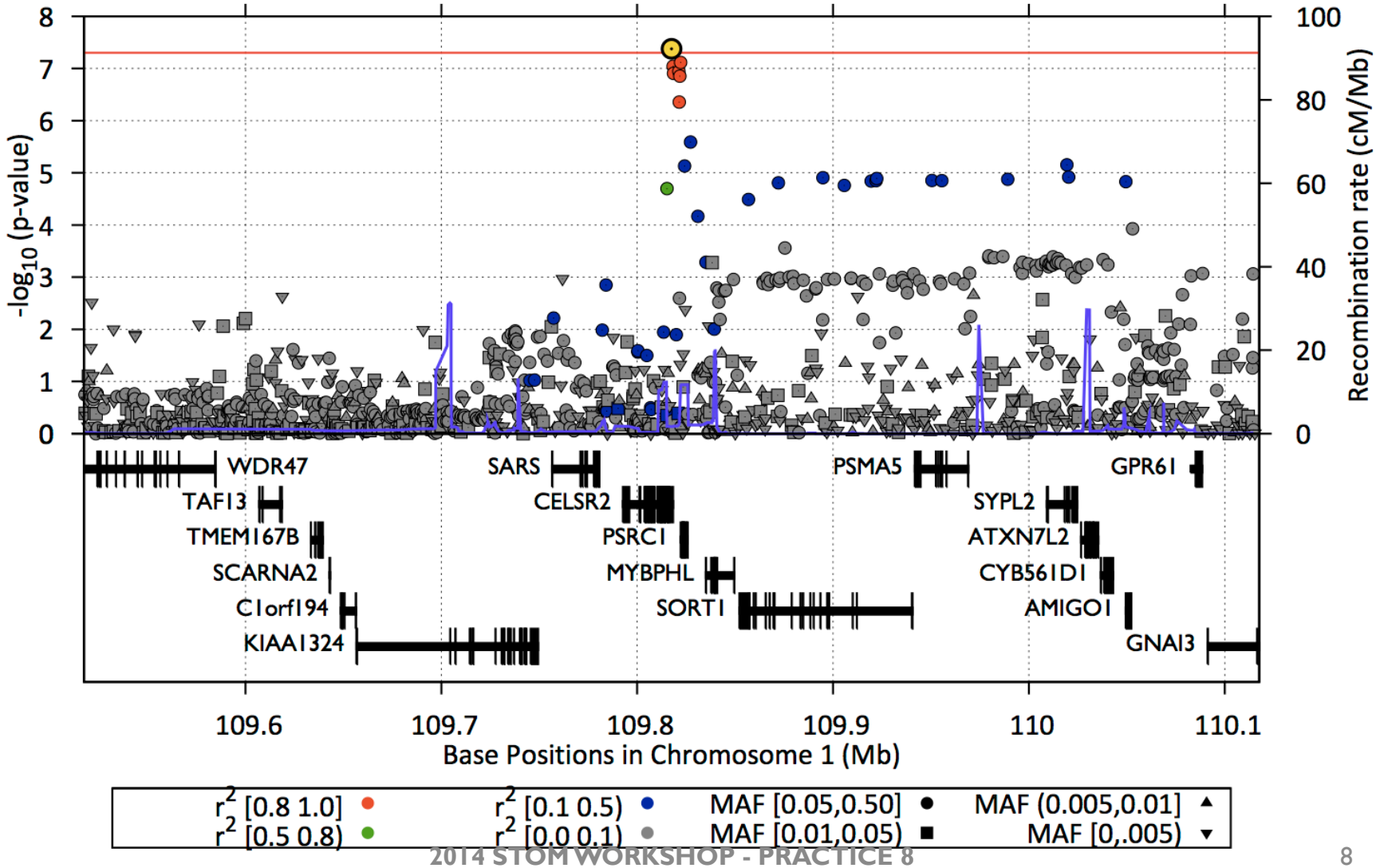
Single Variant Test	Groupwise Test
Wald Test	Collapsing
Score Test	Madsen-Browning*
Likelihood-ratio test	Reverse Regression
Firth bias-corrected LRT	SKAT / SKAT-O
Reverse Regression	VariableThreshold (VT)
Wilcoxon Rank Sum	EMMAX-Collapsing
EMMAX	EMMAX-VT

Example of Manhattan & QQ plots Automatically generated by EPACTS using a genome-wide data

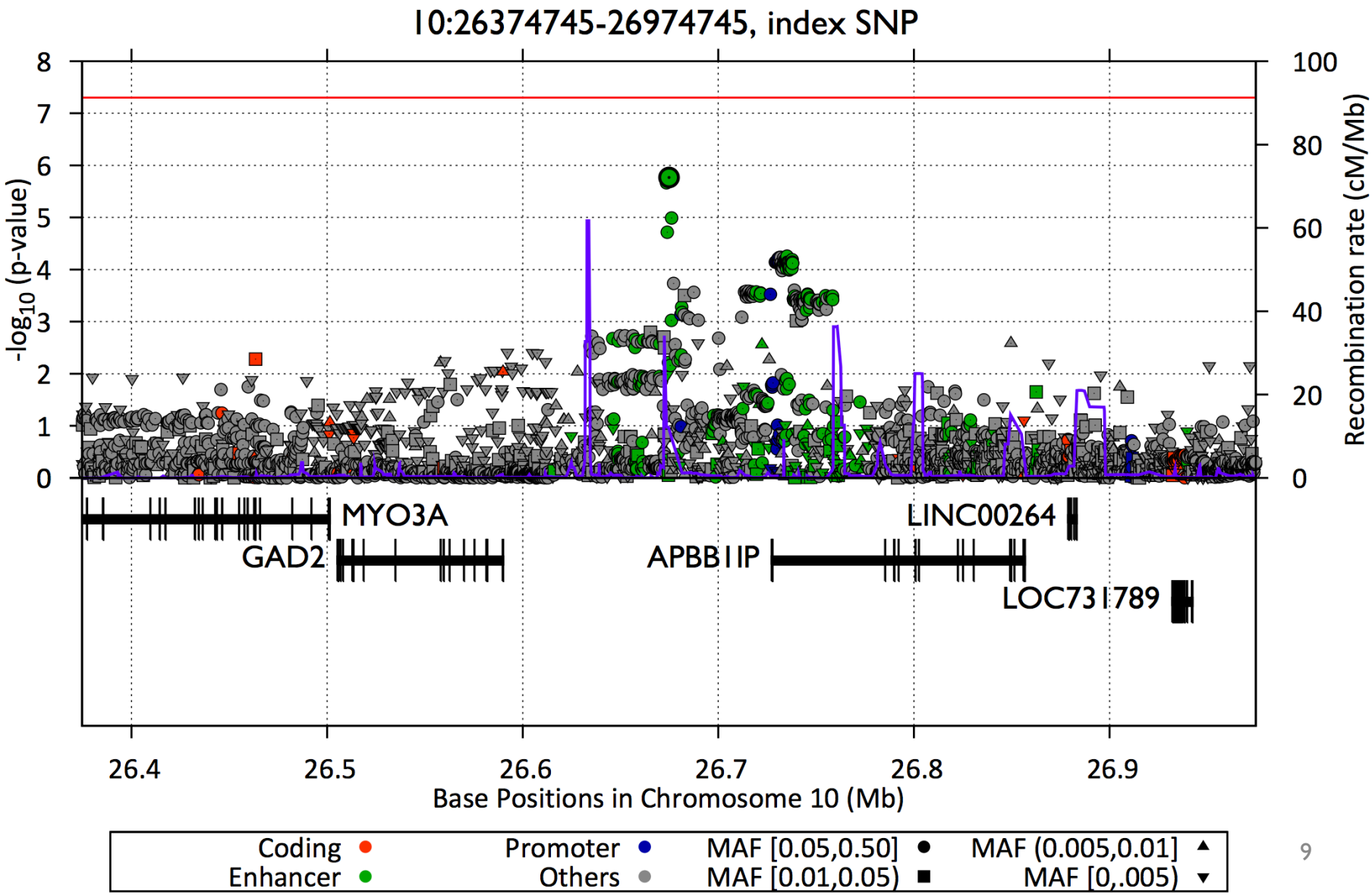




Zoom Plots for top associations



Zoom Plots by Regulatory Regions



GETTING STARTED WITH EPACTS

- Input Files – What should we provide?
  - VCF : genotype data (bgzipped and tabixed)
    - [prefix].vcf.gz and [prefix].vcf.gz.tbi should exist
  - PED : phenotype & covariate data
    - Header can be in a separate file (.dat) or in the first line (starting with #)
- Additional Input Files (Optional)
  - Marker group data (for groupwise test)
  - Reference genome sequence (for annotation)
  - Gene annotation files (in UCSC format)
  - ENCODE chromatin state predictions