

DEPTH: A Novel Algorithm for Feature Ranking with Application to Genome-Wide Association Studies



• Novel algorithm for feature ranking

- Ultra-high dimensional data sets
 - e.g., genome-wide association studies, epigenomewide association studies

• Which features correspond to signal/noise?



- Genome-wide Association Studies
 - Case-control setup
 - N samples, p markers (SNPs)
 - Allele frequency in cases vs. controls
 - Report effect size as an odds ratio





- Conventional approach to analysis
 - Test each marker independently
 - Calculate frequentist *p*-value for each marker
 - Adjust for multiple testing
 - All *p*-values less than threshold considered true associations
 - e.g., Genome-wide significance threshold



Manhattan Plot and Skyline





- Difficult statistical problem
 - Large number of markers
 - Correlated data
 - Disease causing variants not measured
 - Conventional analysis minimises family-wise error rate
 - Highly conservative publications



- Our strategy: DEPTH
 - NHMRC Project grant
 - Designed to run in a parallel environment
 - Exploits data correlation structure
 - Examine all markers, or subset of markers
 - e.g., all markers in a gene or pathway of genes









chr6 (q24.2-q26)



26 6p22.3 21.1 p12.3 12.1 6q12 6q13 6q14.1 6q15 6q16.1 16.3 6q21 6q22.31 q25.3 g2(6q27









ULBP2 ULBP1 AF4252441 RAET1L PPP1R14C



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chr6:1-170,556,128 170,556,128 bp. enter position, gene symbol or search terms

chr6 (p25.3-q27) 26 6p22.3 21.1 p12.3 12.1 p 6q12 6q13 6q14.1 6q156q16.1 16.3 6q21 6q22.31 q25.3q26 6q27





THE UNIVERSITY OF

MELBOURNE





A non-parametric measure of signal





- CCFR Phase I GWAS data set
 - 1,179 cases and 998 controls
 - 2,121,264 markers
 - Standard QC
 - DEPTH genome-wide analysis (NHMRC Project Grant)



 DEPTH identified ~60 genomic regions associated with risk of CRC

- The genomic regions:
 - Some already known (e.g., ERCC6, SMAD7, DCC)
 - Many novel regions (e.g., TUSC3, VIM, LIMA1)

DEPTH and CCFR Colorectal Cancer GWAS data (3)







- DEPTH sub-analyses
 - Proximal colon versus distal colon and rectum
 - Mismatch repair deficient versus proficient tumours
 - Case-case analysis (stratified by age)

 DEPTH analysis of combined CRC GWAS and EWAS data



Future work – Replication (2)



THE EVOLUTION STARTS HERE

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