Using KEGG pathways information for genomic partitioning

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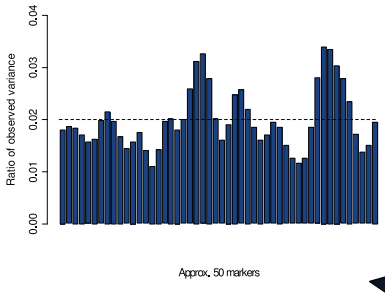
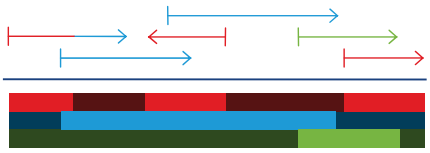
The problem

Estimating single marker effects of a complex trait using 650,000 markers results in marker effects being spread too thin.



A solution

Use prior biological information such as KEGG pathways to partition the genome into two or more non-overlapping sets.



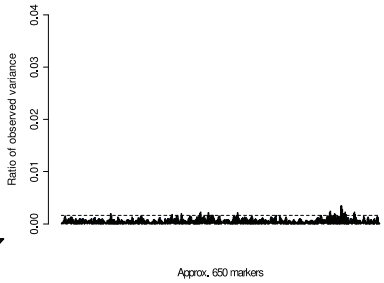
Genes associated with 3 pathways

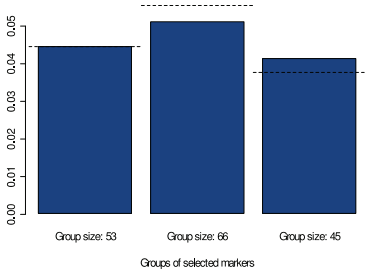
Markers included in group for pathway (light colours)

$$Y = \mathbf{1}\mu + X_1\beta_1 + X_{1^{-1}}\beta_{1^{-1}} + \varepsilon$$

$$Y = \mathbf{1}\mu + X_2\beta_2 + X_{2^{-1}}\beta_{2^{-1}} + \varepsilon$$

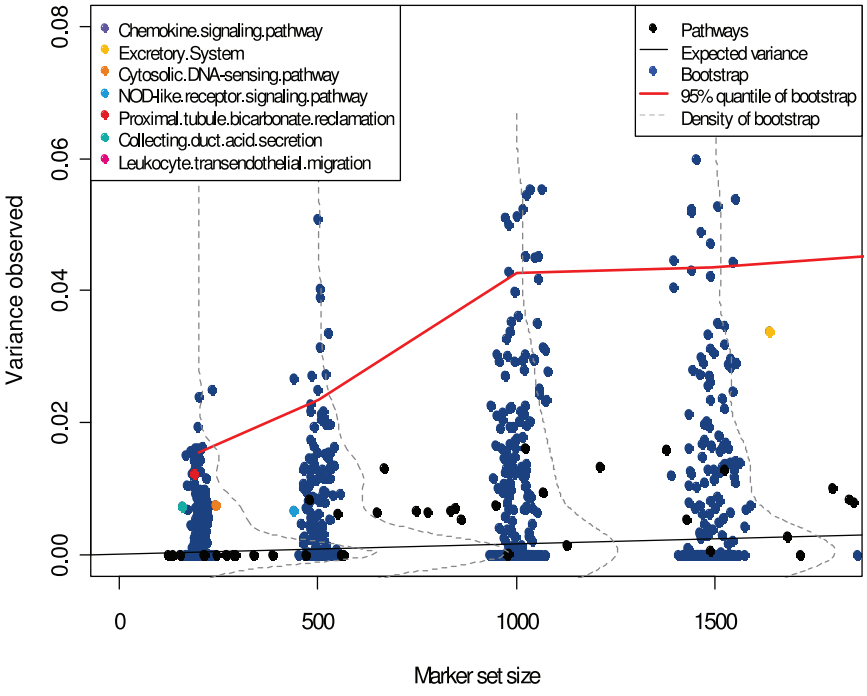
$$Y = \mathbf{1}\mu + X_3\beta_3 + X_{3^{-1}}\beta_{3^{-1}} + \varepsilon$$





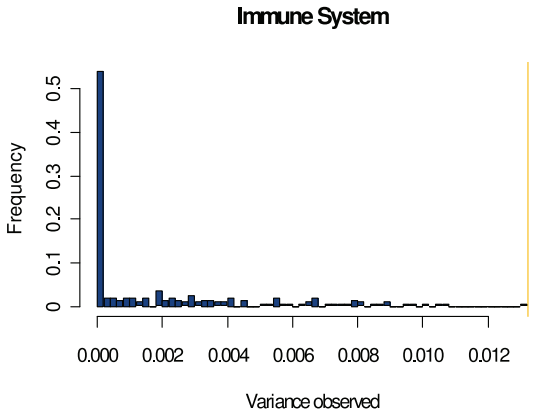
Results

Examination of observed variance on mastitis in dairy cattle on ~650,000 markers.



Test of power

- Null hypothesis: all markers contribute equally to complex trait
- Bootstrapping for estimation of null hypothesis
- Self-contained permutation test for stricter alternative null hypothesis



Conclusion

A large proportion of the genetic variance can be explained by markers located in genes associated with certain pathways.