

GMACwriteup2.RMD

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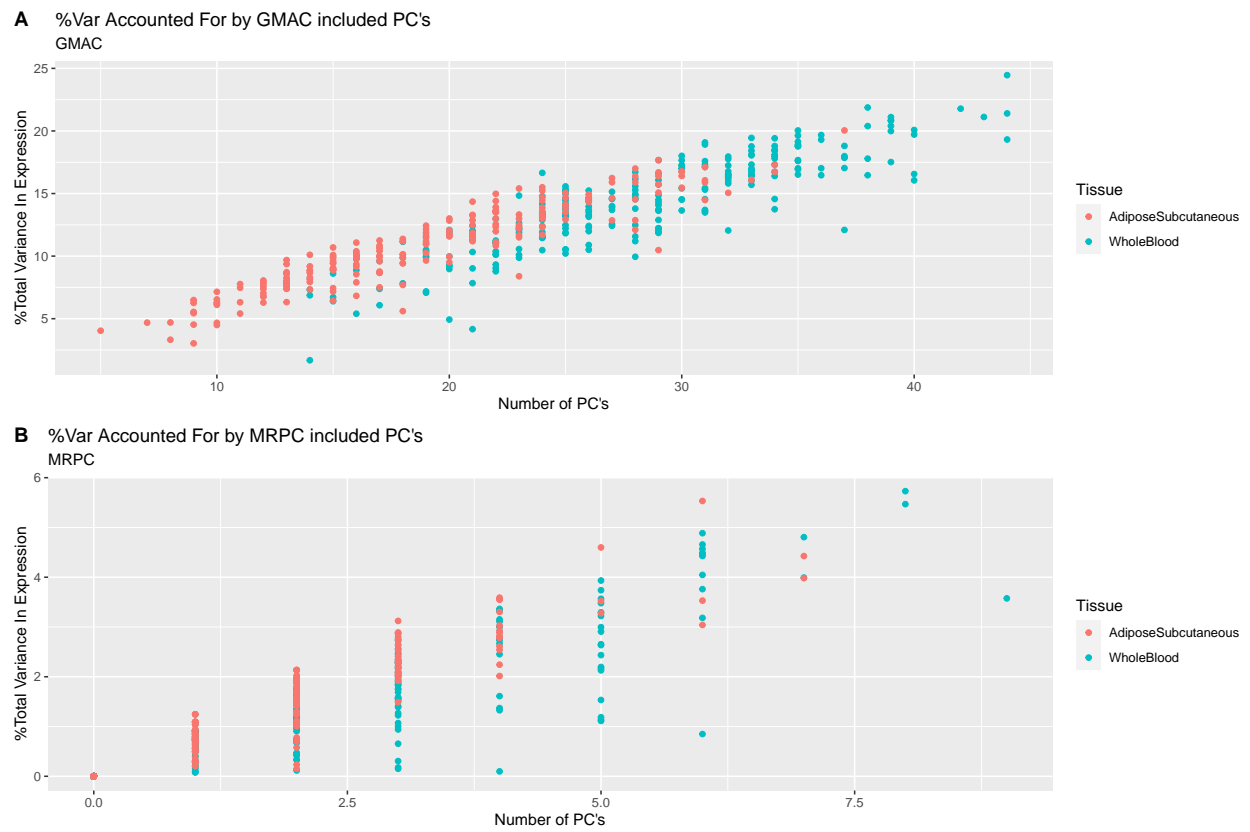


Figure 1: (A) scatter plots for the number of PC's included by GMAC and MRPC (B) and the percentage of total variation in expression summarized by the included PC's for each model

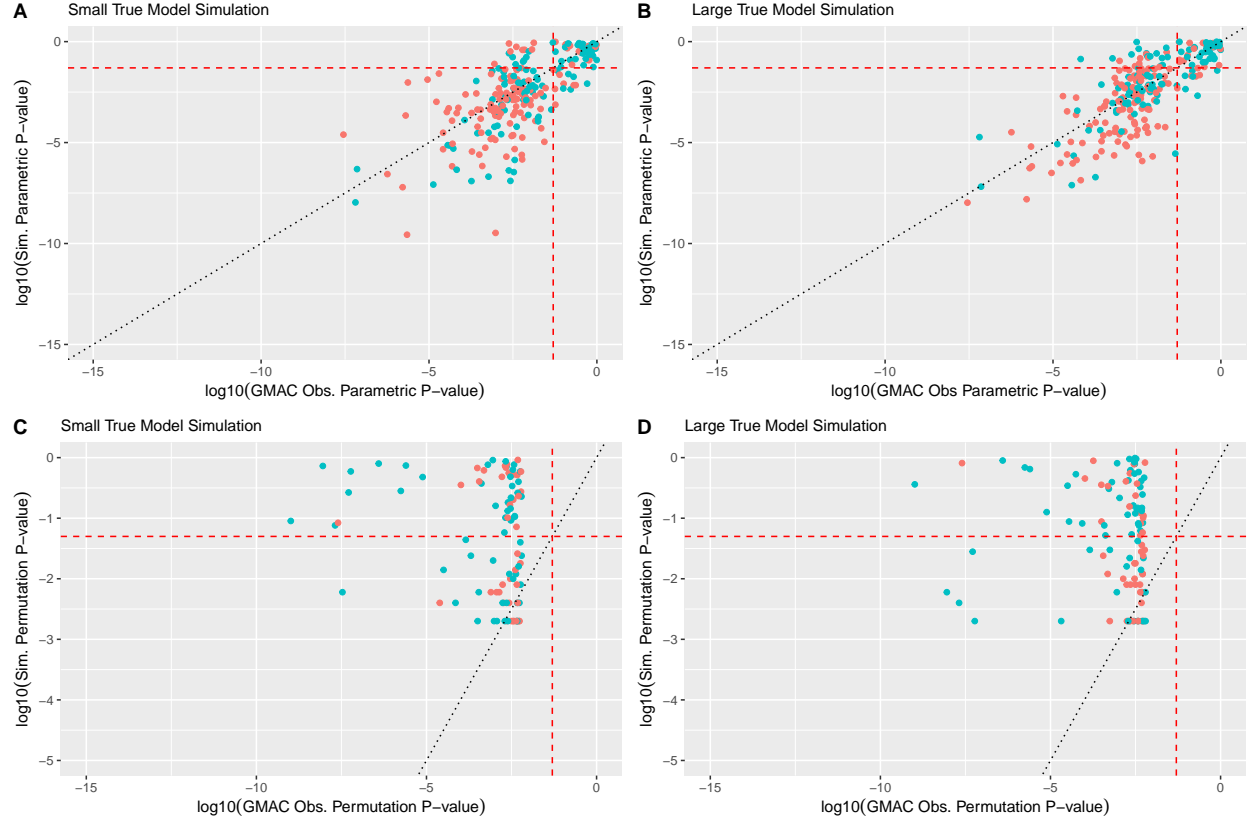


Figure 2: **(A)** and **(B)** the relationship between the observed p -value of the mediation test and the p -value from the simulated mediation test under the STM and LTM scenarios. **(C)** and **(D)** the relationship between the observed p -value of the permuted mediation test and the p -value from the simulated mediation tests under the STM and LTM scenarios. In all plots blue points represent trios with a rare allele observed at the SNP loci e.g having a frequency among subjects below 5%. The dotted lines define the zone of insignificance at $\log_{10}(\alpha) = -1.301$ scale. Note that p -values $< 2e-16$ have been floored to $2e-16$

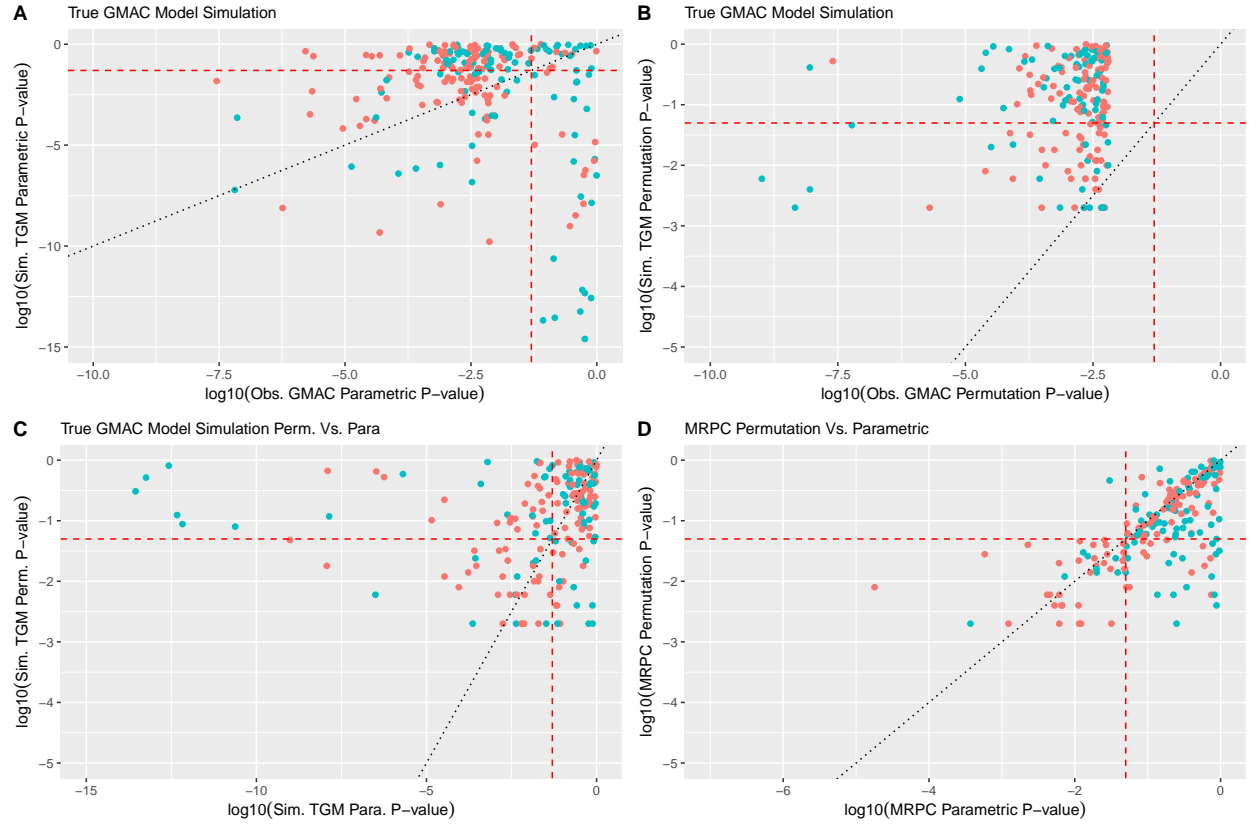


Figure 3: **A and B** Comparison of the observed parametric and permutation p -values to those simulated under the True GMAC model scenario. **C** comparison of the parametric to permutation p -values within the TGM simulation. **D** comparison of the parametric and permutation p -values within MRPC

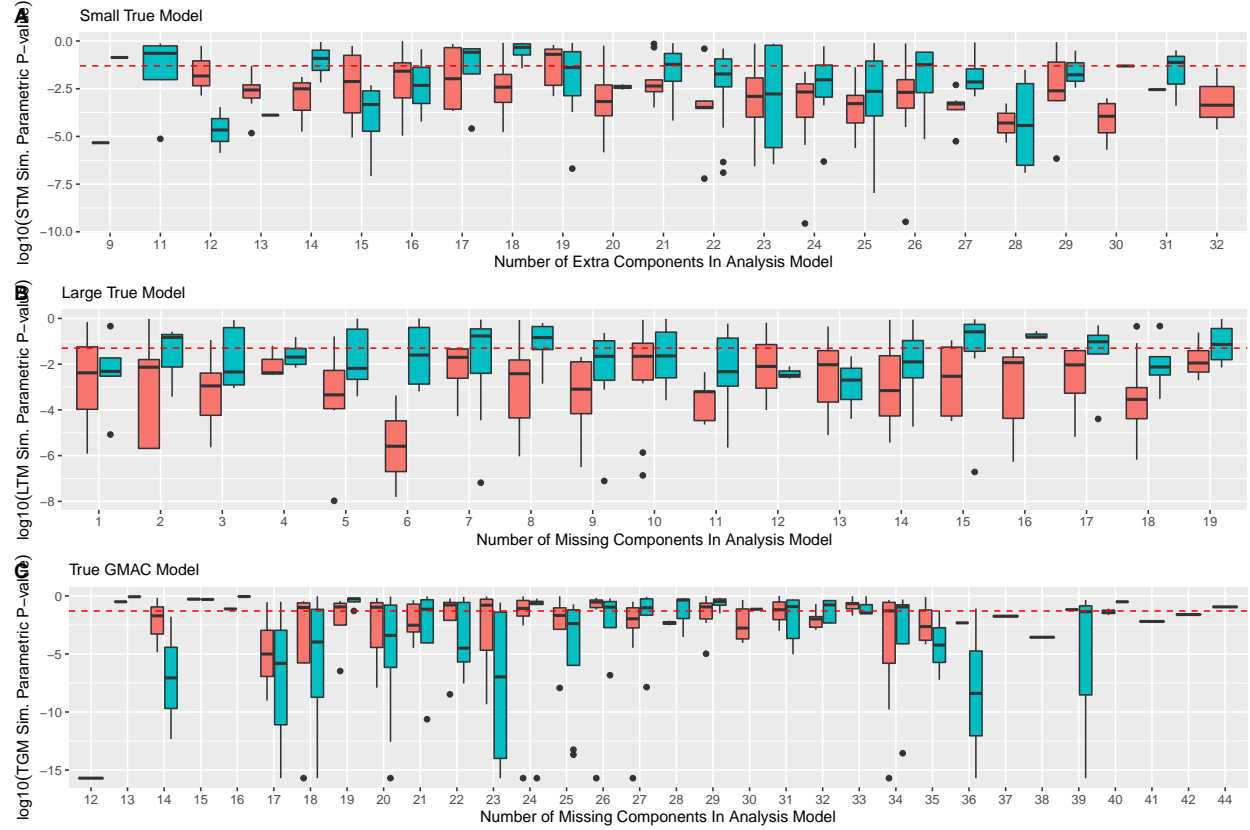


Figure 4: **(A)** and **(B)** The relationship between the simulated mediation p -value and the number of additional (STM scenario) or missing (LTM scenario) confounders in the analysis model relative to the true model generating the trans gene. In both plots blue boxes represent trios with a rare allele observed at the SNP loci e.g having a frequency among subjects below 5%.

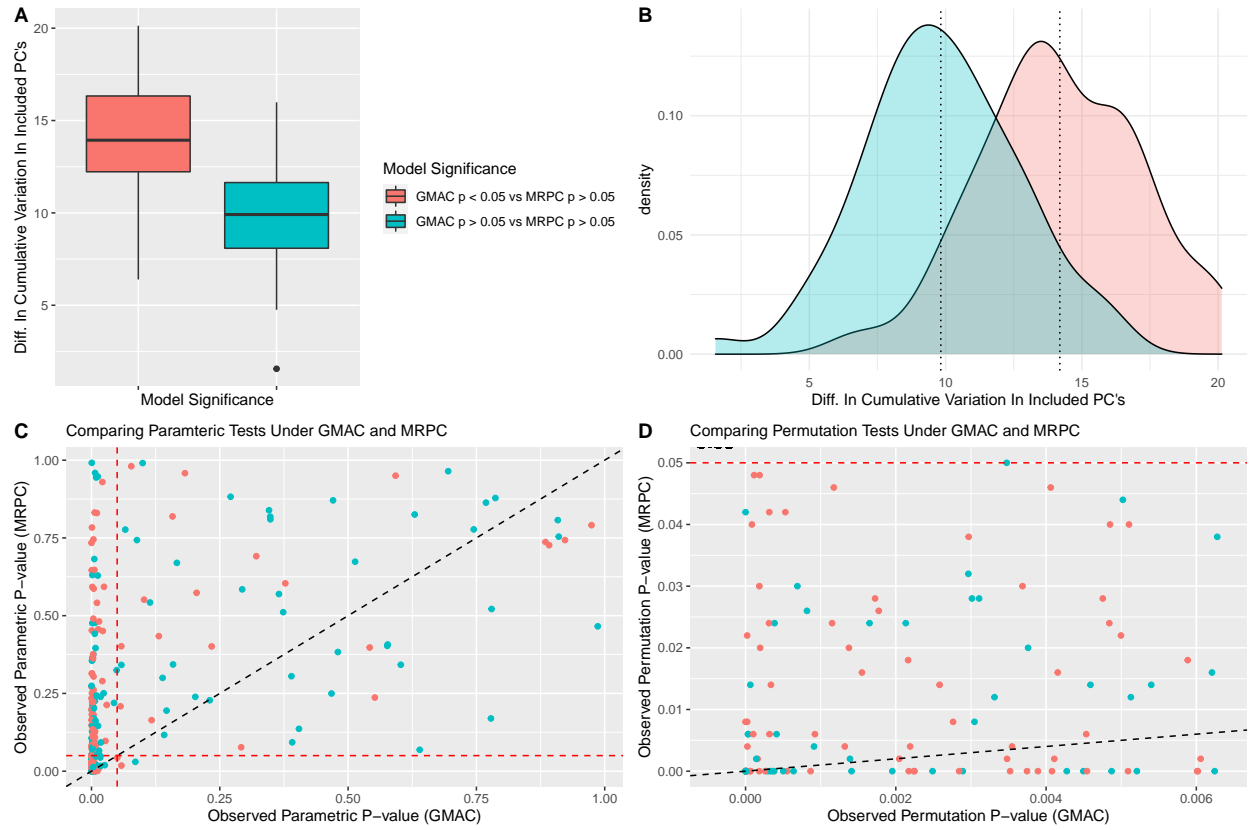


Figure 5: **A** The distribution of the difference between the GMAC and MRPC models in terms of in percentage of variation captured by the PCs/confounders included by each model, and under the special case of trios for which the mediation test was significant under GMAC but insignificant under MRPC **B** The distribution described for **A** but under the alternative scenario when both GMAC and MRPC mediation tests were insignificant (not to be confused with the permutation test which is significant for GMAC). **C** Comparison of the permutation and mediation p -values under GMAC. Blue points indicate trios with a corresponding rare allele at the SNP loci. **D** Comparison of the permutation and mediation p -values under GMAC and excluding trios with a corresponding rare allele for visibility. In **A,B,D** points along the black diagonal lines indicate near 1 : 1 correspondence in the p -values between methods.