

LETTER TO THE EDITOR**Response to ‘Controlling type 1 error rates in genome-wide association studies in plants’ by Andrew W George**

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We thank Andrew George for his interest in our work and his good suggestions for improving computational efficiency (George, 2013). We fully agree with his assessment of computational bottlenecks in our proposed method, which result from our aim to provide an accurate method. It is promising to see that the simplifications he suggests lead to substantial computational savings.

The one simplification results from the approximative assumption that linkage groups are independent. When applying the modified method, it is probably prudent to check that there is indeed little linkage disequilibrium between linkage groups. It would be interesting to see how the approximation works when there is more substantial LD between chromosomes. A similarly spirited, but conservative alternative to speed up computations is to compute the adjusted *P*-values per linkage group by our method, and then to perform a Bonferroni correction across linkage groups. This method, which was suggested in the discussion of Müller *et al.* (2011), is guaranteed to provide strong control of the genome-wide type 1 error rate.

The other simplification suggested by Andrew George is to impute missing marker data so that the number of inversions of variance-covariance matrices can be reduced. Again, this is an approximation. These approximations seem to have worked very well for the data set

studied, which is good news. But it is not obvious that these approximations will always work well. We would therefore encourage simulation studies that compare our method in its original form to the simplified version proposed by Andrew George, and perhaps also to the Bonferroni method proposed in Müller *et al.* (2011). Such studies could be based on real marker data representing diverse population structures and crops.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Müller BU, Stich B, Piepho HP (2011). A general method for controlling the genome-wide type I error rate in linkage and association mapping experiments in plants. *Heredity* **106**: 825–831.