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Dear Editors,

We would like to submit our manuscript entitled "Eagle makes multi-locus association mapping on a genome-wide scale routine" for consideration in *Nature Communications*.

Our goal is to transform the way in which genome-wide association study (GWAS) data are being analyzed in plants, animals, and humans. In the past 12 months, over 1400 papers have been published on GWASs (Web of Science). Of these, only 21 featured multi-locus methods. Single-locus methods are by far the predominant method-of-choice when analyzing GWAS data, despite multi-locus methods having greater power to detect true SNP-trait associations. We believe this poor uptake of multi-locus association mapping is due to multi-locus methods not scaling well, computationally, with study size and many of the multi-locus implementations being at the prototype level. With *Eagle* we have solved these problems.

We show that the *Eagle* method has greater power to find true SNP-trait associations while rejecting false associations than competing single-locus and multi-locus methods. It has a run time that is equal to the fastest single-locus association mapping program. We have also implemented *Eagle* as an R package of the same name. It can handle data larger than the memory capacity of a computer and makes extensive use of multi-threaded computation. *Eagle* comes with a GUI for easy use. We have also built a website (http://eagle.r-forge.r-project.org) to accompany the *Eagle* package.

For the first time, geneticists have access to a multi-locus association mapping tool that makes the analysis of GWAS data routine. We anticipate that this work will impact a large proportion of the readership of *Nature Communications*.

Thank you for considering our paper for publication in *Nature Communications*.

On behalf of the authors,

Dr Andrew George
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