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Dear Editor,

We would like to submit our manuscript entitled “Eagle: Making multi-locus association mapping on a genome-wide scale routine” for consideration in *Nature Genetics*.

Our goal is to transform the way in which genome-wide association study (GWAS) data are being analyzed. We aim to shift the animal, plant, and human genetic communities from using single-locus (or locus-by-locus) association mapping to multi-locus association mapping. In 2018, over 1400 papers had been published reporting findings from GWASs (Web of Science). Of these, only 21 featured multi-locus methods. Single-locus methods are by far the predominant method-of-choice.

We believe several factors are driving the poor uptake of multi-locus methods. First, the findings from multi-locus methods can be difficult to interpret. The size of the SNP effects are often reported but not the significance of the effects. Second, the learning curve for running the computer programs/packages that implement the multi-locus methods can be steep. Several are still at the prototype stage with limited documentation and no error checking. Third, multi-locus methods do not scale well, computationally, with study size. With Eagle, we have solved these problems.

In our paper,

* we present our new multi-locus association mapping method that we are calling Eagle.
* through a simulation study, we will report that Eagle has greater power to detect true associations and reject false associations than competing single- and multi-locus methods.
* we evaluate Eagle’s computational performance against competing implementations and reveal that Eagle is orders-of-magnitude faster than other multi-locus implementations and has the same run time as the fastest single-locus implementations.

We also analyse real data. We chose data from a published study (Nicode et al. 2016, Nature Genetics) where the extra findings of Eagle (due to its high power) could be corroborated against published findings. Eagle found over two times more (true) results and no false results than the competing method-of-choice (single-locus) methods.

We are committed to making Eagle the method-of-choice for the genetics’ community. To this end, to increase Eagle’s (the package) usability, we have developed a GUI for Eagle, absolving users from the responsibility of having to be familiar with R, upon which Eagle is based. We have also created “How To” guides, tutorials, installation instructions, videos, and an interactive demo that can be accessed from the [Eagle website](http://eagle.r-forge.r-project.org) (<http://eagle.r-forge.r-project.org>).

We have developed a new computational tool that we believe will benefit the animal, plant, and human genetic communities greatly.

Sincerely,

Andrew George