

Peter Ralph
Fenton Hall
University of Oregon
Eugene, OR 97403-1222 USA
PHONE: (541) 346-5530
FAX: (541) 346-0987
plr@uoregon.edu

September 29, 2016

To the editor(s) –

We are writing to submit our paper, “Local PCA Shows How the Effect of Population Structure Differs Along the Genome”, for consideration in *PLOS Genetics*. In this paper, we set out to describe how background patterns of relatedness (colloquially, “population structure”) vary along the genome at a scale larger than correlations induced by linkage. It was not certain that we would find significant large-scale heterogeneity in patterns of relatedness; in the field we tend to think of neutral, background population structure as a single thing, uniform across the genome except at a few isolated loci under selection. What we found was not only substantial variation at chromosomal scales, but different underlying causes in the three species we consider. The focus of our paper is on the method we developed to identify and visualize such variation in patterns of relatedness. We believe our method represents a fundamental advance because it lets the data speak for itself, providing an unbiased view of what are the most important variation in patterns of relatedness, rather than looking for specific signals. The method is therefore complementary to more common methods that identify small regions of the genome that are outliers for particular summaries of relatedness (e.g., F_{ST} -based scans for selection). We think the paper will be of interest to readers of *PLOS Genetics* because the method fills an important gap in the genomicist’s toolkit, that is tailored to describing variation in modern, spatially sampled datasets, and because it sheds light on the roles of linked selection and chromosomal inversions in establishing modern genetic diversity.

Potential reviewers for this paper could include: John Novembre (U Chicago, jnovembre@uchicago.edu), Joe Pickrell (NY Genome Center, jkpickrell@nygenome.org), Alkes Price (Harvard, aprice@hsph.harvard.edu), or Andy Clark (Cornell, ac347@cornell.edu).

If the reviewers would like to read a version of the paper that is single-spaced and has figures included, they can download it from <http://biorxiv.org/content/early/2016/08/21/070615>.

The paper has been seen and approved by both authors. All data we use is publically available, and so no permissions or databank submissions are needed; however, all source code and substantial derived statistics are available at our github page. We adhere to all relevant nomenclature guidelines.

Sincerely,

Peter Ralph and Han Li