Author's response to reviews

Title: Visualizing Genomic Information Across Chromosomes With PhenoGram

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Author's response to reviews: see over
September 12, 2013

Dear Editor,

We would like to thank the reviewer for carefully evaluating our submission titled “Visualizing Genomic Information Across Chromosomes With PhenoGram” by Wolfe et al. for publication as a software article in *BioData Mining*. We appreciate the helpful feedback and additional ideas. Attached to this letter are our specific responses. We have made the one essential minor revision requested, and there were no major essential revisions requested by the reviewer.

We look forward to hearing from you.

Sincerely,

Sarah A. Pendergrass, PhD

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Responses to Reviewer:

We would like to thank the reviewer for the time spent reviewing our manuscript, as well as for the very useful suggestions about future directions for our software.

There were not major essential revisions requested, and we fixed the one minor essential revision (Capitalizing "Crohn’s Disease").

As for the discretionary revisions:

1. The authors do an excellent job exploring the broad utility of PhenoGram for visualization in genomics. One of the nice features of this program is the ability to plot coverage/density of certain genotyping arrays throughout the genome, making it easy for users to get a quick look at areas of interest. Likewise this feature could also be used to better understand the coverage of rare vs. common variants on certain genotyping arrays, such as the exome chip, that has a large proportion of rare variants. The author should add this feature for users if possible.

Response to reviewer: This is actually possible with the software already, just by filtering/annotating the input table properly. If the user has information on the chromosome and base pair location of a series of variants, they only need to annotate those base pair locations with a color choice. They can choose one color for more rare variants, and one color for more common variants. Plotting rare vs. common variants to contrast location and density is a great suggestion. It is an additional way to use the feature of PhenoGram that allows users to plot genomic locations, in different colors. We have changed the paragraph referring to plotting CNV coverage with different colors, indicating the same approach can be used to plot SNP coverage with different colors.

2. It might be of interests to population geneticist to plot the different ancestral backgrounds for admixed individuals or groups across the genome. Currently most investigators plot different ancestral backgrounds per individual for the entire genome similar to Figure 3 by Tishkoff et al (PUMID: 19407144). While these figures are helpful for understanding genetic diversity across several populations from a global standpoint, it fails to capture local ancestry. PhenoGram is unique in a sense that it allows users to view results and other important genetic characteristics by chromosome. This feature would be very useful for plotting different levels of ancestry by chromosome (local ancestry) for an admixed individual or population. Recently there has been a shift in the field towards studying admixed populations and understanding how genetic admixture impacts disease. Given the current state of the field, a feature to plot the density of one (or more) ancestral background(s) throughout the genome would be of interest.

Response to reviewer: This is also a great idea. While it is beyond the scope of this paper, we would like to add this as a feature of PhenoGram for the future.
3. The authors use base pair position to determine the location of genetic loci. Is there a feature to plot the genetic position in (cM)? This might be helpful to visualize recombination rates throughout the genome.

Response to reviewer: Again, great idea. We would like to add this as a feature of PhenoGram for the future.