Reviewer Report

Title: iGenomics: Comprehensive DNA Sequence Analysis on your Smartphone

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Reviewer name: Marcos Colebrook

Reviewer Comments to Author:

REPORT ON THE PAPER
"iGenomics: Comprehensive DNA Sequence Analysis on your Smartphone"
by Aspyn Palatnick, Bin Zhou, Elodie Ghedin, Michael C. Schatz
SUMMARY
The authors present iGenomics, a comprehensive genome analysis iOS application that enables read alignment, variant calling, and an easy visualization of results. It was developed in Objective-C using the FM-index, banded dynamic programming and, according to the authors, other high-performance bioinformatics techniques. The app has been benchmarked against real and simulated sequencing datasets, and the results show that its performance is comparable to other desktop tools (i.e. BWA-MEM, samtools, IGV).
HIGHLIGHTS
- The paper is very well written and it is very pleasant to read.
- The app runs the complete analysis on the iOS device.
- Data can be loaded directly from Dropbox or imported via any iOS app capable of sharing files.
- Results can be shared using Dropbox, AirDrop, Google Drive, Mail, etc.
- The performance of the app was benchmarked using simulated and non-simulated data, obtaining very good results in comparison to desktop tools.
- The app is very easy to use for experts and non-experts (citizen scientists).
MAJOR REMARKS
My main concern is regarding the incompatibility of this app with Android devices. There are more than 2 billion Android devices around the planet. I suggest the authors, in a future version, using Ionic [1], Xamarin [2], Xojo [3] or any other cross-platform framework to develop the app for different systems and architectures. Besides, if you move to Android, you can use external APIs and/or Docker containers in order to increase functionality in a fast and efficient way.
Finally, and with the advent of 5G, I guess that calling an API in order to get all the functionality seems the easiest and fastest solution, rather than coding every single algorithm back again in Objective-C (or Swift, see point 8 below).
MINOR REMARKS
1. I suggest changing the title to "iGenomics: Comprehensive DNA Sequence Analysis on a mobile device" since the app runs also on an iPad, not only on a smartphone.
2. Page 11: line 12: there is a cite (Chan et al. 2020) that is not listed in the references.
3. Page 11, lines -8 and -9: change "extract" for "obtain" in "Then, to extract the BWT…", since you have "is extracted" in the following line as well.

4. Page 11: regarding BWT sorting, isn't there any recent advance on this field better than using Quicksort in O(n log n)? (see [4])

5. Page 13, line 6: why a match of a 20bp substring of the read?

6. Regarding the iOS code, have you used any Objective-C design patterns aside from the traditional MVC? If not, I suggest taking a look to [5], [6] and [7]. Using design patterns eases building and maintaining apps, along with the chance to add new functionalities in a fast way.

7. Why Objective-C and not Swift? I have my own opinion, but I want to hear your reasons.

8. The app's Github is a bit cluttered (doc/ppt/image files mixed with code files). I suggest arranging the repository for any prospective user.

9. The tutorial on the web [8] does not match my experience on the iPhone. For example, "5. Select the parameters for mapping the reads" is different from the screen I got in that step.

10. Is the data and software available in the public domain under a Creative Commons license?

IMPROVEMENTS

11. Build a cross-platform app, in particular, for Android devices, and develop using design patterns.

12. Regarding the reference genome, maybe it will be very useful in a near future to move to a graph genome structures [9], rather than working with the actual linear reference.

CONCLUSION

Although I am really aware that the authors cannot fulfill the major requirements or improvements in the next version of the revised paper, I believe that writing some lines in this direction will help the prospective readers.

Thus, the paper can be accepted when the minor comments are completed.

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REFERENCES

[1] https://ionicframework.com/

[2] https://dotnet.microsoft.com/apps/xamarin

[3] https://www.xojo.com/

[4] Okanohara D., Sadakane K. (2009) A Linear-Time Burrows-Wheeler Transform Using Induced Sorting. In: Karlgren J., Tarhio J., Hyyrö H. (eds) String Processing and Information Retrieval. SPIRE 2009. Lecture Notes in Computer Science, vol 5721. Springer, Berlin, Heidelberg.

[5] Chung, C. (2011), Pro Objective-C Design Patterns for iOS, Apress.

[6] https://developer.apple.com/documentation/swift/migrating_your_objective-c_code_to_swift

[7] https://developer.apple.com/library/archive/documentation/Cocoa/Conceptual/CocoaFundamentals/CocoaDesignPatterns/CocoaDesignPatterns.html

[8] http://schatz-lab.org/iGenomics/tutorial/

[9] Schatz, M.C., Cosgrove, A. Graph genomes article collection. Genome Biol 20, 25 (2019). https://doi.org/10.1186/s13059-019-1636-0.

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