As I have mentioned before, we would like to peer review the manuscript next. However, before we proceed with this, we must ask that you make some changes. These, we think, will improve the readability of the manuscript and will hopefully ease its way through the review process. I have listed our comments below. I hope you will find them useful, but please do let us know if you object to any of these suggestions – we are happy to discuss these further with you.

We kindly ask that you revise the manuscript to address the following comments (please note these are in no particular order):

1. We think the introductory section, while giving a nice historical background, is too long: it takes almost a page of text for the reader to actually learn where the piece is going. We suggest that you either completely drop this section, or shorten it substantially to one brief paragraph. Instead, we ask that you provide an introductory paragraph outlining the content of the Opinion and describing the motivation for the piece.

2. Please provide a short section with the conclusions and/or future directions.

3. In the section on the alignment algorithms, we thought it would be interesting to see some discussion of pseudoaligners in addition to the two types of aligners you already discuss. I am not entirely sure how these will fit the narrative of the piece, but we suspect the readers may find the lack of mention of these weird. However, if you think such addition would not provide novel insights here, please can you simply clarify this for us?

4. Finally, we ask that you consider how the language of the manuscript can be edited to make it slightly less formal; for instance, in many places active rather than passive voice could be used: such sentence construction makes is easier for the readers to follow the text. We do appreciate that it may not always be possible, but we would recommend that you have a colleague or a lab member (preferably one who was not involved in writing the manuscript) read it critically with just this aspect in mind.

We ask that you submit a revised version of the manuscript within the next two weeks, but please do let me know if this is not feasible. We are quite flexible about this and can negotiate the submission deadline that will be convenient for you.