

Rebuttal letter

Editorial comments

Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

We have gone over the manuscript in detail and removed spelling and grammatical issues.

2. Lines 191-231: Please write these as numbered steps.

We added numbered steps to the requested lines.

Reviewer 4

The protocol is already improved compare to the initial submission but in the line 302 the user could mention SIM-XL search engine (<http://dx.doi.org/10.1016/j.jprot.2015.01.013>), since this the only XL tool that produces a protein-protein interaction map as result, and can help in this protocol to validate the results.

We have added the requested reference.

Reviewer 5

As fairly pointed out by the authors, the major concern of the work is on the limitation to DSS (K-K) cross-linker only. This will restrict greatly the use of the tool presented here by the community as more and more new cross-links are developed and used. This work is another docking tool integrating cross-links data as several other exist and I am not convinced it will be largely used by the community because of its specificity.

We appreciate the reviewer's comments; adding support for other cross-linking reagents is technically possible but early work has indicated that we need to retrain the machine learning model used in the hrMS1 step. We will add support for all cross-linkers that we have sufficient amounts of data to train and validate the models.

There is quite a number of spelling error in the manuscript that need to be corrected. For example :

line 69 "and" should be removed

Removed.

line 294 "cross=linked" instead of "cross-linked",

Corrected.

line 300 "sessility" instead of "sensibility"

Corrected.