Reviewer's #1 comments:

Proteins displaying non-trivial topologies are a fascinating subject that offers ever new surprises. Whether these topologies are rare, or common because of some robust physical principle, and what is their biological function if any, are very interesting questions. In this manuscript, the authors investigate some features of complex lasso topologies with the aim of advancing the understanding of complex lasso-proteins. In particular, the authors observe that non-trivial lasso proteins are rather common, and compare their occurrence in polymers. The manuscript reports research that is well conducted and of potential interest for a specialized community. I, therefore, recommend the publication.

On a minor note, the English could be improved in several points. In particular, some sentences sound a bit childish (eg "the polymer theory was coined in the past century by great scientists"), or when the authors talk about "statistical probability".

We thank the reviewer for positive comments on our work. To improve our writing, we asked for help English native speakers and introduced the corrections. Next, we again proofread the manuscript and checked the typos with the on-line tools.
Concerning the "childish" expressions, it is the result of the balance we want to keep between scientific rigorous and the manuscript being understandable for the broad community. Still, we corrected the mentioned sentence. We also shorted "statistical probability" to "probability" throughout the manuscript, although in the methods we clarify, that we calculate the fraction of the numbers of observed structures, called by us the "statistical probability", as it is only an approximation to a real probability distribution.

Also, in the discussion, the authors could write and comment more clearly whether lasso-proteins are more common than expected than not, which is one of the aims of the paper, and which in the current form is not so clearly discussed.

We are sincerely grateful for this reviewer's insight! In fact, that was not the original aim of the work, although some expressions could suggest otherwise. However, this definitely lies in the scope of the manuscript. Therefore, we decided to enhance the work by more detailed analysis of the referee's comment. In particular, we added two new paragraphs and modified the last figure, inserting two new panels, showing two approaches to comparison of numbers of polymeric and biological non-trivial lassos.

A list of minor points:

- 4 and 45 phantom and trivial lasso loop ⟶ never defined what they mean
- 5 strictly positive ⟶ non-zero
- 10, 11 rather childish
- 41 not clear what least-polymeric means here
- Figure 2 "Statistical probability" is redundant
- Figure 3 Figures captions should stand on their own, please explain what the
- domination number is. Also in the labels, what is "other"?

We are grateful for those specific comments. We've corrected all of the suggested fragments.