

School of Physics and Astronomy

University of Leeds
Leeds LS2 9JT

T +44 (0) 113 343 3860/3804/3429
F +44 (0) 113 343 3900



UNIVERSITY OF LEEDS

29th September 2023

Thesis Report for Zara Zeenat

Dear Petra

The thesis by Zara Zeenat "Computational Modelling of Biomolecular Interactions in Proteins" focuses on two distinct systems: the PETase plastic degrading enzymes and the GPCR receptor 5HT7R. The thesis has resulted in two published papers (only one of which is described in the thesis), one submitted paper, a book chapter and a review. This is an excellent output from a PhD thesis and demonstrates that the candidate has made a novel contribution to the field of biomolecular simulation and is indicative that she merits the award of a PhD, subject to satisfactory performance in the viva.

The thesis contains a well thought-out description of the background importance and environmental significance of the work, and places the thesis into an appropriate context. A description of the theoretical methods underlying molecular dynamics simulations has also been provided in the introduction.

There are several areas that I would be interested to explore in more detail during the viva exam.

- 1) The structures for GPCRs have been predicted by homology modelling. What is the importance of AlphaFold in this context, and have the structures developed here been compared with those available from AlphaFold?
- 2) The thesis does not describe the computational resources used by the molecular dynamics simulations, which are expected to be significant given the computational expense of the calculations. Were GPUs or CPUs employed during the project, for example? Did they use local or national HPC resources?
- 3) I was surprised by the results reported in Figure 11 A (section 3.1.2) showing that the increased percentage concentration of ionic liquid can reduce the RMSD of the protein. Is there a physical explanation for this result? Would it be expected to persist if more repeat simulations had been performed?
- 4) The two systems chosen for the study seem unrelated – why were these two systems of particular interest, and is there any common theme that connects the studies together?

I look forward to hearing more about this interesting research during the viva exam.

Yours sincerely

A solid red rectangular block used to redact the signature of Dr Sarah Harris.

Dr Sarah Harris (s.a.harris@leeds.ac.uk)
Associate Professor in Biological Physics
Astbury Centre for Structural and Molecular Biology and School of Physics and Astronomy
University of Leeds