Faculty of Biological Sciences
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UNIVERSITY OF LEEDS

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Evaluation report of the PhD thesis from Mateusz Marcisz

Thesis title: Development of novel computational approaches for glycosaminoglycans

The goal of the thesis was to developmental a computational tool for GAGs and interrogate their interactions.

The thesis is composed of five main parts, with a brief introduction about glycosaminoglycans (GAGs) and confounding factors affecting their properties, followed by a Method section, objectives of the PhD, a summary of the studies, with a final appendix section with all the articles published by the candidate.

The thesis first examined and revised the current available model for molecular docking of GAGs, based on GAG monosaccharides, and the consideration of van de Waals radii and use of explicit water model. The thesis then continued to determine the interaction of GAG and proteins. A set of non-redundant was analysed. The role of GAG length in protein binding was studied. Using APRIL and TACI as an example, the candidate has demonstrated that their binding is facilitated by GAG binding. Lastly, the candidate has shown the effect of solvent molecules in sulphated GAGs, demonstrating that TIP5P and OPC water models are superior than the commonly used TIP3P model.

The candidate and the study are highly productive, with the generation of 7 publications, including two from the Journal of Computational Chemistry (one as first author and one 2nd author), two from the Journal of Chemical Information and Modelling (as first author), one in Glycobiology (as first author), one in Biomolecules (as first author) and one in Current Opinion in Structural Biology (as second author).

The organisation of the thesis is appropriate for thesis which is based on a high number of publications. The additional writing of the Introduction and the Summary provide a clear illustration of the candidate's understanding in the area.

While the thesis is self-contained and of high quality, this reviewer felt that some additional aspects should be considered, including the potential implications of GAG-protein interactions in physiology and diseases, an opinion on the general rules of GAG-protein interactions (if there is any), and how this work would advance the field.

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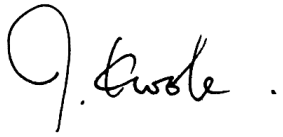
Nonetheless, this thesis has provided valuable tools for studying GAG-protein interactions which are extremely important for the field of carbohydrate biology. As such, this reviewer agrees that the thesis fulfills the criteria of the PhD Thesis to be defended.

Yours sincerely,



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