

Review Form 3

Journal Name:	Current Journal of Applied Science and Technology
Manuscript Number:	Ms_CJAST_130593
Title of the Manuscript:	Performing effective calculations of protein - ligand binding free energy with the help of molecular dynamics methods
Type of the Article	

PART 1: Comments

	Reviewer's comment	Author's Feedback <i>(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.	This manuscript provides a practical approach to accurately calculating protein-ligand binding free energy using molecular dynamics methods. These calculations are vital for drug design, helping predict how well a drug binds to its target protein. Accurate methods save time and resources by guiding experimental efforts. The study offers clear guidelines to improve computational efficiency and reliability, benefiting researchers in drug discovery and molecular biology.	Thanks for your comments.
Is the title of the article suitable? (If not please suggest an alternative title)	yes	Thanks for your comments.
Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.	Required rewrite	Thanks for your comments. Abstract section have been rewritten.
Is the manuscript scientifically, correct? Please write here.	yes	Thanks for your comments.
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.	yes	Thanks for your comments.

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Is the language/English quality of the article suitable for scholarly communications?	Need revised	
<u>Optional/General</u> comments	<p style="text-align: center;">Comments for Authors</p> <p>This manuscript addresses an important topic in computational chemistry, specifically the calculation of protein-ligand binding free energies using molecular dynamics methods. The calculation of protein-ligand binding free energies is a cornerstone of computational drug discovery. Molecular dynamics (MD) methods have emerged as powerful tools for simulating biomolecular interactions at the atomic level, providing insights into binding mechanisms, thermodynamics, and structural dynamics.</p> <p>Prior to publication, the following amendments are required:</p> <ol style="list-style-type: none">1. The introduction is not well-organized; the motivation and statement of the problem are not clearly explained.2. The terms MM/PBSA and MM/GBSA are repeated. Please remove one. Additionally, ensure the first occurrence of abbreviations such as MM/PBSA, VMD, and XA includes their full names.3. Change "material" to "materials."4. Why 1FOR, 1FJS, 1KSN, 1NFU, and 2J34 proteins selected? Please explain?5. In the Results and Discussion section, the statement "These numbers show that, as expected, more calculations can be made per unit time by decreasing the volume of the systems and the number of atoms they contain" is unclear. Please revise for clarity.6. The phrase "as expected" is not scientifically precise. For example: "As seen in Table 3, it was observed that the simulation speeds decreased as the volumes of the systems and the number of atoms they contain increased, as expected." Rewrite this sentence using precise, scientific language.7. Ensure uniform formatting for Figure 2 and Fig 3. Also, compare these results with relevant literature. Figure 2 is not visible; please replot it for better clarity.8. The conclusion is not well-written. Rewrite the conclusion, focusing on the key findings and their implications.	<p>Thanks for your comments.</p> <ol style="list-style-type: none">1. One more citation added to the first paragraph of the introduction section and last paragraph have been rewritten in order to clarify the motivation of the study.2. MM/GBSA is deleted and only MM/PBSA is used in the introduction section.3. "Material" updated as "Materials"4. In this study my aim was to try to calculate the binding free energies of a protein - ligand complex by using only the residues in the binding site. In this way, it will be possible to reach results faster and using fewer resources, according to the calculations we make using all residues in the protein structure. The paper published by Ngo et al. in 2019 was very suitable to test my approach and compare it with existing methods. For this reason, 1FOR, 1FJS, 1KSN, 1NFU, and 2J34 complexes, which were mentioned in the article of Ngo and colleagues and whose study results were given, were selected for experiments and comparisons. In light of the encouraging results I have obtained, I have started to work and develop new projects to apply my method to other Factor Xa inhibitors and other protein-ligand complexes existing in the literature and to evaluate the results I have obtained.5. "as expected" word is deleted. It has been marked with a yellow highlighter and striked through. Strike through words will be deleted in the final version of the manuscript after your review.6. "as expected" word is deleted. It has been marked with a yellow highlighter and striked through. Strike through words will be deleted in the final version of the manuscript after your review.7. "Figure 2" typo mistake have been updated as Fig.2.8. The conclusion section have been rewritten and marked with a yellow highlighter.

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	<u>(If yes, Kindly please write down the ethical issues here in details)</u>	