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REVIEWER'S REPORT

Manuscript No.:50790 Date: 29-03-2025

Title: Optimization of feature extraction for the prediction of macromolecular interactions: OTE-24 Approach

Recommendation:
Accept as it is ……yes……
Accept after minor revision……
Accept after major revision ……
Do not accept (*Reasons below*) ……

Rating	Excel.	Good	Fair	Poor
Originality			Yes	
Techn. Quality			Yes	
Clarity			Yes	
Significance		Yes		

Reviewer Name: **Date:**

Reviewer's Comment for Publication.
The paper's main contribution is the development of a new feature extraction method, OTE-24, which combines bigram and APAAC approaches to improve the accuracy of predicting macromolecular interactions.

Detailed Reviewer's Report

1. *This paper introduces a new feature extraction method, OTE-24, for predicting macromolecular interactions, combining bigram and APAAC approaches. The method demonstrates high accuracy, precision, and recall in tests using the HPRD database. OTE -24 outperforms existing methods, showing improvements in accuracy, precision, sensitivity, and MCC.*
2. *The study uses a rigorous 5-fold cross-validation technique to validate the model's performance.*
3. *However, the ROC AUC value is lower than other metrics, suggesting potential for improvement in reducing false positives or negatives.*
4. *The computational complexity of the Random Forest model is acknowledged as a limitation, particularly during hyperparameter optimization. Future work could explore alternative algorithms or feature selection methods to address this complexity and further enhance performance.*