論文 / 著書情報
Article / Book Information

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Category(English)	Doctoral Thesis
種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
Doctoral Program

論 文 要 旨

THESIS SUMMARY

系・コース： Department of, Graduate major in	Computer Science Artificial Intelligence	系 コース	
申請学位（専攻分野）： Academic Degree Requested	博士 Doctor of	(Engineering)	
学生氏名： Student's Name	Jason Kurniawan		
審査員主査： Chief Examiner	Takashi Ishida		

要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

The prediction of protein stability and its changes is fundamental to understanding protein function in drug design and protein engineering. To facilitate the predictions, various computational methods have been developed. Current state-of-the-art methods for predicting protein stability, predominantly based on machine learning (ML), face critical limitations due to the inherent nature of supervised learning. These include data set biases, the black-box nature of algorithms, and a reliance on static protein information, which overlooks the intrinsic dynamic behavior of proteins. Such limitations can lead to inaccuracies, especially when predicting the stability of proteins under various domain applications. To address these gaps and leverage the dynamic nature of proteins, this research adopts Molecular Dynamics (MD) simulations which have shown successful application in capturing complex, real-time interactions within proteins across various research fields.

In the first phase of our research, we demonstrated the ability of molecular dynamics simulations to assess the quality of predicted single protein 3D structures. This has laid a solid foundation for understanding inherent protein stability through the explicit dynamic information, which is critical for accurate structural prediction and the subsequent rational design of proteins, but still has not been utilized by existing methods in the field. Building upon this, the second phase extends the field from protein stability to stability changes, particularly in the field of point mutations on protein stability, employing alchemical molecular dynamics simulations to predict the resulting stability changes. We introduced a novel protocol to enhance the performance by specifically handling charge-changing mutation cases. Our proposed approach achieves significantly better performance in comparison with state-of-the-art machine learning-based methods.

The main contribution of this thesis is the development of a novel approach that integrates protein explicit dynamics information, obtained from molecular dynamics simulations, into the prediction of protein stability and stability changes in single protein structures. This novel approach addresses and overcomes the inherent limitations found in machine learning-based methods. A key advantage of the proposed method is that it does not require complex feature extraction and extensive training processes typically associated with machine learning models. By incorporating dynamic information from molecular dynamics simulations, this approach not only introduces additional useful information but also enhances the accuracy of protein stability predictions. This offers a more comprehensive and dynamically informed perspective in understanding protein behavior and functionality.

Additionally, further discussions and additional experiments have opened new directions for the application of the proposed methods. The possibility of integrating with machine learning-based methods to tackle computational limitations, enhancing the speed without compromising the accuracy of stability predictions. Further extension of the proposed approach to the field of multiple mutations also represents a positive outcome in the field.

Overall, the research embodied in this thesis has achieved its objectives. The methodologies developed and tested here have proven successful in predicting protein stability and its changes. The potential to extend these methods to more complex scenarios, such as multiple mutations, opens new possibilities for comprehensive and insightful protein stability analysis. They pave the way for more reliable and insightful predictions in protein research and its applications, particularly in the fields of drug design, therapeutic interventions, and protein engineering.

備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。
Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1 copy of 800 Words (English).
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