論文審査の結果の要旨

氏名　　ロジャン　シュレスタ

The candidate, Mr. Rojan Shrestha, has submitted his PhD thesis entitled "Improving de novo model quality and its application in ab initio phasing" and given a presentation in front of his thesis committee on July 28, 2014.

His research was focused on the development of methods to improve the accuracy of de novo models using the fragment assembly approach, and then using these improved de novo models as templates to solve the crystallographic ab initio phasing problem by molecular replacement.

His PhD thesis presented the development of three methods. His first method (MORPHEUS) is designed to improve de novo models by rebuilding the regions with large estimated errors and thus increase the success rate for ab initio phasing. He first proposed a metric to estimate errors for each residue in the predicted models based on the average pairwise residue distance score (AP-RDS). He has shown that this AP-RDS correlates well with the model accuracy when the native structure is known. A Roulette wheel algorithm was used to bias the rebuilding on regions with large estimated errors. He has shown that the rebuilt models were significantly improved and they can be used as templates for ab initio phasing with a higher success rate.

His second method (NEFILIM) is to identify new and better fragments from a pool of initial models and then use them to generate better de novo models using the fragment assembly approach. He has shown that the NEFILIM method was able to generate better models compared to Rosetta judged by CA-RMSD, TM-score and GDT-TS on a test dataset.

His third method (FRAP) deals with cases when the best de novo models are not accurate enough to be used as templates for ab initio phasing by molecular replacement. He proposed to dis-assemble the full models into fragments, to perform molecular replacement with individual fragments, and then to re-assemble them together to form a more complete model that can provide sufficient phase information to enable the solution of the entire structure. He has demonstrated that his FRAP method can solve upto 80% of the difficult structures that couldn't solved by conventional approaches.

Two of above three methods have already been published and the third one is currently under review. He is the first author on all these three papers. In addition, he has contributed to three other papers as a co-author.

The committee felt that he has achieved a very high level of research productivity. His thesis is well written. He has answered well those questions raised

during his thesis defense demonstrating his excellent knowledge in the subject matter related to his research. The committee believes that his research results are significant advancement in the field. The committee felt that his thesis lacks a clear description of his computational work to biology and therefore recommended that he revise his thesis to include some descriptions of the biological significance of his work and the potential impact that his research results might have on benefiting the biologists.

The committee has unanimously agreed to recommend that Mr. Rojan Shrestha be granted the PhD degree in the Dept. of Computational Biology, The University of Tokyo.

以上 3222 words