学位申請論文公開講演会

日時:2025年2月4日 13:00~

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場所:物理会議室(C207)

題目: Modeling Conformational Transitions of Biomolecules from Atomic Force Microscopy Images

(原子間力顕微鏡画像を用いた生体分子の構造変化モデル化)

主論文の要旨

Studies on biomolecular functions necessitate an understanding not only of the structure of biomolecules but also of their dynamics. High-speed atomic force microscopy (HS-AFM) provides information on dynamics; it can observe biomolecules in "action," i.e., molecules performing biomolecular functions in solution in real time.

In this study, we would like to develop a new flexible fitting method, called NMFF-AFM, combine normal mode analysis and AFM image to construct the 3D model from 2-D images.

The algorithm was tested on proteins for which two distinct conformations were experimentally known: Adenylate Kinase, ABCB1 transporter and Elongation Factor 2. To evaluate the algorithm's performance, an AFM target image was simulated from one conformation, while the structure optimization process was initiated from the second conformation. In addition, to evaluate the robustness, misalignment tests were performed. Across the test cases of the three systems, a noticeable reduction in the overall conformational difference between the initial conformation and the target conformation was observed.

Furthermore, aiming to evaluate the performance of NMFF-AFM under experimental data, simulated AFM images were used as the target to perform the flexible fitting. For the initial conformations, we utilized another stand alone software called Simulator, belongs to AFMize program, to prepare the initial conformations by rigid-body fitting. We tested NMFF-AFM by running flexible fittings with the result of the rigid-body fitting of Adenylate Kinase, ABCB1 transporter, and the results showing reducing of the difference between the initial and target conformation. The orientation error caused by rigid-body fitting matches the results of the previous tests, which indirectly illustrates the accuracy of NMFF-AFM.

From the various test cases, the accuracy of the NMFF-AFM can be highlighted, this method can help characterize 3D structure modeling large-scale conformational changes observed in 2D AFM images.