disk were frequently observed. These results indicate that rTMVCP retains the properties of self-association similar to those of wtTMVCP although it is not expected to have a modified N-terminal residue specific to wtTMVCP.

3H1458 抗腫瘍細胞活性を示すオレイン酸-蛋白質巻き戻り中間体複合体の NMR 及び生物学的研究

NMR and Biological Studies of Anti-tumor Complex between Oleic Acid and Protein in the Molten Globule State

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Svensson *et al.* reported that human α -lactalbumin (α -LA)-fatty acid complex, named HAMLET, induced apoptosis-like death in tumor cells. α -LA in HAMLET is stable in the molten globule (MG)-like conformation, but the structural details are not fully understood. Peterson *et al.* reported that goat α -LA-fatty acid complex (GAMLET) also induced apoptosis in tumor cells. In this study, we examined the hydrodynamic radii of HAMLET and GAMLET by pulse field gradient NMR to check the oligomer formation of HAMLET and GAMLET. As a result, both in HAMLET and GAMLET, monomeric and oligomeric forms were observed under physiological conditions.

From our previous NMR studies, we assume that oleic acid in the anti-tumor complex may act as an apoptosis inducer in tumor cells and that α -LA in the complex may act as a carrier. According to this hypothesis, we made complexes between oleic acid and other proteins (canine milk lysozyme (CML), apo myoglobin (apoMg) and β 2 microglobulin (β 2m)), which form the stable MG state, and tested their anti-tumor cell activity. As a result, all oleic acid-protein complexes exhibited anti-tumor cell activity. CML-oleic acid complex exhibited an anti-tumor activity comparable to HAMLET, and apoMg-oleic acid complex and β 2m-oleic acid complex exhibited less anti-tumor activities than HAMLET. This finding strongly supports our hypothesis that α -LA in the anti-tumor complex acts as a carrier of oleic acid into tumor cells.

9:00~12:00 |会場/ Room I

蛋白質計測・解析の方法論 1

Protein: Measurement & Analysis 1

3I0912 分子動力学の時系列データ解析-側鎖の構造変化と運動-

Time-series analysis of in molecular dynamics : Conformational change and movement of the side chain

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Our study aims to analyze time series data of molecular dynamics simulation for proteins to extract collective behavior involving side chains. Our methodology consists of the following two steps: (1) the wavelet transformation and (2) singular value decomposition(SVD).The wavelet transformation enables us to investigate time-varying features of oscillatory motions, and SVD extracts collective variables involving multiple amino residues [1] [2]. Our system is chignolin, the first designed protein consisting of ten amino residues. The protein exhibits conformational changes wondering around multiple stable conformations. Thus, it is a convenient molecule to develop methodology to investigate dynamical behavior involving multiple conformations. In particular, we aim to extract collective behavior involving not only the main chain but also the side chain [3]. By analyzing relationship of collective behavior between the main chain and the side chains, we can understand to what extent collective behavior involving the main chain provides us with information concerning collective behavior with the side chains.

[1] N. Sakurai, M. Toda, S. Fichigami, A. Kidera, Time series analysis using wavelet toward molecular dynamics simulation of proteins, in preparation.

[2] M. Kamada, M. Toda, M. Sekijima, M. Takada, K. Joe, Chem. Phys. Lett. 502 (2011) 241-7.

[3] T. Yamane, H. Okamura, Y. Nishimura, A. Kidera, M. Ikeguchi, J. Am. Chem. Soc. 132(2010)12653-9.

3I0924 Exploring Feature Extraction Method for Time Series Data Obtained by Molecular Dynamics Simulation

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Protein dynamics within an organism are deeply involved in their functions and include multiple modes with different time scales and frequencies on their time-evolution. To analyze changes over time of these protein dynamics, we have been using the wavelet transform, which is one of the methods for time-frequency analysis. In previous work, we have applied the method with singular value decomposition (SVD) to short time series data of molecular dynamics (MD) simulation and have shown its usefulness [1]. There have been the needs to consider the number of dimensions of principal components to be used and apply to longer time scale data. In this work, we apply log time series data obtained by all-atoms MD simulation of Myoglobin[2,3], and explore the index to express the motion features and the method for extracting principal component from the features obtained by the wavelet transform. At first, we introduce the indexes using several singular vectors of SVD and analyze the difference between principal components. Furthermore, we validate other dimensionality reduction techniques for the vector space, for instance, Non-negative matrix factorization.

References:

[1] M. Kamada et al., Chem. Phys. Lett. 502(4-6):241-247 (2011)

[2] Scorciapino MA et al., J Am Chem Soc. 131(33):11825-32 (2009)

[3] Scorciapino MA et al., J Am Chem Soc. 132(14):5156-63 (2010)

3I0936 蛋白質の遅いダイナミクスを観察するための Transform and P28 relax sampling

Transform and relax sampling to enhance slow protein dynamics

Akio Kitao^{1,2} (¹IMCB, The University of Tokyo, ²JST, CREST)

Protein dynamics contains relatively slow components that are diffusive and/or stochastic in nature. Sampling of slow dynamics is a challenging problem for molecular simulation because we need to spend long computational time before observing slow dynamics. Transform and relax sampling (TRS) is proposed as a conformational sampling method to enhance slow dynamics in highly anisotropic systems such as protein in solution. This method consists of three stages; transform, relax and sampling. In the transform stage, molecular dynamics simulation is performed with randomly assigned force bias to enhance the fluctuations along relatively soft collective movements, as expected from the linear response theory. After relaxing the heated system to equilibrium without force bias in the relax stage, Monte-Carlo-type determination is made as to whether the generated state is accepted or not. The sampling stage is then conducted for conformational sampling by conventional molecular dynamics simulation. After test calculation for a coarse-grained model system, TRS was applied a few protein systems to enhance domain motion of proteins and accelerate folding of mini-proteins. We were successful in enhancing open-close domain motions in T4 Lysozyme and glutamine binding protein within 20 ns and also in observing folding-unfolding transitions several times within 100 ns.

3I0948 スクリプト言語を用いた分子力学プログラムの高速化

Coding Molecular Dynamics by an Interpreted Scripting Language with Uncompromising Performance

Yutaka Ueno (AIST, Biomedical Research Institute)

While recent advances of high performance microprocessor allowed large scale molecular dynamics simulations, programs still need improvements in calculation model of target molecular systems including interactions with other proteins. Computational tasks to automate, customize or develop required molecular simulation are facilitated by an interpreted scripting language. Among feasible implementations of such language, Lua language was employed as a software platform for molecular dynamics simulations to support various biophysical studies using atomic coordinates of proteins. To overcome performance degradation by an interpreted scripting language that takes computer resource at run time, a critical portion of code can be implemented in a native code as fast as existing programs. Using a custom vector data type, the code written in C language are linked to Lua to be called from a script. Furthermore, it is also possible to run the code on a recent acceleration hardware such as graphics processing unit (GPU). Once the fast calculation code is fixed, a large program code are described and managed by a interactive script. In addition, Lua provides very efficient interpreter to run most calculation program fast enough even though they were written in Lua. This software platform provides both programming flexibility and processing performance within a comprehensive programming grammar of Lua language.

3I1012 Decomposition Analysis for Binding Enthalpy of Protein-Inhibitor Complex