2P019 Hras-GTP 複合体と Hras-GDP 複合体の分子動力学シミュレーションにおける水分子ネットワークの解析
Analysis of network of water molecules in molecular dynamics simulations of Hras-GTP and GDP complexes

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In order to understand the mechanism of hydrolysis of GTP in the Hras-GTP complex, we study the structures of Hras-GTP and GDP complexes in water solvent by molecular dynamics (MD) simulations.

We evaluated the potential parameters and the atomic charges around Mg²⁺ in Hras-GTP and GDP complexes by quantum chemical calculations. We performed MD simulations of the Hras-GTP and GDP complexes in water solvent using parameters of AMBER03 and our parameters around Mg²⁺. We found that the angular distribution of water around GTP is different from the distribution around GDP. We proposed that this difference of causes the difference of hydrolyzability between GTP and GDP.

In this study, we analyze the network of water molecules using the site-dipole introduced by Higo et al.

2P020 分子動力学シミュレーションによる GLP-1 の最適構造探索
Optimized structure study of GLP-1 by Molecular Dynamics Simulation

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We have performed simulated annealing of glucagon-like peptide-1-(7-36)-amide (GLP-1) with molecular dynamics approach using GROMACS software package. GLP-1, a 30 amino acid peptide with the sequence: HAEGTFTSDVSTLSGQAQAEFIWLVKGR [Protein Data Bank at RCSB code: 1D0R], has the function to increase insulin secretion.

Simulated annealing is a method of optimizing the protein structure. We analyze Coulomb energy of the system without the interaction between water molecules because the energy between water molecules is much larger than the energy concerning proteins, and we observe the secondary structures.

2P021 エネルギー表示溶液理論を用いた分子動力学シミュレーションによる蛋白質複合体モデルの評価
Evaluation of protein complex model using molecular dynamics simulation with the solution theory in the energy representation

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In protein-protein complex prediction, 10³ ~ 10⁴ complex structure models are typically generated and evaluated. Accurate evaluation of generated complex models is a key to predict correct complex model. We recently developed a method to evaluate binding free energy differences of generated complex models through molecular dynamics simulation using the solution theory in the energy representation. Using this method, we can select “near-native” models, which are similar to crystal structure, as low energy structures. To consider a larger number of complex models, we are developing a procedure to combine the free energy evaluation with a method in which ~10⁶ complex models can be clustered and reranked.

2P022 チオエステル周辺の AMBER 力場の開発および評価
Determination and evaluation of AMBER force field parameters for thioester

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Sulfur atoms frequently play important roles in biomolecules. Several enzymes include acetylcysteine or acetyl CoA in the active center, and these molecules contain a thioester sulfur. In this study, the AMBER force field parameters around the sulfur atom of the thioester moiety were determined by high-accuracy quantum chemical calculations. Because the atomic charges are mostly indispensable to classical force field calculations, the atomic charges of acetylcysteine were also calculated. To evaluate the newly determined parameters, quantum chemical and molecular mechanical calculations of short peptides including acetylcysteine were carried out, and the results were compared to evaluate the new parameters.

2P023 アミロイド β の構造探索
Conformational Search of Amyloid β Peptide

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The cause for Alzheimer's disease is considered to be due to the accumulation of amyloid β peptides in the brain. The excess amount of amyloid β peptides leads to the formation of aggregates which are neurotoxic. Therefore, it is important to obtain the conformation of the aggregate of amyloid β peptides. Recently, we have examined the growth process of the aggregates of the amyloid β peptides by FCS and obtained the size of the aggregates. However, we could not identify the conformation of the aggregates. Here, we carry out MD simulations to explore the conformational space of an amyloid β peptide to understand the possible structures and the build-up mechanism.

2P024 Photo synthesis of protein-based drug delivery nanoparticles for active tumor targeting

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In this work, we present a novel method to photo synthesize protein based drug delivery system with active targeting function to tumor site. The disulfide bonds in protein bovine α-lactalbumin (BLA) can be ruptured by controlled UV illumination, which triggers the formation of nano-sized protein aggregates and releases free thiol groups for the modification of active targeting ligand of circular RGD. The synthesis approach is very convenient and cost-effective and can be accomplished in physiological condition. Both in vitro and in vivo experiments validate that this DDS system possesses much greater drug delivery efficiency to the tumor sites and better inhibition capability to tumor growth than the unmodified counterparts.