the sequence, raising the following question. How is the hydration related with the conformational properties of DNA? To address this question, we analyzed the deformability and hydration of various DNA sequences using the ensembles of DNA conformations generated by molecular dynamics simulations. The result showed a correlation between the DNA deformability and the hydration pattern. Most of rigid sequences had a particular type of water localization where two bases diagonally opposite were mediated by a single water bridge. There were a few exceptional sequences where two water molecules participate in the bridge formation. Flexible sequences did not have any specific hydration. Detailed analysis of the conformation ensembles suggests that the obtained relation is associated with the coupled motions of DNA base-pair steps and hydration water. A possible mechanism for this linkage will be shown in the presentation.

2P-115 DNA Dynamics in Solution and on Metal Surface

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Single-stranded oligonucleotides play significant roles in both biology and biomimetic technologies. Despite these observations, the dynamics of single-stranded oligonucleotides have seen little investigation. Thus motivated, we have measured the end-to-end collision dynamics of a series of oligonucleotides by monitoring the quenching of a long lived fluorophore covalently attached on the 3' terminus by a contact quencher attached on the 5' terminus. We find that the collision rate observed for a thymine homopolymer (polythymine) is effectively indistinguishable from that of a more complex sequence, suggesting that the dynamics of the chain are relatively sequence independent. The end-to-end collision dynamics are, however, strongly dependent on the length of the oligonucleotide, and scale with the theoretically expected 1.8 power. This implies that, despite its significant negative charge, single-stranded DNA behaves similarly to a polymer exhibiting only excluded volume effects. We also find that end-to-end collision rates depend linearly on solvent viscosity with a non-zero intercept (the rate extrapolated to the limit of no viscosity) that is independent of chain length. Finally, we have also characterized the dynamics of polythymine when covalently linked to a metal surface, in an effort that to harnesses these dynamics in a potentially promising biomimetic application.

2P-116 分子動力学シミュレーションによる環境条件の違いにおける DNA のコンフォーメーション変化の解析

Analysis of environment-dependent conformational transition of DNA by molecular dynamics simulations

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Sequence-dependent conformational properties of DNA play important roles in various biological processes involving DNA. For example, interactions of proteins with DNA are known to be affected by the conformational properties of DNA. Proteins such as TBP change the conformation of the DNA recognition site to be bent significantly. On the other hand, catalytic protein DNaseI induces the recognition site to A-form. It has been recognized that these conformational transitions in DNA among various canonical forms are biologically relevant. It has also been known that these conformational transitions are induced by environment. Variations in ionic strength and identity, sequence, water activity, and ligand/protein binding can modulate DNA structure. In this study, we examined how the sequence and water activity influence the DNA conformations.

We have carried out 8 kinds of 10-ns molecular dynamics simulations for the dodecamer DNAs by parmbsc0 force field in AMBER8.0. We prepared the structures; d(CGCGAATTCGCG)₂ in B-form (AATT_B) and A-form (AATT_A), and d(CGCGTATACGCG)₂ in B-form (TATA_B) and A-form (TATA_A). We calculated all 4 structures in water(wat) and in 85 % (v/v) Ethanol / H₂O(eth). Only TATA_A in eth was equilibrated in A-form. The others were in B-form. Especially, AATT_A in wat were changed from A-form to B-form conformation in less than 200 ps. These results indicate that the environment is important for the DNA conformations. The detailed results will be shown at the presentation.

2P-117 DNA まわりの水分布の塩基配列依存性に関する理論化学的研究

Theoretical study on the base-sequence dependency of water distribution along DNA groove

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Water molecules at the DNA surface play important roles in DNA-protein and DNA-ligand recognition. However, the base-sequence dependency of water distribution along DNA groove is not well investigated yet. Here we calculate the interaction free energy (ΔG) between a water molecule and 32 kinds of 3bp DNA. To sample the conformational space efficiently, a multicanonical Monte Carlo (MUCAMC) sampling is used. A water molecule moves around the space around the fixed DNA during the MUCAMC sampling. The space around DNA is divided into small cubic cells and the frequency (the number of times water visited the cell) is counted during the simulation. ΔG values are obtained by reweighting technique of the frequency at each cell. Thus obtained ΔG value is the index of stability and ΔG values around DNA represents the spatial distribution of water around DNA. Calculated ΔG values for the 32 kinds of 3bp DNA are combined and utilized to get ΔG values for longer DNA sequences. In

this way, we can predict water distribution for any DNA sequences. We compare the predicted water distribution with the position of water molecules found in the Protein Data Bank (PDB).

2P-118 ピストンモーションを実現した DNA ナノマシンの構造解析

Structural analysis of a DNA nanomachine with a piston motion

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DNA is an ideal material for nanofabrication because its self-assembly can be controlled by base-pairing and it is simple to execute. Four single strands of DNA were synthesized with three different complementary parts in each strand so that they self-assemble into a tetrahedron, with its five edges being double helices but the remaining one edge containing a centrally positioned hairpin loop. The hairpin loop is a reconfigurable structural motif. When the hairpin is formed in its 'closed' state, the length of the sixth edge is expected to be 3.4 nm. This hairpin loop can be extended by adding a 'fuel' strand of DNA that has the complementary sequence to the hairpin region. As a result, the tetrahedron changes its conformation from a closed to an open state. When the double helix forms in the sixth edge by hybridization of the fuel DNA, the length of the helix is expected to be 10.2 nm. An 'anti-fuel' DNA strand can remove the fuel DNA from the open tetrahedron, and the structure returns to the closed state again. This dynamic change like a piston can be controlled by the fuel and anti-fuel DNAs. The driving force of the motion is the binding free energy of the fuel DNA strand. We have successfully visualized the structures of this DNA tetrahedron in the two conformational states by cryoEM. I will discuss the structures in more detail.

2P-119 ヒト IgG に結合する RNA アプタマー複合体の立体構造

X-ray structure of RNA aptamer in complex with human immunoglobulin G

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Aptamers, which are short DNA or RNA folded molecules, bind target molecules with high affinity and specificity. We have recently identified an RNA aptamer specific for the Fc fragment of human immunoglobulin G1 (IgG1), and also showed that an optimized 24-nucleotide RNA aptamer binds to the Fc fragment of human IgG1, but not to other IgG's. To clarify the structural basis for the high specificity of a RNA aptamer, we have performed a crystallographic study of RNA aptamer in complex with the Fc fragment of human IgG1. The complex has been crystallized in 20% polyethylene glycol 1000, 0.2M calcium acetate, 100mM Tris-HCl (pH 8.0), at 294 K by the vapor diffusion method. Preliminary X-ray diffraction studies reveal that the crystals belong to the orthorhombic space group P21212 with unit-cell parameters $a = 83.7$, $b = 107.2$, $c = 79.0$ Å. The crystals diffracted beyond 2.2 Å resolution. We have determined the molecular structure of the aptamer in complex with human IgG. The electron density has clearly proved two aptamers bound to dimeric IgG. The tertiary structures of the recognition sites on the Fc fragment differ significantly between human IgG and other species of IgGs. The structure also explained high specificity and affinity of the selected aptamer to human IgG.

2P-120 超好熱古細菌由来 TATA-box 結合蛋白質の SELEX 解析

SELEX experiments of a hyperthermostable TATA-box-binding protein at different temperatures

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Genomic DNA in thermophiles do not have an intrinsically high thermal stability, because there is no correlation between the overall G or C base content of a given genome and the optimum growth temperature (OGT) of that organism. However, strong correlations have been identified between characteristics of genomic sequences and the OGT from complete genomic sequence analysis of various biological species. Therefore, it has been proposed that sequences in genomic DNA are optimized to function in a particular environment, analogously to the case of proteins. For example, TATA-box sequences are reportedly affected by the temperature at which they function. We carried out SELEX experiments and studied the thermodynamics of the interaction between thermophilic TBP and double-stranded DNA at several temperature. SELEX experiments were performed using a library of 68 bp oligonucleotides containing a central randomized region of 24 bp, and distinct sequences of DNA were consequently selected at 298 and 323 K, respectively. At both temperatures the identified DNA fragments consisted of A/T-rich sequences, but they differ in their nucleotide sequence. At 323 K, box A-like sequence DNAs (e.g. TTTT, TTTA) were selected (ODN50s). This result at high temperature is consistent with the base sequences of the consensus TATA-sequence of Archaea. On the other hand, at 298 K different TATA box-like sequences (e.g. TATA, TTAT) were selected (ODN25s), which were similar to the consensus TATA-sequence of Eukaryote organisms.