that the neck linker-less monomer stably bound to the microtubule even in the presence of saturating ATP. Cryo-EM observation of the neck linker-less mutant on the microtubule in the presence of saturating AMP-PNP displayed a structure similar to that of nucleotide-free wild-type kinesin. These results are consistent with the idea that the neck linker acts as an activator of ATP hydrolysis reaction, and also explains the front head gating mechanism for dimeric kinesin: the neck linker of the leading head is pulled backward so that the head cannot proceed ATP hydrolysis cycle until the trailing head detaches from microtubule.

1P185 Conformational Spread as a Mechanism for Cooperativity in 1B1420 the Bacterial Flagellar Switch-from structure to dynamics

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The switch that controls the direction of flagellar rotation during bacterial chemotaxis has a highly cooperative response. This has previously been understood in terms of the classic two-state, concerted model of allosteric regulation. Here, we used high-resolution optical microscopy to observe switching of single motors and uncover the stochastic multistate nature of the switch. Our observations are in detailed quantitative agreement with a recent general model of allosteric cooperativity that exhibits conformational spread, namely the stochastic growth and shrinkage of domains formed by neighboring subunits sharing a particular conformational state. We propose a structural model for this conformational spread mechanism and discuss its implication in understanding the recent observed switching-load dependence.

1P186 F1-ATPase の回転のメカニズムにおける水のエントロピーの 1YA1115 重要性 Crucial importance of translational entropy of water in rotation mechanism of F₁-ATPase

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We report a recent progress in elucidating the rotation mechanism of F₁-ATPase. The water entropy, which has been shown to be the key factor in a variety of biological self-assembling and ordering processes [1], plays crucially important roles in the mechanism. We first calculate the water-entropy changes upon the formation of the α - β , α - γ , and β - γ subunit pairs, respectively. The change is given as the difference between the hydration entropy of a subunit pair and the sum of the hydration entropies of subunits forming the subunit pair [2]. The calculations are made using a hybrid of the angle-dependent integral equation theory combined with the multipolar water model and the morphometric approach. Our result is quite consistent with that obtained by the MD simulation with all-atom potentials [3], indicating that the packing of the α -, β -, and γ -subunits and their interfaces is highly asymmetrical. We then calculate the hydration entropies of three different groups comprising the γ -subunit, one of the β -subunits, and the two α -subunits adjacent to them. In the presentation, we will argue that the high asymmetry plays essential roles in the rotation mechanism of F₁-ATPase and propose its novel physical picture [2]. [1] M. Kinoshita, Int. J. Mol. Sci. 10, 1064 (2009). [2] T. Yoshidome, Y. Ito, M. Ikeguchi, and M. Kinoshita, to be published. [3] Y. Ito and M. Ikeguchi, J. Comp. Chem., in press.

1P187 滑り運動を可能にするアクチン・ミオシン間相互作用の自由エ ネルギーランドスケープ Free energy landscape of the interaction between actin and myosin underlying the sliding movement of the myosin head

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A single molecule measurement has shown that myosin moves along actin filament with successive two to five mechanical steps of about 5.3 nanometers, which corresponds to hydrolysis of a single ATP molecule (Kitamura et al., Nature 397, 129, (1999)). This phenomenon cannot be explained by the conventional "lever-arm model". It has been shown that unidirectional Brownian motion can arise from the energy landscape with an asymmetric slope due to the electrostatic interactions between actin and myosin (Takano et al., PNAS 107, 7769, (2010)). However it remains unclear the role played by the conformational change within the myosin head. Using a coarse-grained model of proteins with Go-like interactions, we generate the structural ensemble of actin-myosin complex by molecular dynamics to obtain the free energy landscape, which allows us to study the correlation between the conformational

change within the myosin head and the movement of the myosin head along the actin filament. In addition, we decompose the free energy into conformational entropy and various interaction energies to determine a factor important for the sliding movement of the myosin head.

1P188 キネシンヘッド間張力の全原子シミュレーションによる評価 Kinesin internal tension for the coordinated walk estimated by all-atom MD simulation

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Kinesin-1 is a two-headed motor protein that moves along microtubules (MT) in a hand-over-hand manner, however the mechanism for the coordinated movement is still not clear. To elucidate the mechanism, we recently solved the crystal structure of nucleotide-free kinesin motor domain, and modeled dimeric kinesin bound to MT under various nucleotide conditions (Makino et al. this meeting). Based on these structural modeling, we propose a model to explain the coordinated processive movement: 1) In the one-head-bound state, the tethered head cannot release ADP until the partner head binds ATP, because if both heads become nucleotide-free (apo-apo), the neck linkers that connects two motor heads would be stretched out. 2) In the two-head-bound state in which the leading head is nucleotide-free and the trailing head is in ATP state (apo-ATP), the leading head cannot bind ATP because the neck linkers will be stretched out in ATP-ATP state. To test these hypotheses, we carried out all-atom MD simulations based on the atomic models of kinesin-microtubule complex, and estimated the tension posed to the neck linker at the following states: apo-apo, ATP-ATP and apo-ATP. We found that the neck linker tensions in apo-apo and ATP-ATP states are significantly larger than that in the apo-ATP state. These results support the idea that off-pathway transitions are prohibited due to the tension increase, so that kinesin can coordinate two motor heads to move processively.

1P189 溶媒和を通じた化学反応の仕事への変換過程のシミュレーション Molecular Dynamics Simulation of Conversion from Chemical Reaction to Work via Solvent

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Conversion process from chemical reaction to work in a solution is simulated by the molecular dynamics simulation (MD). A model colloidal particle which has a reaction site on the surface is immersed in solvent. The interaction between the reaction site and the solvent is changed during the "chemical" reaction. In the present simulation the strong attraction appears in the "reaction period" and disappears except the period. The simple model is adopted as a solvent molecule, too. However, this reaction mimics the ATP-hydrolysis on the protein surface in aqueous solution. The Brownian motion of the colloidal particle is modulated at the beginning of the reaction. However, the directions and the migrating distances depend on the event. So we can observe the forward step events and the back step events for same parameter. Then we take an average over the events and the trajectory converges. Various parameters are examined. The efficient of the conversion is dependent on the interaction change, the reaction period, the packing fraction of solvent molecules and so on. The direction also depends on the reaction period in case of the averaged trajectory. Here, we do not maintain that the mechanism of this type molecular motor is important in the bio-molecular motor. However, the exploration of this type motor could be interesting.

1P190 キネシン 1 の協調的な二足歩行運動を可能にする構造基盤の解 析 1B1435 Structural basis for the coordinated processive movement of kinesin-1 studied by structural and single molecule analyses

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Kinesin-1 is a dimeric motor protein that moves processively along microtubules. Kinesin's two motor domains alternately hydrolyze ATP to drive hand-over-hand type movement, however the structural basis for the coordinated walking mechanism remained unknown. At the last annual meeting, we reported the first crystal structure of nucleotide-free kinesin-1 and presented atomic-detailed structural models of kinesin dimer on microtubule at various nucleotide states. Here, we remodeled kinesin dimer structures based on the high-resolution cryo-EM density maps (Sindelar et al. 2010) and refined the neck linker structures using MD simulations. Based on the analysis of these