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Abstract of Doctoral Dissertation

Degree requested Doctor of Life Science Applicant's name: Noushaba Nusrat Mafy

Title of Doctoral Dissertation

Driving and Regulation of Macroscopic Motile Functions in Artificial and Living Systems by Molecular Photoswitches

光分子スイッチによる人工系および生体系での巨視的運動機能の駆動と制御

Life on nature is fantastically diverse. All life is composed of microscopic building block cells, which are themselves composed of nanoscale molecules. Where, microscopically cells are using nanoscale molecules to perform several motile functions, including transport of metabolites across cell membranes, signaling of nerve impulses, transport of chromosomes during cell division, generating force etc. By using these cellular events, macroscopically plants are growing, animals are moving and doing work, insects are crawling or climbing etc. After examining this relation between microscopic and macroscopic activities in living organisms, I can claim all the macroscopic movements and other functions in living organisms are governed by these nanoscale molecules. Amplification of such molecular scale motions to produce a controlled macroscopic change is the main challenge in the development of molecular devices. This doctoral thesis focused on amplification of novel photoisomerization event of azobenzene based molecules in both artificial and living system to drive the rotational motion and regulate the cell division, respectively. By illuminating with a specific light, the azobenzene molecule undergoes *trans*-*cis* isomerization, which involves reversible change in the geometry and charge of the molecule. These reversible changes in the structure by light induce different affinity toward the protein or liquid crystals without further addition of another molecule and reversibly reorganize the molecular systems.

In case of artificial system, I introduced a molecular system which induced an accumulative unidirectional rotary motion of glass flakes with about 100 μm. The molecular system was a chiral nematic liquid crystal doped with chiral azobenzene derivative which showed different texture change paths upon UV and visible light irradiations inducing "*trans* to *cis*" and "*cis* to *trans*" photoisomerizations, respectively, of the chiral azobenzene dopant. Namely, a polygonal fingerprint texture accumulated the ordered molecular motion of each molecule in macroscopic film and induced the rotation of glass flakes on the film surface during UV irradiation, while scattered domain in focal conic texture induced no rotation of glass flakes emerged during visible light irradiation. As a result, cycles of the alternative irradiation of UV and visible lights afforded many rotations toward a single direction of the glass flakes which can be considered as a continuous conversion of light energy to mechanical work. I may compare the effect of this molecular system converting "back and forth" structural change between *trans* and *cis* isomers of the chiral azobenzene to a continuous rotational motion of glass flakes with the crankshaft effect converting a piston-like motion to a rotational motion seen in engines in the real world.

In cellular system, I have demonstrated the reversible control of mitosis cell division by transferring the reversible photoisomerization information of azobenzene based molecule. During eukaryotic cell division, the replicated chromosomes are transported from the centrosomes (spindle poles) towards the plus end of spindle microtubules by the kinesin-like motor protein, centromere-associated protein E (Cenp-E / kinesin 7), which can hydrolyze ATP to produce the mechanical works. While, *trans-cis* photoisomerization of azobenzene allowed us to manipulate both activation and inhibition of motor activity of Cenp-E in cells and *in vitro* system. By regulating the Cenp-E activity, it is possible to control the chromosome movements in a reversible mode. Cenp-E was inhibited under *trans* state and induced miscongression of chromosomes and stopped the cell cycle progression, whereas it was not under *cis* state. By using light irradiation, reversible and dynamic control over Cenp-E-driven chromosome movements were addressed in living mitotic cells. This work illustrated the amplification of molecular change under light irradiation to regulate the motor activity of kinesin as well as dynamic cellular processes in living system.

Overall, these findings add a significant contribution to the broad field of amplification of molecular motion to macroscopic system. Specifically, here azobenzene photoswitches efficiently transferred it's switching information to control the chromosome dynamics in living cells and mimic the rotational motion in artificial molecular machine.