論文の内容の要旨

Molecular-Level Precision Functionalization of Surface Nanostructures by Noncovalent Interactions

(非共有結合的相互作用を用いた表面ナノ構造の分子レベル精密修飾)

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1. Introduction

Functional groups on surface of materials strongly affect the physicochemical properties such as solubility and binding affinity to other materials. Noncovalent immobilization of functional molecules to the surface is often selected for the modification of materials due to the facility in operation. For example, surface functionalization is often achieved by solvophobic interactions for self-assembled objects such as in solution. In another case, nanocarbon materials can be noncovalently functionalized by using chemically-modified aromatic molecules through π–π interaction. However, these noncovalent approaches often lack the control of interactions at the molecular level precision for construction of objects and cause nonspecific adsorption of the molecules to the surface. In addition, the ill-controlled molecular immobilization methods often induce destabilization of self-assembled objects and decrease of cost-effectiveness of the surface modification. Therefore, more precision surface functionalization methods are needed.

In this thesis, I developed two kinds of supramolecular surface modification methods to overcome these problems. One is post-surface modification of a self-assembled nanocapsule via fluorous interaction. Another is shape-dependent surface modification of a nanocarbon via hydrophobic host-guest interaction.

2. Hierarchical Construction of Protein-Coated Capsule by Orthogonal Noncovalent Interactions

In the field of pharmacotherapy, self-assembled capsules that can bind to a specific membrane protein of target diseased cells have attracted much attention as a drug carrier for the efficacy control. To bind the capsules to the target cells, surface functionalization with protein ligands is often employed. However, immobilization of the protein ligands into a membrane of self-assembled capsules, especially liposomes, often destabilizes the membrane structure due to competitive interactions between the membrane formation and the ligands immobilization.

Herein, I report a noninvasive ligand display method on the surface of a self-assembled vesicle of fluorous fullerene amphiphile **F8K**. A part of this result had been already reported in my master theses.[1] Our group has reported water-soluble fullerene pentaadducts that are composed of nonpolar fullerene core, polar cyclopentadienide anion, and nonpolar (perfluoro)alkyl groups form structurally robust sub-100-nm sized vesicles in water.[2] This structural robustness of fullerene membrane enables the surface modification without dissociation of the vesicular structure. Similar to other fullerene amphipiles, **F8K** forms the vesicle **V1** with the perfluorooctyl substituted groups expored to water phase.[3] Modification of the perfluorinated surface of **V1** succeeded with fluorous-tagged (FT)-ligands such as FT-mannose (FT-Man **1**) (Figure 1). FT-ligands were easily and densely immobilized on the surface of **V1** by just mixing the solutions of FT-ligands and **V1**.

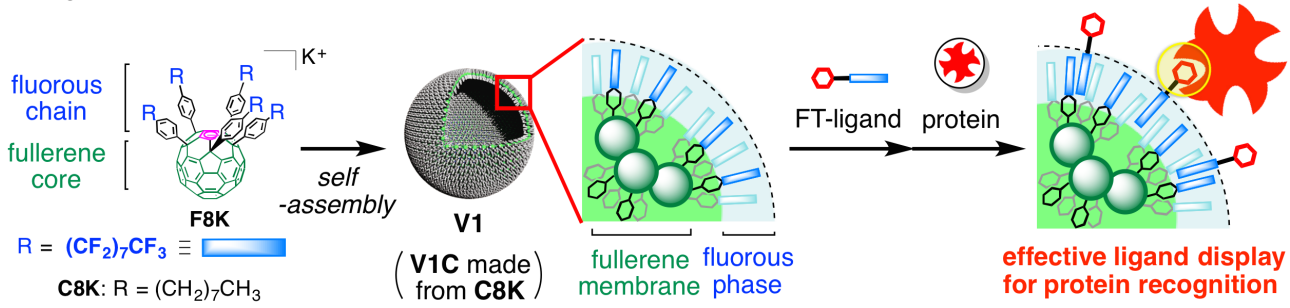

Figure 1. A fluorous fullerene vesicle noncovalently decorated with protein molecules by sequential addition of FT-ligands and proteins.

The surface modification of fullerene vesicles was evaluated more focusing on combination of functional groups on fullerene amphiphiles and ligand molecules. Mannopyranose substituted with a short fluorous tag (FT-Man **2**) and an alkyl tag (AT-Man **3**) were synthesized (Figure 2a). A vesicle **V1C** composed of a fullerene amphiphile substituted with octyl group (**C8K**) was used as an aliphatic template. Upon mixing of each vesicle solution and ligand solution, size of the vesicles increased due to the ligand immobilization, and the combination of **V1** and FT-Man **1** showed significant increase that indicates the ligand display on the surface of **V1**. FT-Man **1**-coated **V1** was strongly bonded to concanavalin A (ConA) via mannose-ConA binding. In contrast, other combinations (**V1**–AT-Man **3**, **V1C**–FT-Man **1**, and **V1C**–AT-Man **3**) did not show significant protein bonding property due to the ill-ordered and weak immobilization of the ligands. Combination of **V1** and small-sized ligand FT-Man **2** did not show protein bonding property. This result suggests that FT-ligands are precisely immobilized on the self-assembled membrane of **V1** with angstrom level. High resolution scanning electron microscopy (SEM) provided visual evidence that **V1** maintained its spherical shape after addition of FT-Man **1** and ConA (Figure 2b). Ligand display and the following protein bonding on the self-assembled membrane of the fullerene vesicle were achieved using fluorous interaction without collapse of the vesicle.

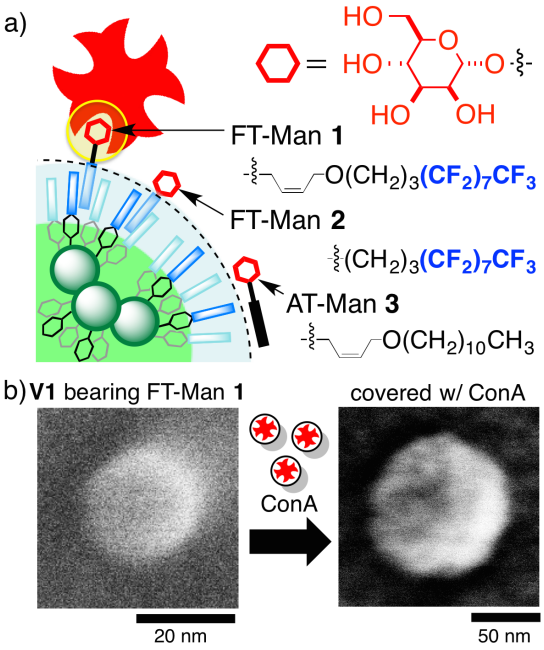

Figure 2. Structure evaluation of ligands and ConA-bearing fullerene vesicles. (a) An illustration of the ligand displays on **V1** indicated by the size increase and protein bonding property. (b) SEM images of **V1** bearing FT-Man **1** (left) and ConA-bonded **V1** (right).

3. Shape-Selective Surface Modification of a Nanocarbon via Host-Guest Interaction of Cyclodextrins

Carbon nanohorn (CNH) aggregates are 50–150 nm-sized aggregates of cone-shaped carbon nanotubes (Figure 3).[4] Because of the unique dahlia-shaped morphology, they have large surface area that is useful for occlusion materials and catalyst supports. In addition, recently our group reported a transmission electron microscope (TEM) observation technique for organic molecules using CNH aggregates as a specimen support. Functional groups bonded to the tip of CNH are observed in near-atomic resolution.[5] Surface modification of CNH aggregates has been performed in a similar manner to that of carbon nanotube, such as adsorption of aromatic molecules by π-π interactions and surfactants by hydrophobic interactions. However, as generally found in functionalization of other nanocarbons, modification sites on the surface of CNH aggregates are difficult to control.[6]

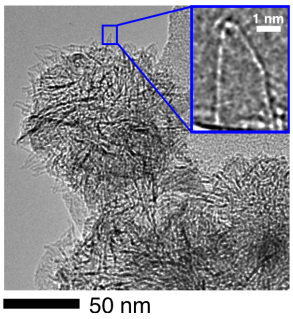

Figure 3. TEM image of CNH aggregates.

To overcome this problem in the surface modification of nanocarbons, I focused on morphology difference in nanocarbons, for instance, conical tip structure of CNH aggregates that is as large as fullerene. For the development of a shape-selective surface modification method for the nanocarbon, I chose host-guest interaction as a key to modify a specific site on solid surface precisely. Cyclodextrins (CDs) are usually used as a host molecule for encapsulation of small guest molecules in water. In particular, γ-CD is known to encapsulate fullerenes into its inner cavity and forms a stable water-soluble complex.[7]

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γ-CD formed a complex with the tip of CNH aggregates and made water-insoluble CNH aggregates dispersed in water well than other-shaped sugars (glucose, starch, and small-sized CDs; α-CD, β-CD). Complexation of CNH aggregates and sugars were evaluated by qualification of the dispersion property of sugar/CNH hybrids macroscopically (Figure 4). In addition, I succeeded in visualizing the host-guest complex on a single CNH by high-resolution TEM. Furthermore, a specimen molecule, high-contrast iodine atom, bonded to γ-CD was also observed (Figure 5).

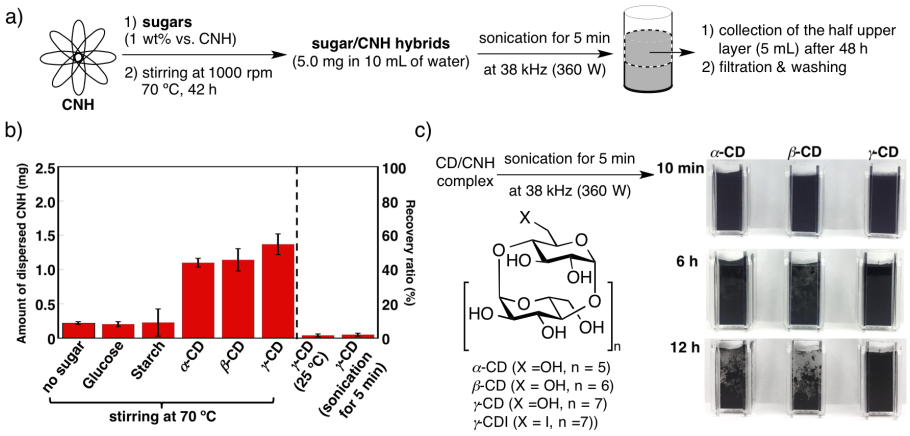

Figure 4. Evaluation of surface modification of CNH aggregates with sugars. (a) A procedure for quantification of dispersion property of sugar/CNH hybrids. (b) Recovery ratio of sugar/CNH hybrids. (c) Re-dispersion of CD/CNH complexes in water for evaluation of the stability.

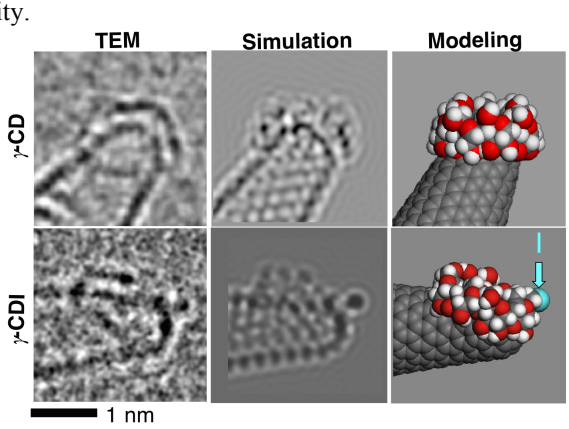

Figure 5. TEM images of γ-CD and monoiodinated γ-CD (γ-CDI, The molecular structure is denoted in Figure 4c.) and their simulations and modelings.

By using the shape and size-selective solid surface recognition by CDs, I achieved separation of nanocarbon particles with different shapes. CNH aggregates were dispersed better than hornless graphitic carbon particles that are produced during their production process. These impurities impair the utilities of CNH aggregates due to the small surface area. I found the CNH aggregates can be separated from other nanocarbons by the addition of with 1 wt% of γ-CD in the dispersion liquid of CNH aggregates. Compare with usual purification method with surfactant as the dispersant,[8] the cost-effectiveness of CNH aggregate/dispersant in this method is 2500 times higher due to the precise surface modification.

4. Conclusion

Two kinds of methodologies for precision surface modification on a self-assembled vesicle and a nanocarbon were developed. Noninvasive ligand display on the surface of fluorous fullerene vesicle was achieved by orthogonal interactions for the formation of the vesicle membrane and the immobilization of ligand molecules on the surface. Robustness of fullerene membrane and fluorous interaction are keys to effective ligand display for the following protein recognition. On the other hand, site-specific and high cost-effective surface modification of a nanocarbon was achieved by applying shape-selective host-guest interaction of cyclodextrins for recognition of the specific surface structure.

References

[1] (a) Mizuno, S. *Master Thesis* **2011**. (b) Yamada, J. *Master Thesis* **2013**.
[2] Homma, T.; Harano, K.; Isobe, H.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 6364–6370.
[3] Homma, T.; Harano, K.; Isobe, H.; Nakamura, E. *Angew. Chem. Int. Ed.* **2010**, *49*, 1665–1668.
[4] Iijima, S.; Yudasaka, M.; Yamada, R.; Bandow, S.; Suenaga, K.; Kokai, F.; Takahashi, K. *Chem. Phys. Lett.* **1999**, *309*, 165–170.
[5] Gorgoll, R. M.; Yücelen, E.; Kumamoto, A.; Shibata, N.; Harano, K.; Nakamura, E. *J. Am. Chem. Soc*. **2015**, *137*, 3474–3477.
[6] (a) Tasis, D.; Tagmatarchis, N.; Bianco, A.; Prato M. *Chem. Rev.* **2006**, *106*, 1105–1136. (b) Zhu, S.; Xu, G. *Nanoscale*, **2010**, *2*, 2538–2549.
[7] Yoshida, Z.; Takekuma, H.; Takekuma, S.; Matsubara, Y. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 1597–1599.
[8] Zhang, M.; Yudasaka, M.; Miyawaki, J.; Fan, J.; Iijima, S. *J. Phys. Chem. B* **2005**, *109,* 22201–22204.