# Imaging life with programmable supramolecular interaction

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Developing strategies to assemble molecular components within the complexities of cells and tissues is of great interest in biology. It drives advancements in various domains of fundamental and medical research, including protein modification, assay development, therapeutic targeting, and cell surface engineering. Importantly, such strategies play a crucial role in applications that require molecular tagging or labeling, such as imaging. Supramolecular non-covalent structural motifs are particularly attractive for this purpose as it allows molecular−level design approach to control properties of the systems in a manner that is life-like (i.e., dynamic behavior, environmental responsiveness, and adaptability). However, the application of synthetic recognition motifs for programming molecular assemblies in living systems remains a challenging task due to the chemical complexities of the living system and lack of selectivity in conventional non-covalent interactions. In my talk, I will describe our recent success of programming molecular assemblies in the living system based on a synthetic host-guest system featuring Cucurbit[7]uril (CB[7]). We demonstrated that highly selective and ultrastable host-guest interaction in CB[7] provides a non-covalent mechanism for assembling imaging agents in cells and tissues. Importantly, we have shown that CB[7]−ADA interaction fulfills the demands of specificity and stability that is required for bioorthogonal assembly in the living cell. We demonstrated this by labeling and imaging the distribution and dynamics of microtubule in HeLa cell. We used the dynamic nature of the supramolecular interaction to develop a new technique for super-resolution imaging with ~20 nm resolution. This technique, which we call SPIN (Supramolecular Probe-based Interaction mediated Nanoscopy), exploits repetitive and transient binding of the fluorescently labeled guest to complementary CB[7] host to obtain stochastic switching between fluorescence ON- and OFF-states. By connecting CB[7] guest to targeting ligands, we demonstrated that this autonomous blinking enables two-dimensional (2D) and 3D super-resolution imaging of biomolecules in cells. We expect that this simple and easy to implement strategies will be easily applicable to address various questions in a wide range of biological and materials research.

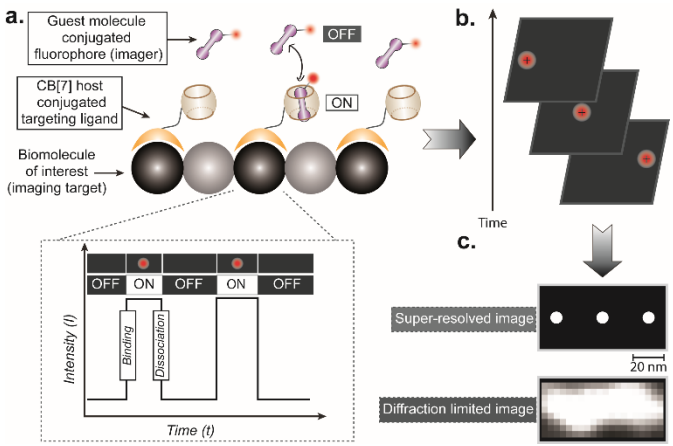


**Figure 1. The concept of host-guest mediated super-resolution imaging.**

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