Project #14: **Shuming Nie** and **Peng Xi**: *Super-resolution Imaging of Cellular Dynamics with Quantum Dots and STED*

Optical microscopy is one of the most widely used techniques in biology and medicine, but its spatial resolution has been constrained by the optical diffraction limit (about half of the light wavelength). With stimulated emission depletion (STED), the barrier of the diffraction limit can be broken, therefore opening up new possibilities in studying molecular dynamics in living cells. A major engineering challenge is to develop fluorescent probes that are highly photostable and have minimal overlap between the excitation and emission spectra (to avoid re-excitation during the depletion process). Semiconductor quantum dots (QDs) are tiny light-emitting particles on the nanometer scale and are emerging as a new class of fluorescent labels for imaging applications. Compared to organic dyes and fluorescent proteins, QDs have unique optical and electronic properties such as size-tunable light emission, narrow and symmetric emission spectra, and broad absorption spectra that enable the simultaneous excitation of multiple fluorescence colors. However, their use in high-resolution cellular imaging is still limited by the large hydrodynamic size of bioconjugated QDs and by their overlapping absorption and emission spectra. This seed grant application aims to address these problems by combining the research expertise of the Xi Group in STED super-resolution imaging at PKU and the QD development expertise of the Nie Group at Emory/Georgia Tech. The proposed research is at the cutting edge of imaging science and is part of a large effort to develop next-generation QDs for molecular and cellular imaging at ultrahigh resolution and sensitivity.