Investigating structure-dynamics-function relationship of biomacromolecules at single-molecule level with submicrosecond time resolution

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In the first part of the talk, I will continue discussions on my efforts in developing new and advanced variants of two-dimensional fluorescence lifetime correlation spectroscopy (2D FLCS),[1] which reveals biomolecular structural dynamics at the single-molecule level with submicrosecond time resolution, and its applications to address important chemical and biological problems. On the method development front, I will present the framework of pulsed-interleaved-excitation (PIE) 2D FLCS which significantly improves the sensitivity of the 2D FLCS method in detecting different fluorescent species.[2] On the application front, I will discuss the use of 2D FLCS in understanding transition state and transition path time of biomolecules,[3] in investigating spontaneous structural dynamics around the chromophore moeity of the novel fluorescent protein "LSSmOrange" (which is important for multicolor fluorescence imaging),[4] and our preliminary efforts in understanding the mechanism of enzymatic action of CRISPR-Cas13a gene editing system which cleaves RNA targets colaterally.[5]

In the second part, I will present my future research plan, which is to study the structure-dynamics-function relationship of noncoding RNAs, especially therapeutically important gene-regulatory noncoding RNAs from bacteria (e.g., riboswitches) and viruses (e.g., viral encoded microRNA), using state-of-the-art single-molecule fluorescence spectroscopy and microscopy. I will discuss how the proposed single-molecule based approach can provide a new perspective in understanding the molecular mechanisms of gene regulation by noncoding RNAs through simutaneous/quasi-simultaneous investigation of their structures, dynamics, and functions.

References

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[5] J. S. Gootenberg *et al. Science*, 356 (6336), 438-442.