NANOSCALE TOOLS FOR SENSING AND IMAGING SINGLE MOLECULES

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Advances in fluorescence imaging and microscopy techniques have provided the ability to detect and monitor biomolecules and the interactions between them at the ultimate sensitivity of a single molecule. In this talk I will discuss how single-molecule fluorescence imaging can be synergistically combined with a technique that allows one to also place and position single molecules on the nanoscale, namely, DNA origami, in the pursuit of building new single-molecule sensors and imaging tools. I will discuss how, using DNA as a building material, we can create light antennas on the nanoscale and amplify fluorescence signals of single molecules by up to few hundred-fold, enabling their detection on a smartphone camera [1]. I will also discuss our work on building modular and tunable sensors with high FRET contrast and single-molecule sensitivity. Utilizing a DNA origami nanostructure as a scaffold to arrange and decouple different sensor components we developed a single molecule sensing platform adaptable to a variety of biomolecular targets, such as nucleic acids, proteins, as well as enzymatic activities. The developed platform also offers mechanisms to tune the dynamic window and specificity of the sensor as well as to implement more complex multiplexed sensing schemes [2]. Finally, I will briefly touch on our efforts to develop strategies to increase the robustness and stability of DNA origami sensors and labels in challenging chemical and biochemical environments [3].

[1] *Nat. Commun.* 2021, *12*, 950; *Acc. Chem. Res.* 2021, *54*, 3338-3348; *iScience* 2021, *24*, 10302; *Adv. Mater. Interfaces* 2022, 200255; *ACS Nano* 2023, *17*, 1327.

[2] *bioRxiv* 2023, doi: https://doi.org/10.1101/2023.11.06.565795.

[3] *Angew. Chem.* 2020, *60*, 4931; *Adv. Mater.* 2023, *35*, 2212024.