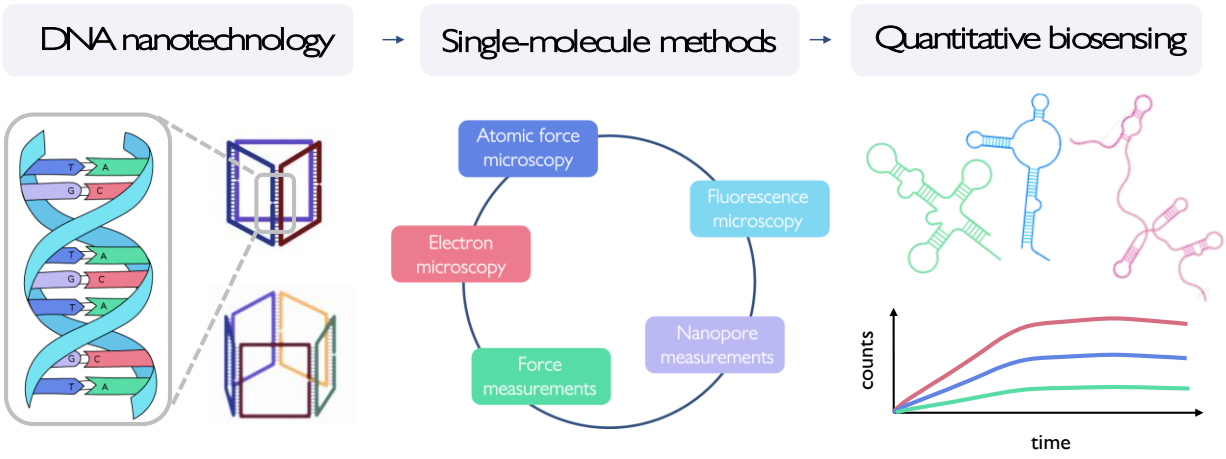
One-by-one: Single-molecule techniques for quantitative bioanalysis

DNA, RNA, and proteins are the key biomolecules responsible for regulating cellular processes, making these biopolymers exceptional targets for the development of new biosensing platforms. In particular, the detection of proteins and nucleic acids present within biofluids (*e.g.* serum or saliva) enables the assessment human health, facilitating early cancer diagnosis and supporting sensitive diagnostic tools for viruses and bacteria. While the importance of DNA, RNA, and proteins as versatile biomarkers is undisputed, technological advances are still required to enable quantitative readout and facile multiplexing.

My work combines the principles of nucleic acid nanotechnology with state-of-the-art single-molecule techniques towards the development of new, quantitative bioanalysis platforms. In this talk, I will describe the use of single-molecule fluorescence methodologies to probe the function of dynamic, surface-grafted DNA nanostructures which respond specifically to sequences of interest.[1] These nanostructure probes may also be constructed using a fully automated microfluidic method, enabling the formation of a monodisperse layer of sensing units on a microscope slide for direct imaging.[2] The high spatiotemporal resolution of fluorescence allows for the differentiation of nanostructure assembly mechanisms with single-molecule precision.[3] By combining simple chemical approaches to reshape RNA with inexpensive and versatile nanopore sensing, I have also demonstrated single-molecule detection of pathogenic RNA. Using this approach, specific RNA sequences can be readily identified, even amid the complex background of total cellular RNA.[4] Finally, I will discuss how nanopore techniques may also be extended to examine critical protein-RNA interactions. Taken together, these methods may be employed to fully leverage the power of the single-molecule approach towards the next generation of quantitative biosensors.



References:
(1) Platnich, C. M. *et al. ACS Nano* **2018**, *12* (12), 12836-12846.
(2) Islas, P. & Platnich, C. M. *et al. Advanced Materials* **2024**, *36* (36), 2403477.
(3) Rizzuto, F. J. & Platnich, C. M. *et al. Nature Chemistry* **2021**, *13* (9), 843-849.
(4) Platnich, C. M. *et al. Journal of the American Chemical Society* **2024**, *146* (19), 12919-12924.