DNA nanorulers as superresolution standards

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The field of fluorescence microscopy achieved tremendous improvements in resolution by the emergence of novel techniques breaking the diffraction limit, summarized under the term super-resolution microscopy. Now resolutions down to 20 nm and less can be achieved but validating and testing those super-resolution microscopes remains challenging due to the lack of precise and nano-scaled fluorescence standards. The gap between top-down and bottom-up techniques – ranging from a few to a few hundred nanometers – could be bridged by means of DNA nanotechnology allowing to specifically design molecular structures with programmed shapes and functionality. The technique behind is called DNA origami and offers the possibility to precisely attach fluorescent dyes at preassigned positions and subsequently establish defined point-to-point distances of fluorophores [1,2]. The flexibility and versatility in the design of DNA origami-based microscopy standards makes them ideally suited for the broad variety of emerging super-resolution microscopy methods. As DNA origami structures are durable and portable, they can become a universally available specimen to check the everyday functionality of a microscope. For instance, nanoscopic rulers qualify for the quantitative determination of resolution in a statistically firm and reproducible way and allow for the comparison of the resolution of different super-resolution techniques. Rulers are developed for different applications such as STED and SIM as well as localization-based super-resolution microscopy in 2D and 3D.
