

Electron microscopy of DNA nanostructures and their hybrid assemblies

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Programmable DNA nanostructures have attracted increasing attention for nanoparticle engineering and assembly, as well as for templating lithographic structures with nanoscale features [1]. Their exceptional spatial addressability enables the precise positioning and functionalization of molecular components, allowing the bottom-up construction of increasingly complex architectures. The assembly of heterogeneous, higher-order hybrid structures further expands their potential for applications ranging from biomedicine to nanophotonics [2].

Imaging these structures by electron microscopy, particularly without contrast-enhancing stains, remains challenging because DNA is composed predominantly of low atomic-number elements and therefore provides relatively weak electron-scattering contrast. Nevertheless, optimized electron microscopy approaches can provide detailed structural information on DNA nanostructures and their hybrid assemblies. Here, we explore different electron microscopy approaches for imaging these systems and investigate their stability and response to electron irradiation across a range of substrates and imaging conditions. We imaged the nanostructures and hybrid assemblies using cryogenic and high-resolution transmission electron microscopy (TEM), scanning electron microscopy (SEM), and, in preliminary experiments, low-energy electron microscopy (LEEM). Several representative examples are shown in Figure 1, including systems in Figure 1A and 1B that can be imaged without additional staining or contrast-enhancing agents while maintaining exceptional structural stability over typical imaging times. These results demonstrate the capabilities and limitations of different electron microscopy modalities for DNA-based nanostructures and provide insights into their compatibility with electron-beam-based characterization and lithographic workflows. They also highlight the potential of DNA nanostructures as model systems for studying electron–matter interactions in biologically relevant materials.

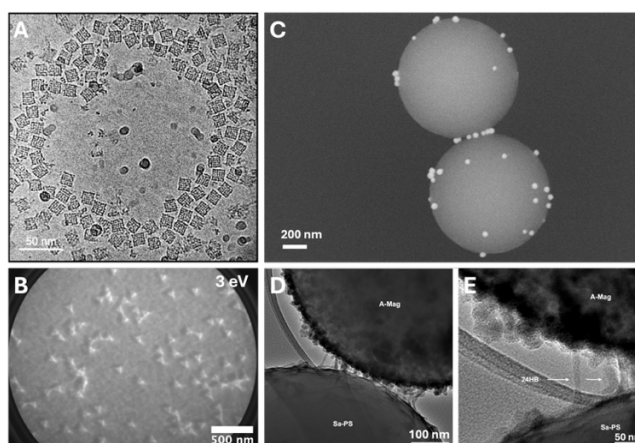


Figure 1. Images of DNA nanostructures and DNA nanostructure hybrid assemblies obtained using various electron microscopy techniques: (A) cryo-TEM image of $6 \times 6 \times 64$ nt DNA nanoblocks, (B) DNA origami triangles imaged by LEEM, (C) polystyrene microparticle dimers decorated with Au nanoparticles via a DNA origami linker scanned by SEM, and (D, E) the connecting point between a polystyrene microparticle and a magnetic nanoparticle bridged by a 24HB DNA origami linkers visualized by TEM [2].

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References

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