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Summary

Soft matter has historically been an unlikely candidate for investigation by electron microscopy techniques due to damage by the electron beam as well as inherent instability under a high vacuum environment. Characterization of soft matter has often relied on ensemble-scattering techniques. The recent development of cryogenic transmission electron microscopy (cryo-TEM) provides the soft matter community with an exciting opportunity to probe the structure of soft materials in real space. Cryo-TEM reduces beam damage and allows for characterization in a native, frozen-hydrated state, providing direct visual representation of soft structure. This article reviews cryo-TEM in soft materials characterization and illustrates how it has provided unique insights not possible by traditional ensemble techniques. Soft matter systems that have benefited from the use of cryo-TEM include biological-based "soft" nanoparticles (e.g., viruses and conjugates), synthetic polymers, supramolecular materials as well as the organic-inorganic interface of colloidal nanoparticles. Many challenges remain, such as combining structural and chemical analyses; however, the opportunity for soft matter research to leverage newly developed cryo-TEM techniques continues to excite.

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