Studying Stimuli-Responsive Polymeric Nanomaterials via Liquid-Cell Transmission Electron Microscopy

Thermoresponsive polymers are used in numerous technological applications, including biomedicine, insulator materials, and tissue engineering. Despite their wide use, we lack well-established, direct techniques for elucidating their elevated temperature, solution-phase, nanoscale morphologies and dynamics. Presently, the accepted workflow for analyzing these materials at elevated temperatures consists of scattering techniques with static imaging via electron microscopy. However, scattering techniques require raw data to be fit to models, often creating challenges in assigning nanostructure morphologies. Alternatively, direct imaging by traditional transmission electron microscopy (TEM) methods at temperature is typically not feasible for nanomaterials that can undergo thermally-reversible transitions.

To address this unmet need in the fields of nano and polymer science, we examined thermoresponsive polymeric materials by variable temperature liquid-cell TEM (VT-LCTEM), a nascent technique for imaging solvated nanomaterials and their dynamics with heating capabilities. We studied phase transitions of thermoresponsive poly(diethylene glycol methyl ether methacrylate) (PDEGMA)-based polymers, specifically a homopolymer, diblock, and triblock. We mitigated sample damage by screening imaging and solvent conditions during LCTEM and evaluated polymer survival via matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI-IMS). Additionally, we employed variable temperature small angle X-ray scattering (VT-SAXS) to correlate LCTEM data. Our multimodal approach, utilizing VT-LCTEM with MS validation and VT-SAXS, is generalizable across polymeric systems and can be used to study solvated nanomaterials and thermally-induced transitions. Moreover, utilizing SAXS with LCTEM provided direct insight into transient nanoscale intermediates formed during the thermally-triggered transformation of a PDEGMA-based triblock. Notably, we observed the temperature-triggered formation and slow relaxation of core-shell particles with complex microphase separation by both techniques.

