Cryo-EM in the Study of Nanostructured Liquids
State-of-the-Technology

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Cryogenic-temperature transmission electron microscopy (cryo-TEM) is now a standard tool for the study of complex liquids, i.e., liquid systems with aggregates or building blocks on the nanometric scale. Methodologies have been developed to help capture the nanostructure of liquid systems, while preserving their original state at a given concentration and temperature. Cryo-TEM is now widely used to study synthetic, biological, and medical systems. Originally developed for aqueous systems, it has been also applied successfully in the study of non-aqueous systems, even in unusual solvents, such as strong acids.

Recent developments in high-resolution scanning electron microscopy (HR-SEM) have made it an ideal tool for the study of nanoparticles and colloids in viscous systems or in systems containing large objects, hundreds of nanometers and larger, in which small (nanometric) features are to be imaged, e.g., hydrogels or body cells. Such system cannot be studied by cryo-TEM. Liquid nanostructured systems can now be studied by cryogenic-temperature scanning electron microscopy (cryo-SEM), using much-improved cryogenic specimen holders and transfer systems, even without conductive coating. In recent years we have developed a novel specimen preparation methodology for cryo-SEM specimens that preserves the original nanostructure of labile complex liquids at specified composition and temperature, quite similarly to what has been done in cryo-TEM.

In my talk I will describe briefly the principles and the state-of-the-technology of cryo-TEM and cryo-SEM, and, through examples of our recent work, will demonstrate various variants of the methodology that allow us to study a wide range of soft matter systems, taking advantage also of the combination of cryo-TEM, cryo-SEM, and non-imaging, e.g., scattering techniques.