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# In-situ Liquid Phase TEM of Soft and Active Matter

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Imaging soft materials in solution is essential for the understanding complex mechanisms involved in molecular self-assembly. Liquid phase transmission electron microscopy (LP-TEM) is an capable of directly monitoring morphological changes of materials in solution with a unique combination of temporal and spatial resolution. LP-TEM has been used to study a wide range of soft materials and molecular assemblies including polymers, peptides, proteins, small molecules and metal−organic frameworks [1]. These studies provided an unprecedented insight into nanoscale reaction mechanisms that have significantly improved our understanding of nanomaterial synthesis. The primary challenge for the field of LP-EM is understanding the role that the electron beam plays in the observed mechanism. It is common to perform control experiments to establish a critical dose limit with which a process can be observed. A consequence of having to work below a critical dose limit is that LP-EM experiments are mostly performed at the limit of signal-to-noise, making data interpretation and analysis extremely difficult. Furthermore, even after a critical dose has been established, it is impossible to completely rule out the role of the electron beam using LP-EM experiments alone. Consequently, in-situ Liquid Phase TEM of soft matter required a series on control experiments, detailed imagine analysis methods and supporting data using complementary methods.

In this talk will discuss examples of how control experiments and additional data can be used to understand and interpret in-situ Liquid Phase TEM of polymers, small molecules. [2] We show how automated data processing and computational simulations can be used to obtain molecular level insights from low contrast, low resolution data. We also discuss the effects of confinement in the liquid cell environment. We will also discuss why CryoTEM is a complementary tool imaging modality. [3] Cryo-EM can also provide direct high-resolution information on reaction mechanisms in solution. The advantage of cryo-EM is that electron beam effects are well understood and, using appropriately low doses, are insignificant. The disadvantage of cryo-EM is that it is impossible to know the history or future of any individual particle being imaged. Finally, we will discuss the role of “in-flask” experiments and how they can be used to better interpret the in-situ data, considering electron beam effects as well as confinement and surface effects.

References:

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