

## Challenges in Revealing Soft Matter Structural Dynamics by Liquid Phase Electron Microscopy

Joe Patterson<sup>1\*</sup>

<sup>1</sup> Department of Chemistry, University of California, Irvine, USA.

\* Corresponding author: patters3@uci.edu

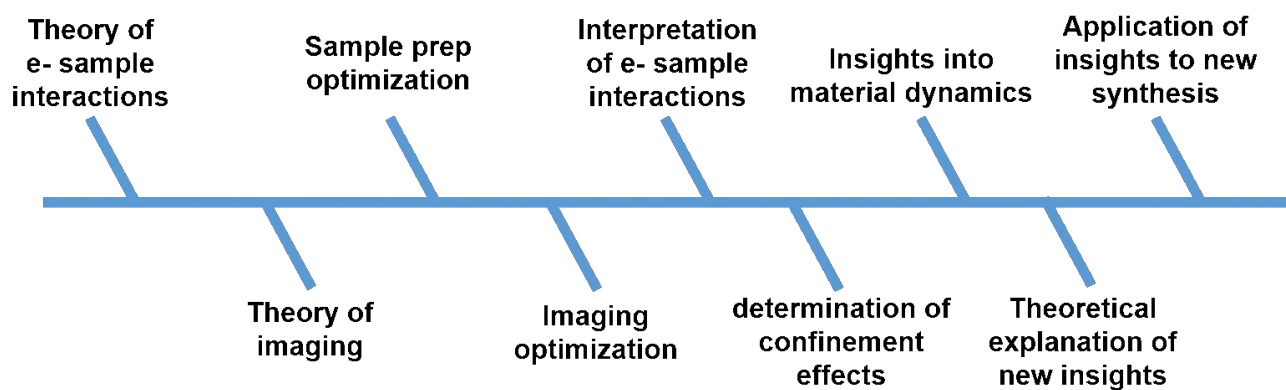
Liquid Phase Electron Microscopy (LPEM) has already begun to revolutionize our understanding of nanomaterial dynamics by providing real-time direct observations of fundamental processes such as nucleation and growth, morphology evolution and particle-particle interactions.[1] However, there are many challenges to overcome before we can translate our observations into quantitative data that can guide us synthetically (Figure 1). These challenges include, understanding and controlling beam-sample interactions, the effect of confinement within the liquid cells and extracting data from noisy, low contrast images.[2][3]

In conventional and cryoEM,[4] electron-sample interactions have been well studied, and for new systems can readily be determined by application of a dose series. Here, a series of images is recorded and changes in the structural features of interest can be measured with each additional image (corresponding to an increase in total dose). If there are changes to the structural features of interest then 'low dose' images should be recorded when these changes are negligible. For liquid phase electron microscopy, electron-sample interaction present a unique challenge. Firstly, all liquids will undergo some degradation when exposed to an electron beam, even at very low doses. However, due to the high mobility of the system the energy input from the electron beam can be rapidly dissipated. Therefore, it is now recognized that in LPEM, dose rate is often much more important than the total dose, as the dose rate establishes a steady-state of energy input/output. This has been discussed in detail previously, but here it is important to note the differences in establishing dose limits for a system in conventional/cryo and liquid phase EM. In conventional/cryo EM, the sample is static and therefore measuring changes in an image series will provide information on how the electron beam is effecting the sample structure. Since the goal of the experiment is to capture the structure which was prepared outside of the microscope, any changes to the structure by the electron beam can be considered as 'damage'. In LPEM, the sample is inherently dynamic, meaning that changes to the structure with sequential images are not necessarily directly related to the interaction with the electron beam, although the electron beam is likely to have some effect on all dynamic processes. The important point here is to understand in what respect and to what degree the electron beam is influencing the observations. One way of achieving this is to perform a detailed analysis of all the dynamic processes in question, over a range of electron doses. For soft matter systems this has been most rigorously demonstrated by Parent et. al. [3] where it was demonstrated that although the electron beam had an influence on dynamic processes such as particle motion, the underlying mechanisms of motion, fusion and growth were related to the specific organization, composition and environment of the structures – thereby relieving useful information on their structural evolution. A second approach for understanding electron-sample interactions is by performing a series of control experiments and comparing in-situ and ex-situ observations.

In this talk we will discuss the philosophies and strategies for overcoming these issues. We will also give some examples of how unique insights provided by LPEM can result in new design opportunities for controlling the structure and properties of materials.

## References:

- [1] FM Ross, *Science* **350** (2015), p. 6267.  
[2] LR Parent et al., *Accounts of Chemical Research* **51** (2017), p. 3.  
[3] JP Patterson et al., *J. Am. Chem. Soc.* **137** (2015), p. 7322.  
[4] JP Patterson et al., *Accounts of Chemical Research* **50** (2017), p. 1495.



**Figure 1.** Example of potential work flow for addressing the challenges in revealing soft matter structural dynamics by liquid phase electron microscopy.