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AXON Dose: A Machine Vision Solution for Accurate, Quantifiable Dose Management in the Transmission Electron Microscope

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All transmission electron microscopy (TEM) experiments are, on one level or another, fundamentally affected by the interaction between the sample and the energy of the electron beam used to form the image. Thus, dose management is an area of electron microscopy that touches nearly every corner of the field.
The effort to mitigate the damaging effects of electron/sample interactions such as knock-on damage and radiolysis has spurred the development of low-impact imaging (low-dose) techniques that minimize these interactions to a level where they do not substantially impact the sample or the analysis results [1]. These efforts to quantify and control both the cumulative electron dose (electrons/ Å2) and the fluence (electrons/ Å2s-1) are well documented in the literature both for conventional (in-vacuum) TEM, as well as in-situ experiments, specifically techniques sensitive to radiolysis, such as liquid-EM. [2-4].

Until now, a robust solution for managing the electron dose during TEM experiments, one that enables an operator to track and manage beam effects, has been hampered by several key issues. First, the calibration of a TEM's beam current and area can be a tedious and difficult process that requires many steps to accurately account for all the variables [1]. Furthermore, once calibrated, a typical workflow requires the operator to either remain at a specific magnification or work within other severe limitations to keep dose rates constant and simplify dose calculations. Finally, the identification of an individual sample's dose threshold, the level at which beam damage occurs, requires a user to carefully dwell on, or step through a series of slowing increasing conditions to manually determine the specific point where damage occurs. Once such a threshold is determined, the operator must keep track of imaged regions within the sample and compensate when the measured limit is approached. Thus, freely operating the instrument through various spot sizes or magnifications while keeping track of the total accumulated dose and/or dose rate over the sample area isn't practical without some form of assisting technology.

Here, we review the development and utilization of AXON Dose, a machine-vision solution designed to address and eliminate the specific pain points with calibrating, managing, and tracking a sample's electron dose exposure throughout the course of a TEM experiment. To achieve this goal, a platform was required that could account for both dose and dose rate on a per-pixel basis while compensating for sample drift and mechanical slop. The AXON core, once installed on the microscope, can streamline adjustments to stage, beam and camera acquisition conditions, while continuously collecting images and metadata produced by all three primary components during an experiment, automatically saving the information to the image metadata. Integration of that dose information into the image metadata enables robust analysis and visualization through heat maps from which accurate, quantifiable information on cumulative dose and fluence can be obtained from any point on the experimental timeline. Figure 1 shows an example of the user interface, which allows the users to easily visualize the dose exposure at any point in the image series and graphically visualize any of the collected metadata associated with the images.

The AXON Dose platform provides a state-of-the-art solution to calibrating, monitoring, and tracking both the electron fluence and the total dose delivered to specific areas of the sample on a pixel-by-pixel basis. This ability unlocks a new paradigm for imaging dose sensitive samples and understanding the electron beam interactions that can affect the rigor and reproducibility of in-situ and operando TEM experiments.

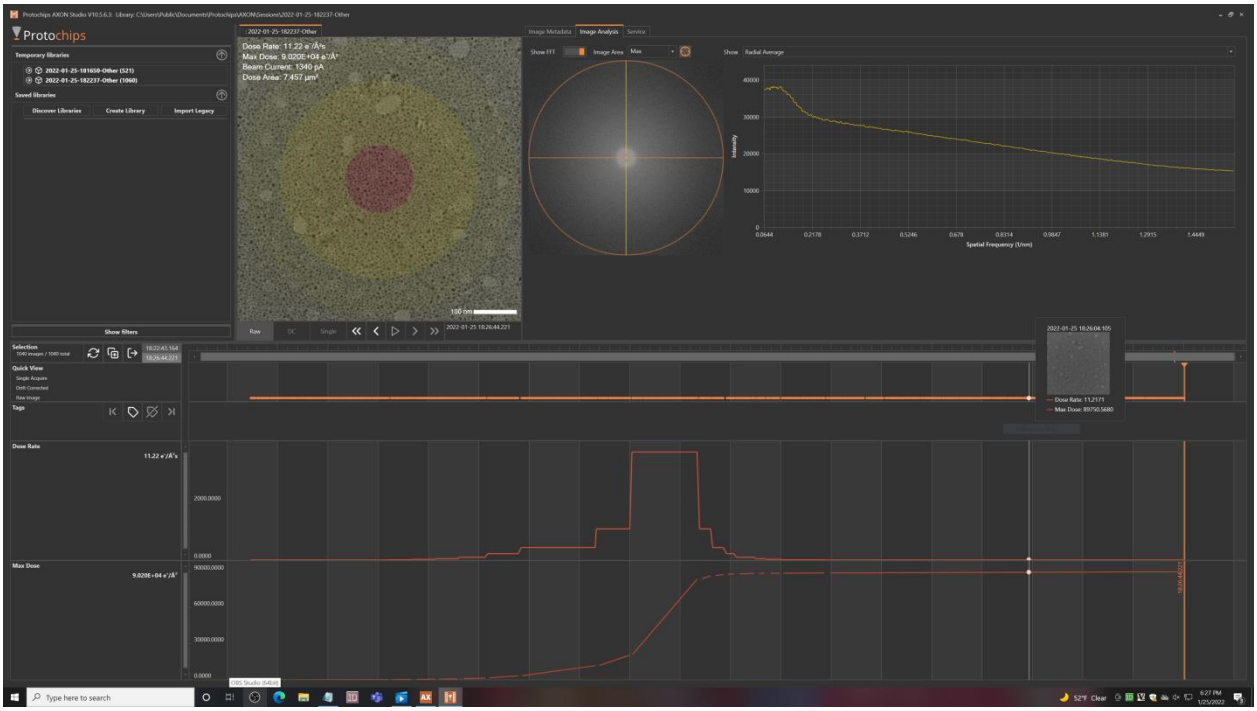

Figure 1: The AXON Dose User Interface. The cumulative electron dose exposure is easily visualized using heat map overlays for any image collected during the series. The available metadata obtained from the microscope, detector and other systems can be plotted graphically enabling the user to holistically identify trends and behaviors that occur over the TEM imaging session.

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